The transmission of anxiety and stress states from parent to infant mechanisms of emotion dysregulation in dyads at elevated likelihood of mental health conditions

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The transmission of anxiety and stress states from parent to infant: mechanisms of emotion dysregulation in dyads at elevated likelihood of mental health conditions

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‘Science was false by being unpoetical. It assumed to explain a reptile or a mollusk, and isolated it - which is hunting for life in graveyards. Reptile or mollusk or man or angel only exists in system, in relation.’

Ralph Waldo Emerson

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On a personal note, I would like to thank family and friends for their part in my academic journey. My parents were unconditionally supportive; my brothers cheeringly irreverent. Diran reliably kept a desk in his spare room for the many occasions I did not have one. James Hutton and Raphael Underwood fielded all my queries about how to put a thesis together. Jamie Enoch, Isabella Mighetto, Alise Kirtley, Emmanuelle Smith, Jac Bell, and Laura Joyner were on-call for regular boosts of optimism.

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DECLARATION

This thesis focused on data from two main studies. Firstly, chapters 4 and 5 used data from the Baby Learning and Infant Sensitivity to the Environment study (BLAISE), headed by Sam Wass and funded by an Economic and Social Research Council (ESRC) Future Research Leaders grant. I was primarily responsible for the data collection for this study. I was also responsible for training two other research assistants in naturalistic ECG and audio-visual data acquisition, and for managing and securing the data. Alongside Sam Wass, I was the main contributor to the development of the novel miniaturised wearable monitors described in the relevant Methods sections. I also wrote the ethics application for this study and conducted all of the recruitment. This work occurred immediately prior to my PhD, following which I was then in charge of formulating hypotheses, as well as analysing and interpreting the psychobiological data, under the guidance of Sam Wass, Emily Jones and Tony Charman.

Secondly, analyses presented in chapter 6 were based on two cohorts from the British Autism Study of Infant Siblings project (phases one and two, BASIS; www.basisnetwork.org), led by Tony Charman, Emily Jones and Mark Johnson. The participants for these cohorts were previously recruited by the BASIS team, who carried out a number of behavioural, eye-tracking and neurophysiological tests as part of data collection. I was in charge of formulating hypotheses and carrying out the analyses, under the guidance of Tony Charman, Emily Jones, and Sam Wass.

Finally, for the review presented in chapter 7, MSc students Cassie Fitzpatrick and Dean Jacobs conducted the title and abstract screening as well as a selection of bias assessments. All other elements of the review were conducted by me, with guidance from my supervisors.

The present thesis represents my own work.

A note on publications

Chapters 4 and 6 represent the publications detailed below. King's College London stipulates that, for a thesis incorporating publications, chapter text must be the same as the published paper, with any supplementary materials included in the thesis appendices.

Smith, C. G., Jones, E., Charman, T., Clackson, K., Mirza, F., & Wass, S. (2021). Anxious parents show higher physiological synchrony with their infants. *Psychological Medicine,* 1-11. doi:10.1017/S0033291720005085.

Smith, C. G., Jones, E., Wass, S. V., Pasco, G., Johnson, M. H., Charman, T., Wan, M. W., & BASIS Team (2021). Infant Effortful Control Mediates Relations Between Nondirective Parenting and Internalising-Related Child Behaviours in an Autism-Enriched Infant Cohort. *Journal of Autism and Developmental Disorders*, doi:10.1007/s10803-021-05219-x. Advance online publication.

COVID-19 IMPACT STATEMENT

It is worth highlighting that a substantive amount of time during my PhD was dedicated to a clinical research project that could not be completed due to the COVID-19 pandemic. This study was known as the 'Heart 2 Heart' study (H2H), developed in collaboration with the South London and Maudsley NHS Foundation Trust's perinatal services. Tony Charman and Trudi Seneviratne provided senior oversight. I received further supervision from Sam Wass and Emily Jones.

H2H replicated the protocol of the BLAISE study (chapters 4-5). However, the sample was recruited from a population of adults with moderate to severe levels of anxiety, via local outpatient and inpatient perinatal services. The study was intended to contribute to the external validity of the thesis, allowing for generalisation to clinical populations. Moreover, the study investigated two central hypotheses: (1) relative to dyads with a parent with less severe anxiety, the physiological activity of dyads with more severe anxiety will be characterised by greater synchrony, and (2) relative to dyads with a parent with less severe anxiety, the physiological activity of dyads with more severe anxiety will be characterised by more instability (Smith, 2020). I had also hoped to explore how physiological dynamics between parents and infants differed by individual anxiety disorder.

I requested and received ethical approval for H2H from the London Queen Square Research Ethics Committee (IRAS 263692), and gained access to clinical sites on the 17th of December 2019. I initiated recruitment by building relationships with principal clinicians and their wider teams in each of the outpatient and inpatient services; these were responsible for identifying eligible participants. I collected the first participant's data in February 2020. Soon afterwards in March, the UK national lockdown began and all non-urgent clinical studies were suspended, including my study.

To mitigate risks of COVID-19 transmission, and to make up for lost time, the study was then scaled down to a small, proof-of-concept study limited to the Mother and Baby Unit (MBU) at the Bethlem Hospital in south east London. I regained access to the hospital site in October 2020, after fixing equipment that had degraded over lockdown. Shortly after this, the study was again suspended due to the spread of the alpha variant and ensuing UK winter lockdown.

By January 2021, the coronavirus pandemic was at a peak in the UK, and I had entered the final nine months of my PhD. Given multiple outbreaks of COVID-19 at the MBU, and increased risk to a vulnerable member of my household, the decision was taken to suspend the study until further notice. As a contingency, I trained myself in systematic review methodologies and conducted a review focused on clinical populations presented in chapter 7. I also wrote a qualitative article on my experience of conducting clinical research during the pandemic, which is included for reader interest in Appendix F.

ABSTRACT

Clinically elevated levels of anxiety represent the most prevalent child mental health condition in the world. Available evidence suggests a key role of environmental influences in the development of anxiety, with recent research suggesting that early childhood is a crucial period for identifying environmental risk factors. As yet, though, our understanding of the early life causative factors that contribute to the development of anxiety conditions are limited.

One area that may elucidate the intergenerational transmission of anxiety is that of parent-infant dynamics, as these early relational patterns are thought to play an influential role in later socio-emotional development. Investigations into these dynamics have typically been focused on observable behaviour in short segments of lab-based interaction, despite the need for ecologically valid and multi-method approaches in investigating anxiety precursors.

Using a mixture of naturalistic biobehavioural recording techniques, longitudinal modelling and time series analyses, the present thesis examines the mechanisms of emotion dysregulation in dyads at elevated likelihood of anxiety conditions and other psychiatric disorders.

Evidence is presented showing biobehavioural atypicality in parent-infant dynamics in the context of elevated parental anxiety. Evidence also shows that the development of anxiety-related distress in early childhood is shaped by parental behaviour and infant temperament dimensions.

Discussion is focused on the contribution of the findings to developmental theories of atypical emotion regulation. Past, present and future directions for intervention studies focused on parental anxiety and infant socio-emotional development are also considered.

Key words: anxiety, stress, parent-infant relationship, early development, psychophysiology, emotion dysregulation, quantitative naturalistic research methods, interventions

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LIST OF ABBREVIATIONS

ADHD	Attention deficit hyperactivity disorder
ANS	Autonomic nervous system
AR	Autocorrelation
BPM	Beats per minute
BS	Bootstrapped
c.	Circa
CBT	Cognitive behavioural therapy
CI	Confidence Intervals
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECG	Electrocardiogram
EL	Elevated likelihood
EU-AIMS	European Autism Interventions - Multicentre Study
GAD-7	Generalized Anxiety Disorder 7-item screening tool
GPS	Global positioning system
HPA	Hypothalamic-pituitary-adrenal
HR	Heart rate
HRV	Heart rate variability
Hz	Hertz
IBI	Interbeat interval
ICD	International Classification of Diseases
ITT	Intention-to-treat
MAR	Missing at random
MBU	Mother and Baby Unit
MCAR	Missing completely at random
MeSH	Medical Subject Headings
MI	Multiple imputation
min	Minutes

MNAR	Missing not at random
mos	Months (occasionally abbreviated further to ‘m’ if space restricted)
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
PICO	Population, Intervention, Comparison, and Outcome
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PROSPERO	International prospective register of systematic reviews
QRS complex	Combination of three graphical deflections seen on a typical electrocardiogram
rho	Spearman's rank correlation coefficient
RoB	Risk of bias
RR intervals	Time elapsed between two successive R-waves of the QRS
RSA	Respiratory sinus arrhythmia
s	Seconds
SCQ	Social Communication Questionnaire
SM	Supplementary materials
t	T-test statistic *or* time, as specified in the text
TAU	Treatment as usual
Ti ab	Title and abstract
TL	Typical likelihood
UK	United Kingdom
USA	United States of America
WL	Wait-list
β	Standardised beta coefficient
η^2	Eta squared

DEFINITIONS OF KEY TERMS

Affect	Arousal states sometimes characterised by intensity or valence; these are nonconscious precursors to emotions, identified early in development (Shouse, 2005).
Allostasis	An 'active process through which internal equilibrium is achieved and maintained' (Wass, 2021a, p. 5); dynamic and rebalancing (Atzil et al., 2018).
Anxiety	Defined broadly in clinical terms by features of persistent anxiety, fear out of proportion to the threat posed, and avoidance behaviours; 'anxiety' refers to apprehension in the context of distal, uncertain threat cues, while 'fear' refers to concern with immediate, unambiguous threats (Craske et al., 2017).
Arousal	Autonomic arousal; the total levels of activity within the autonomic nervous system (the fast-acting neural substrate of the physiological stress response; Cacioppo et al., 2007).
Bidirectional	Describes the 'relative impact of child behaviour on parent behaviour, and of parent behaviour on child behaviour' (Pettit & Arsiwalla, 2008, p. 713).
Contagion	'Exchange or transfer of some aspect of emotion from one person to another' (Butler, 2011, p. 375); this term may be operationalised in terms of emotions, affect or arousal, and is often assessed using time-lagged analyses that focus on the target partner's prior emotion as a predictor (Almeida et al., 1999). Contagion also describes a process by which dyadic states become altered or amplified over time, particularly via cognitive or behavioural mechanisms (Waters et al., 2014, 2017, 2020). Contagion overlaps with the term 'synchrony' (Butler, 2011).
Coregulation	'Psychobiological connectedness [allowing] the caregiver to directly regulate the physiological and emotional functions of the infant, thereby providing critical scaffolding for the child to develop self-regulatory capacities' (Butler, 2011, p. 369).
Dysregulation	Impaired or atypical regulation dynamics. With respect to older children and adults, this often relates to goal-interfering behaviour (Cole et al., 2019). With respect to physiology, this often relates to hyperarousal and slower recovery from a challenge episode (Beauchaine & Thayer, 2015).
Emotion	'A collection of psychological states that include subjective experience, expressive behaviour (e.g., facial, bodily, verbal), and peripheral physiological responses (e.g., heart rate, respiration)' (Gross & Barrett, 2011, p. 9).
Metastasis	The dynamical principle underlying dysregulation; '[involves] small initial increases and decreases in arousal becoming amplified over time' (Wass, 2021a, p. 9).

Reciprocal	Describes an 'ongoing concept of adjustment as environments are influenced by individuals, and individuals are influenced by environments' (Wille et al., 2012, p. 307). This term is used interchangeably with the term 'bidirectional' (Pettit & Loulis, 1997), though reciprocal relations may imply a more dynamic pattern of change.
Regulation	Of affect, arousal, or emotion; during early development, regulation describes behavioural and attentional processes that modulate arousal (Derryberry & Rothbart, 1988; Eisenberg et al., 1998; Thompson, 1994). In adulthood, regulation describes actions used to influence 'which emotions we have, when we have them, and how we experience and express them' (Gross, 2002, p. 282).
Stress	An umbrella term encompassing a wide range of human experience, including biological, affective, and cognitive states. Stress may describe both circumstances ('stressors') and responses ('stress response'). The course of stress may be acute or chronic (Epel et al., 2018). Throughout this thesis, 'arousal' is used as a proxy for stress.
Synchrony	'Coordination of biological and social processes during social contact' (Feldman, 2015, p. 369); in dyadic contexts, synchrony may be operationalised as 'concurrent' ('when A is high, B is high') or 'sequential' ('changes in A forward-predict changes in B'; Helm et al., 2018; Wass et al., 2020). Synchrony is associated with data analysis techniques such as cross-correlations using time series analysis, or conditional probabilities. Synchrony is also sometimes used interchangeably with the term 'contagion'. For a theoretical rapprochement of the two terms, see Butler (2011).
Transactional	Generally, this term describes 'behavioural outcomes as the mutual effects of context on child, and child on context' (Sameroff & Fiese, 1990, p. 136). In reference to anxiety, the term describes interactions between infant exposure to parental anxiety, and both parent and child characteristics (Aktar & Bögels, 2017).

I. INTRODUCTION CHAPTERS

CHAPTER 1 - Thesis Overview

This thesis attempts to elucidate the dyadic mechanisms of emotion dysregulation in young children, particularly in the context of parental anxiety.[1] In doing so, this thesis contributes to our understanding of how stress and anxiety states might be transmitted from parents to infants, and subsequently mitigated. In order to complete this project, different research methods were required. Firstly, methods for measuring physiological and behavioural processes had to be adapted for use in a naturalistic context. Secondly, it was necessary to adopt both longitudinal and systematic review methodologies to establish how infant self-regulation is shaped over time, and if infant socio-emotional functioning can be improved through interventions for perinatal anxiety. Of note, the present thesis incorporates two publications (chapters 4 and 6). These have been presented in the version they were accepted, but formatted and put into context within the framework of the thesis.

In chapter 2, the background material and rationale for the thesis are presented. This includes an overview of anxiety, including its aetiology and pathophysiology, as well as a summary of how perinatal anxiety may relate to emotion dysregulation in early developing relationships. Finally, gaps in the literature that this thesis attempts to address are outlined. In chapter 3, the principal research aims and contributions are also described.

In chapters 4 and 5, the first two empirical studies are presented. In chapter 4, wearable technologies are used in participants' home settings to determine whether infants of more anxious parents display higher parent-infant physiological synchrony, compared to infants of less anxious parents. In addition, these wearables are used to detect whether, in line with developmental theories, parents with elevated anxiety show atypical patterns of dyadic coregulation. In chapter 5, the same methodologies are used to examine whether infants of more anxious parents are more physiologically reactive to stimulating parental behaviour, compared to infants of less anxious parents. Mechanisms underlying intra-dyadic 'arousal contagion' are examined. The chapter ends by identifying differences between more and less anxious parents that may help explain how infant emotion regulation becomes compromised in early life.

While chapters 4 and 5 examine parent and infant characteristics at the state-level, chapters 6 and 7 look instead at the trait-level. Chapter 6 presents a longitudinal study, investigating how specific parenting behaviours associate with individual differences in infant temperament in relation to self-

[1]A note on terminology: the terms 'affect dysregulation' and 'emotion dysregulation' are used to refer to earlier and later stages of emotional development respectively. The literature suggests that a less mature instantiation of emotion exists in infancy ('affect') compared to later on in childhood ('emotion'; Shouse, 2005). However, the literature does not consistently distinguish between the two terms (e.g., Keenan, 2000; Thompson & Waters, 2020), indicating their comparability.

regulatory problems in early childhood. This is examined among infants at elevated likelihood of developing co-occurring neurodevelopmental and mental health conditions. Chapter 7 then reviews if and how perinatal clinical treatments lead to improvements in parental anxiety symptoms, the parent-infant relationship, and infant socio-emotional functioning.

Chapter 8 concludes the thesis with a general discussion of the findings from each study and review, in the context of the current literature. Strengths and limitations of the methods used throughout the thesis are outlined, along with their implications for interpreting findings. The thesis ends by discussing the potential for the findings to inform future research on the development of emotion dysregulation, and the intergenerational transmission of anxiety; implications for clinical work relating to the care of anxious parents and their infants are also outlined.

CHAPTER 2 – General Introduction

This chapter provides an overview of anxiety, including its causes, its pathophysiological mechanisms, and its manifestation in the perinatal period. It then goes on to discuss the role of perinatal anxiety in the early development of emotion dysregulation, examining micro-behavioural, transactional and physiological processes. Finally, existing methodologies used to investigate joint physiological processes are outlined; limitations of these and knowledge gaps in need of further study are highlighted.

2.1 Overview of anxiety

2.1.1 Preface

In his interdisciplinary study, Dylan Trigg (2018) documents how anxiety is typically presented as an insular and internal experience. Drawing on the perspectives of clinical anxiety specialists Rollo May (2015) and David Barlow (2004), as well as philosophers such as Heidegger (2010), he describes how anxiety is characterised as 'a state of mind, a placeless experience, or (…) something that individuals undergo alone' (p. 187). This conceptualisation appears to minimise interactive aspects; 'it leaves to one side the richly situated quality of anxiety' (Trigg, 2018, p. 188). The present thesis seeks to depart from the prevailing account; it aims to understand how anxiety-related states come to be shared and transmitted between individuals; particularly in the context of close parent-infant relationships found in early development. While the emphasis is on anxiety, the thesis may also illustrate how, more generally, affective states come to be expressed and regulated in a relational sense.

2.1.2 Measurement of psychopathology

Before any formal definitions of anxiety can be put forward, it is first necessary to address the broader debate regarding measurement of mental health conditions. Researchers contest whether such phenomena should be conceptualised discontinuously, according to discrete diagnoses, or continuously, as the negative extreme of a broader dimension (Haslam et al., 2012; Ruscio, 2019). Both perspectives may have pragmatic utility. Discontinuous views of mental health are necessary for treatment decisions in clinical contexts, while continuous views may be applied when devising public health policies. Meta-theorists suggests that the two perspectives have more in common than in difference with regard to their empirical bases, and that proving the empirical advantage of one over the other is 'more trouble than it's worth' (Angold & Costello, 2009; Pickles & Angold, 2003). A measurement-agnostic position is therefore proposed: investigations ought to be informed by questions of when a given measure is appropriate for its context, and whether the measure has specific advantages in terms of operationalisation, measurement, analysis, or communication (Pickles & Angold, 2003). The present thesis is guided by this measurement-agnostic position.

2.1.3 Clinical manifestation of anxiety

In clinical research, categorical perspectives on anxiety are dominant. In this context, the phenomenon of anxiety is understood in terms of discrete medical diagnoses. This involves classing individuals as cases or non-cases of a specific disorder. Multiple individual anxiety disorders are classified across two official nosologies: the Diagnostic and Statistical Manual of Mental Disorders (5th edition; DSM-V; American Psychiatric Association, 2013) or the International Classification of Diseases (11th edition; ICD-11; World Health Organization, 2018). Figure 2.1 presents the diagnoses classified under the broad anxiety disorder heading, which are unified by features of persistent anxiety, fear out of proportion to the threat posed, and avoidance behaviours (American Psychiatric Association, 2013).[2] Differences between diagnoses have been documented (Fonzo et al., 2018; Hook & Valentiner, 2002) and there is evidence to suggest that narrowly defined anxiety disorders (e.g. panic disorder, social anxiety disorder) display phenotypic heterogeneity (Barzilay et al., 2020; Lau et al., 2007). However, there is also evidence that individual anxiety disorders share phenotypic overlap (particularly among 'stress-related' disorders: Smoller, 2016; Smoller et al., 2008; Smoller & Tsuang, 1998) as well as transdiagnostic aetiological and maintenance pathways (e.g., emotion dysregulation; Norton & Paulus, 2017).

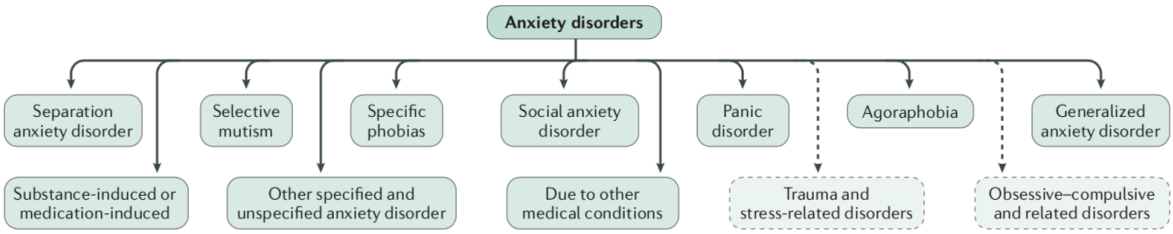

Fig. 2.1 Multiple individual anxiety disorders classified within the DSM-V; dashed arrows represent disorders previously but no longer listed under the anxiety disorder classification. Reprinted by permission from the Copyright Clearance Center (CCC): Springer Nature GmbH, Nature Reviews Disease Primers, *Anxiety disorders*, Craske et al. Copyright © 2017.

Quantitative research has demonstrated that anxiety disorders, as well as the experience of subthreshold symptoms, are associated with compromised quality of life and psychosocial functioning (Mendlowicz & Stein, 2000). Qualitative research has also shed light on the lived experience of distress that accompanies anxiety. Young people with generalised anxiety describe feeling 'stuck', 'trapped,' confined to a 'shrinking world,' and 'assaulted' by their symptoms; they describe anxiety as a 'monster' permeating all aspects of their life, contributing to feelings of loss, fear and pain

[2]'Fear' and 'anxiety' constitute two threat responses, typically distinguished by the immediacy of the threat; fear relates to imminent, unambiguous threat, and usually subsides after the threat passes, whereas anxiety relates to distal, ambiguous threat cues, and has a longer time course (Craske et al., 2017).

(Woodgate et al., 2021). Adults with generalised anxiety describe their experience as an 'endless cycle', a 'struggle for autonomy,' and a 'battle with uncertainty' (Young, 2019); in frail older adults, there are also expressions of desperation, worry, and a fear of leaving the house alone (Frost et al., 2020).

2.1.4 Epidemiology and the course of anxiety

Anxiety disorders are both highly prevalent and debilitating, and are associated with substantive economic costs. They are among the most common classes of psychiatric disorders globally (lifetime prevalence, ~16%; Kessler et al., 2009; Wittchen & Jacobi, 2005) and are the most frequent mental disorders in children and adolescents in the world (6.5%; Polanczyk et al., 2015). In 2017, anxiety disorders were responsible for over 27, 000 years lost due to disability globally (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). In the last decade, the costs associated with anxiety disorders were estimated to be greater than 74 billion euros per year for the European economy (Haro et al., 2014; Wittchen et al., 2011).

The course of anxiety is defined by early onset, gender differences, and co-occurring diagnoses. The average peak onset for all anxiety disorders is estimated at five and a half years old (with a second, smaller peak at 15.5 years; Solmi et al., 2021). There is also evidence to suggest that, for individual anxiety disorders, earlier onset is associated with greater severity and a more enduring course (Ramsawh et al., 2011). There are higher rates of any anxiety disorder in women compared to men, with ratios of 1:1.5 in adolescence (Merikangas et al., 2010) and 1:2 in adults (McLean et al., 2011). Rates of anxiety disorders are also higher in trans and non-binary people compared to cisgender people (Thorne et al., 2019). These gender differences may reflect differential experiences of socialisation or environmental stressors arising from gender inequalities (e.g. exposure to abuse and victimisation; Chew et al., 2020; Christiansen, 2015). Added to this, anxiety disorders represent a significant risk factor for the development of other mental health conditions, such as depressive disorders (Wittchen et al., 2011; Wittchen & Jacobi, 2005). They also commonly co-occur with neurodevelopmental conditions such as autism and attention deficit hyperactivity disorder (Schatz & Rostain, 2006; Simonoff et al., 2008).

2.1.5 Pathophysiology of anxiety

Research on the neurophysiological processes underlying pathological forms of anxiety has produced mixed results, though some generalities have been established. Several brain regions have been implicated in anxious individuals' responses to threat-based stimuli, including the brain stem, amygdala, hypothalamus, hippocampus, and medial prefrontal cortex (for summary and review, see: Brehl et al., 2020; Doyle et al., 2021; Shin & Liberzon, 2010). Meta-analyses of functional magnetic resonance imaging studies have also shown that there are neural patterns associated with cognitive processes in anxiety disorders (e.g., Wang et al., 2018).

A related but independent approach to establishing biomarkers for anxiety is the examination of physiological signals. This includes those derived from the slow-acting endocrine system, including the hypothalamic-pituitary-adrenal (HPA) axis, which has been shown to be hyperactivated in numerous stress and anxiety disorders (though not all: Chrousos, 2009). Acting in concert with the endocrine system is the fast-acting autonomic nervous system (ANS), the neural substrate of the body's stress response.[3] This comprises two complementary subsystems; the sympathetic nervous system – activated for 'fight or flight' – and the parasympathetic nervous system – activated to 'rest and digest' (Cacioppo et al., 2007). Of note, the ANS has been studied in a range of contexts, with research indicating that the same autonomic processes mediate responses to positive, attention-eliciting stimuli, as well as adverse, unexpected or threatening stimuli (for reviews, see: Wass, 2018, 2021b).

Autonomic arousal (henceforth 'arousal') refers to the total levels of activity within the ANS. The preclinical literature has shown that hyperarousal underlies anxious emotion, following a pattern of reciprocal sympathetic activation and parasympathetic deactivation (Kreibig, 2010). Arousal dysregulation has also been identified as a maintaining factor of adult generalised anxiety disorder (Thayer et al., 1996), social anxiety disorder (Bögels & Lamers, 2002), and panic disorder (Brown et al., 1998; Brown & McNiff, 2009); it has been implicated in the literature on childhood anxiety (Cho & Buss, 2015; Peltola et al., 2016; Root et al., 2016), and has been demonstrated in young children of adults with anxiety disorders (Nikolić et al., 2016, Nikolić, Brummelman, et al., 2018). Recent research has suggested that autonomic hyperarousal in infancy acts as a dispositional factor for anxiety disorders; prenatal parental anxiety has been shown to predict infant hyperarousal and, in turn, fearful child temperament (a precursor to later anxiety; de Vente et al., 2020; Möller et al., 2016). However, our knowledge of how arousal operates as a mechanism within the development of anxiety remains limited.

2.1.6 Aetiology of anxiety and intergenerational transmission

The causes of anxiety disorders have been widely investigated, with researchers suggesting that a range of factors – genetic, biological, and environmental – all exert an influence from childhood. Of note, the term 'intergenerational transmission' is also commonly used to refer to ways in which states of anxiety in children arise as a result of parental characteristics (e.g., Aktar et al., 2019; Murray et al., 2008; de Vente et al., 2020) though the term is conceptualised slightly differently by epigeneticists, discussed below.

[3]Stress is an umbrella term encompassing myriad experiences and sensations. Given the role of the ANS in physiological responses to acute and daily stressors, 'arousal' is used throughout this thesis as a proxy for stress. For broader definitions of stress, see: Epel et al. (2018).

One possible explanation for understanding the development of anxiety in children involves biological mechanisms. Specifically, the aetiology of anxiety has been related to the fetal programming hypothesis (also known as the 'socialisation of stress neurobiology'; Thompson & Waters, 2020). This hypothesis suggests that alterations in utero, associated with adult anxiety or stress, represent a risk factor for offspring (Tibu et al., 2014). Alterations in utero include: placenta function (O'Donnell et al., 2012), fetal HPA axis function (McLean et al., 2020; O'Donnell et al., 2013), and fetal amygdala volume (Buss et al., 2012). These and other prospective studies have indicated that increased stress, or anxiety, during pregnancy associates with a greater likelihood that offspring will develop symptoms of anxiety and other mental health problems (Glover, 2011). The fetal programming hypothesis has also been related to other theories suggesting that offspring characteristics develop as a consequence of epigenetic changes experienced by the parent in response to a traumatic event (i.e., the 'intergenerational transmission of trauma'; Bowers & Yehuda, 2016). One key issue with the fetal programming hypothesis is that it does not explain why most children are not affected by prenatal stress, or why those that are can be affected in diverse ways (Glover et al., 2016). In addition, the evidence base is largely correlational (Davis, Hankin, et al., 2018) and associated with modest effect sizes (Leis et al., 2014; Loomans et al., 2011).

Another mechanism that has received substantive attention for its role in the development of anxiety is genetics. Anxiety disorders run in families, and have a strong heritable basis. Twin studies' heritability estimates range from 30 to 40%, depending on the disorder, trait or age under investigation (Craske et al., 2017; Polderman et al., 2015). There is also evidence that gene-environment interactions and associations partly explain the development of anxiety disorders (Hicks et al., 2009; Jaffee & Price, 2007; Lau et al., 2007), and that cross-generational relations exert an influence on children and parents' anxiety symptoms (Ahmadzadeh et al., 2019). It is also possible – though not yet demonstrated in the context of anxiety - that nontransmitted parental alleles can affect a child through their impact on parent characteristics (a phenomenon known as 'genetic nurture'; Kong et al., 2018). Despite this, numerous candidate gene studies of anxiety disorders have not found robust associations (Smoller, 2016), and there is a growing consensus that - as with other mental health conditions - a multitude of common genetic variants with relatively small effects, added to environmental factors, probably underlie the risk for anxiety disorder (Otowa et al., 2016; Purves et al., 2020; Wray et al., 2018). Findings from children-of-twins studies, in particular, highlight the role of direct environmental transmission (Creswell & Waite, 2015; Eley et al., 2015).

Although the environmental factors implicated in the development and maintenance of anxiety are multifarious (see reviews, Bögels & Brechman-Toussaint, 2006; Murray et al., 2009), the present thesis focuses on those implicated in early childhood. This is due to the early onset of anxiety disorders (Solmi et al., 2021), the rationale for preventative and early intervention strategies for anxiety disorders (Hirshfeld-Becker & Biederman, 2002), as well as theoretical accounts emphasising

the general importance of understanding the complex ontogenesis of developmental psychopathology (Karmiloff-Smith, 1998).

Parenting behaviour is an environmental factor that has been widely linked with the aetiology of anxiety. One behaviour thought to play an important role in the early development of child anxiety is parental expression or modelling of anxiety (Aktar et al., 2013; Aktar & Bögels, 2017; Murray et al., 2008). For instance, socially anxious adults' higher levels of parental threat attribution in a school representation task have been found to predict a higher likelihood of social anxiety disorder in their children the following term (Murray et al., 2014; Pass et al., 2012). Other parenting behaviours such as low encouragement (among socially anxious adults; Murray et al., 2007), increased overprotectiveness or intrusiveness (discussed later in more detail; Möller et al., 2016; van der Bruggen et al., 2008) and reduced 'challenging' behaviour (e.g., rough-and-tumble play, encouraging children to move outside their comfort zone; Majdandžić et al., 2018) have all been linked with children's subsequent development of anxiety symptoms too. The extent to which a child is securely attached to her parent has also been associated with the development of childhood anxiety disorders, though firm conclusions are restricted by methodological limitations of the evidence base on attachment (cross-sectional designs, use of groups with small age ranges, and heterogeneous assessment measures; Esbjørn et al., 2012; see also reviews: Colonnesi et al., 2011; Manassis, 2000).

Parenting behaviours are also thought to exacerbate 'anxiety precursor symptoms' in early childhood, and shape the self-regulatory strategies of young children. Anxiety precursor symptoms represent behaviours observed in very young children that are associated with elevated likelihood of anxiety disorders later on; these include characteristics such as behavioural inhibition, fearful reactivity to novel stimuli, attentional orienting to fear-provoking stimuli (Fox et al., 2005, 2020; Möller et al., 2016) and internalising behaviour, i.e., the outward expression of intropunitive emotions including fear, guilt and worry (Broeren et al., 2013; Zahn–Waxler et al., 2000). These characteristics are thought to be reinforced by the behaviour of family members, who may have a tendency towards anxiety symptoms, and who may support the child's principal self-regulatory strategy of avoiding fear-provoking scenarios; this approach may provide relief in the short term, but is associated with augmenting rather than reducing anxiety risk in the long term (see accounts of family accommodation: Lebowitz et al., 2013, 2019; and functionalist emotion theory: Thompson & Waters, 2020). Of note, physiological correlates of anxiety precursor symptoms have been identified, such as infant hyperarousal in response to a lab stressor, but the role of physiological mechanisms in the intergenerational transmission of anxiety have yet to be elucidated (de Vente et al., 2020; Fox et al., 2005).

Early developing anxiety disorders may therefore be conceptualised in two fundamental ways. Firstly, anxiety develops as a result of complex, interactive biopsychosocial influences. Any factor alone (e.g., behavioural inhibition) will not necessarily be deterministic, but, taken as a collective, multiple

factors will exert an additive influence on the pathway to later anxiety. In addition, anxiety appears to develop in part due to the establishment of dysregulatory processes in the management of emotion (henceforth 'dysregulatory processes'; Thompson, 2001). One promising signal for understanding how children first develop dysregulatory processes lies in the interaction between anxious parents and their infants – in particular, the dyad's arousal dynamics – as discussed in part two of this chapter.

2.1.7 Anxiety in the perinatal period

The above discussion has mainly described the manifestation and development of anxiety as it applies to the general population. However, anxiety has also been observed in the perinatal period, among pregnant people and new parents. Over the last decade in particular, this subgroup has become the subject of increased research attention, owing to high prevalence rates combined with an awareness that perinatal anxiety has been traditionally overlooked compared to other perinatal conditions (e.g., depression; Howard et al., 2014). Anxiety in the perinatal period is also associated with a range of negative outcomes for young children (Rees et al., 2019), suggesting that further research with this population may help shed light on mechanisms for the intergenerational transmission of anxiety. The following section gives a brief overview of perinatal anxiety, before moving on to discuss the role of perinatal anxiety in the early development of children's dysregulatory processes.

Some degree of anxiety during and after pregnancy is typical, giving the major transition it represents (Matthey, 2010). However, extreme or persistent experiences of anxiety that inhibit daily function may require clinical attention (Ayers et al., 2015). Clinical levels of perinatal anxiety may be classified as one of the individual anxiety disorders discussed above, though three core symptoms are thought to feature in any given presentation: cognitive distortions, elevated physiological arousal states, and behavioural avoidance (Harrison & Alderdice, 2020).[4]

The prevalence of perinatal anxiety is high among all genders. Rates of self-reported anxiety symptoms among women range from between 18 to 25% during pregnancy, and are calculated to be 15% during the first four months postpartum (Dennis et al., 2017). Prevalence rates for a clinical diagnosis of any anxiety disorder are similar; the overall rate is 15% during pregnancy and the postpartum period (Dennis et al., 2017). Prevalence of perinatal anxiety in men is also thought to be high, with rates estimated at 11% during both pregnancy and the first year of the infant's life (Leiferman et al., 2021). Due to the dominance of cisnormativity within reproductive healthcare, only one country worldwide records information about parent gender in perinatal services. Consequently, in most countries it is not possible to identify trans and non-binary parents within maternity data, impeding systematic examination of differential mental health difficulties in these communities

[4]Further detail on the content of cognitive distortions have been detailed in relation to anxiety within the general population (see: Leung & Poon, 2001). Detail is limited regarding the specific content of cognitive distortions within perinatal anxiety, though evidence is available in the context of depression (see: O'Mahen et al., 2012).

(Greenfield & Darwin, 2021). However, evidence suggests rates of perinatal affective disorders are likely higher among trans men and non-binary people, on the basis of increased vulnerability to mental health difficulties in the general population (Wisner, 2018). Across all genders, prevalence rates of perinatal anxiety are likely to be underestimates due to the inadequacy of present screening tools (Fairbrother et al., 2019).

With respect to the course of perinatal anxiety, two onset peaks have been identified. The first of these is during the initial trimester during pregnancy (Figueiredo & Conde, 2011). The second peak onset is soon after childbirth, following which there is a progressive drop in anxiety levels (Dennis et al., 2013; Paul et al., 2013). Reasons for the development of perinatal anxiety are manifold. Risk factors range from broad social factors (e.g., low parental education, couple relationship problems, poor social support) to more pregnancy-specific factors (e.g., prior miscarriage or perinatal loss; poor pregnancy health; difficult birth experience); a prior history of low self-esteem or psychological distress may also increase susceptibility (Leach et al., 2017).

Both for parents and for their children, perinatal anxiety has been associated with a series of negative outcomes. For the parent, this includes increased likelihood of birth complications (Dowse et al., 2020), maladaptive coping strategies (George et al., 2013), and suicidality (Farias et al., 2013). Neonates of parents with perinatal anxiety are more likely to be born preterm and have low birth weight (Ding et al., 2014), while children are more likely to have chronic abdominal pain (Ramchandani et al., 2017), emotional or behavioural problems (O'Connor et al., 2002; O'Donnell et al., 2014), and impairments in socio-emotional development (Polte et al., 2019). Of note, the majority of research on the impact of perinatal anxiety on children involves self-report measures of parental anxiety symptoms - as opposed to diagnostic interview assessments (Glasheen et al., 2010; Rees et al., 2019). This suggests that high anxiety symptoms are clinically significant in terms of their impact on offspring and others (Ayers et al., 2015).

Due to the influence of perinatal anxiety on both members of the parent-infant dyad, effective clinical treatments for perinatal anxiety are paramount. Cognitive behavioural therapy (CBT) is the treatment formally recommended under NICE guidelines to support individuals with perinatal anxiety in the UK (National Collaborating Centre for Mental Health, 2014). Informed by cognitive and behavioural theories, CBT aims to reduce anxiety by restructuring distorted cognitions, and by increasing exposure to fearful stimuli without recourse to maladaptive coping behaviours; such behaviours provide initial relief but exacerbate difficulty in the long term (Bolton & Perrin, 2008; Clark, 2013). While CBT for anxiety is characterised by a high degree of heterogeneity (varying by disorder, clinical setting, and intensity; Simos & Hofmann, 2013), one underlying principle is that distress is maintained by interactive cognitive, physiological and behaviour factors. For example, the misinterpretation of bodily sensations can lead to heightened arousal states, which can lead to behaviours that amplify hyperarousal, subsequently reinforcing initial misinterpretations (Clark et al.,

1997; Ohst & Tuschen-Caffier, 2018). Recent research has focused on modifying CBT for specific anxiety disorders during the perinatal period (Challacombe et al., 2021; Challacombe & Salkovskis, 2011). However, trials examining the efficacy of perinatal anxiety treatment – particularly with respect to both parent *and* infant outcomes - are scant. This may partly be a consequence of our relatively limited understanding of the mechanisms by which perinatal anxiety leads to socio-emotional difficulties in young children.

2.2 Perinatal anxiety and the early development of emotion dysregulation

2.2.1 Theoretical frameworks for infant affect regulation

Having briefly summarised the evidence regarding how anxiety develops in children of anxious parents, attention now turns to a related inquiry regarding how perinatal anxiety exerts an influence on young children's dysregulatory processes. Emotion dysregulation is fundamental to anxiety, both in terms of aetiology (Cisler et al., 2010; Suveg et al., 2010; Thompson, 2001) and maintenance (Amstadter, 2008; Hofmann et al., 2012; Norton & Paulus, 2017). A greater understanding of the development of emotion dysregulation is therefore likely to help us establish the early life causative factors that contribute to the development of anxiety conditions. To frame the following discussion of perinatal anxiety and early dysregulatory processes, definitions of emotion regulation, and theories regarding its development, are informative.

Emotion regulation typically refers to behavioural and attentional processes that modulate arousal (Derryberry & Rothbart, 1988; Eisenberg et al., 1998; Thompson, 1994).[5] In infancy, arousal states may be characterised by intensity or valence, and described in terms of 'affect.' While non-conscious, these states are thought to be related to the later development of emotions (Shouse, 2005), which are – themselves – understood as 'a collection of psychological states that include subjective experience, expressive behaviour … and physiological responses' (Gross & Barrett, 2011, p. 9). The establishment of affect regulation in infancy is important, as it is considered an essential precursor to competent emotion regulation in later childhood and adult life (Schore, 2015).

There are two key hypotheses regarding the development of affect regulation in infancy. Firstly, the 'mutual regulation model' hypothesis suggests that infant affect regulation – like temperature regulation – is principally dyadic; that is, not accomplished solely by the infant (Tronick, 1998). Though infant affective states are regulated partly by their own neurophysiology, the parent's

[5]In the adult literature, emotion regulation may be alternatively described as a set of actions used to influence 'which emotions we have, when we have them, and how we experience and express them' (Gross, 2002, p. 282). Such actions may include processes associated with better adjustment outcomes (e.g., reappraisal, acceptance) or psychopathology (e.g., suppression, avoidance; Aldao et al., 2010). Suppression and avoidance are positively associated with anxiety disorders, though evidence has traditionally been based on self-report measures and top-down executive processes that come online later in development (Cisler et al., 2010).

behaviour also has an influence. For this to work, a cognitive component is suggested; each partner has an implicit understanding of the other's behaviour. Hence the explanation:

> 'The infant's [affective] states are (…) regulated dyadically. The principal components are the infant's central nervous system (e.g., limbic sites) and the behaviors it organizes and controls (e.g., facial and vocal emotional displays) and the caregiver's regulatory input (e.g., facial expressions, touches, gestures). The dyadic emotional regulatory system is guided by (…) the capacity of each of the interactants, to appreciate the meaning of the affective displays of their partner, and to scaffold their partner's actions so that they can achieve their goals' (Tronick, 1998, p. 293).

By administering a discrete stressor to the infant in the form of a temporary aberration in parental expression, Tronick and others sought to show that this relational system operates through a process of mismatch and reparation (Tronick & Cohn, 1989). Mismatch states occur when one partner does not accurately interpret the meaning of the other's affective display, and in turn responds inappropriately; reparation occurs when mismatched coordination is corrected. It is the recurrent transition between mismatch and reparation, over a wide range of interactive scenarios, that constitutes the regulatory function of the dyad (Beebe & Lachmann, 1994; Tronick, 1998). More recent work has suggested that quicker reparation of mismatched states is associated with lower stress reactivity in infants, indicating that latency is a potentially important element in infants' psychobiological regulation (Müller et al., 2015). In addition, it has been suggested that infrequent transitions between mismatch and reparation are likely in the presence of parental psychopathology. Postpartum depression, for example, is thought to generate 'chronic exposure to reparatory failure' within the dyad, leading to the development of maladaptive strategies for regulating affective states (Varga & Krueger, 2013, p. 284; see also: Manian & Bornstein, 2009; Reck et al., 2004).

The ideas about mutual regulation of affect are expanded through the 'dyadically expanded states of consciousness hypothesis' (Ham & Tronick, 2009; Tronick, 2004; Tronick, 1998).[6] This hypothesis incorporates principles of open systems theory, specifically nonlinear dynamic systems theory (Layek, 2015; von Bertalanffy, 1969). For example, the notion that human beings function by incorporating increasing quantities of information, subsequently becoming more coherent and complex. This suggests two ideas: (1) neurodevelopment of the infant is fundamentally contingent on external sources, i.e., the parent, and (2) the dyadic regulatory system as a whole is more elaborate than either member's part, i.e., 'more complex and coherent than either the infant's (or the mother's) endogenous state of consciousness alone' (Tronick, 1998, p. 296). More recently, these ideas have been reflected in the construct of 'coregulation', that is, 'psychobiological connectedness [allowing] the caregiver to

[6]The term consciousness may be substituted for 'brain organisation, for the materialists' (Tronick, 1998).

directly regulate the physiological and emotional functions of the infant, thereby providing critical scaffolding for the child to develop self-regulatory capacities' (Butler, 2011, p. 369).

2.2.2 Micro-behavioural processes

To examine how coregulatory parent-infant dynamics alter in the context of perinatal anxiety, studies have largely examined micro-behavioural processes. These are measured using behavioural observations of dyadic interaction, at varyingly fine-grain units of analysis. There are three main techniques for assessment: global rating scales of pre-specified combinations of behaviour (which generate a single score); frequency counts of a specific target behaviour (e.g., vocalisations), or measures of temporal relatedness (near continuous ratings of each member of the dyad's behaviour over a set time interval; Kaitz & Maytal, 2005).

Some parental micro-behaviours have been associated with positive or negative emotional adjustment outcomes in children, while others have not been studied in this way. For example: parental sensitivity, understood broadly as behaviour characterised by appropriate, contingent responding, is thought to predict secure child attachment (Bakermans-Kranenburg et al., 2003). By contrast, parental intrusiveness, understood broadly as overcontrolling behaviour that restricts child autonomy, has been related to decreased regulatory control in early childhood (Graziano et al., 2010; Stevenson & Crnic, 2013). However, there are numerous other micro-behaviours observed among anxious parents and their infants that have not been studied with respect to longer term child outcomes. Consequently, in this section we coin the term 'patterns of relating' to refer to the ways in which parents and infants interact in the presence of anxiety, as an alternative to other terms that may imply optimal or suboptimal parenting behaviour (e.g., 'caregiving quality').

Myriad micro-behavioural patterns of relating have been observed between anxious parents and their infants. These are presented in Figure 2.2. The majority of studies are focused on the parent and have found evidence of: more intrusive behaviour (Feldman et al., 1997; Hakanen et al., 2019; Ierardi et al., 2019; Kaitz & Maytal, 2005; Stein et al., 2012; Wijnroks, 1999); more intense behaviour (Kaitz et al., 2010; Murray et al., 2008); more stimulating behaviour (Beebe et al., 2011), and more unpredictable behaviour (Holmberg et al., 2020). There are mixed findings on positive affect; whether anxious parents display more (Murray et al., 2008) or less (Nicol-Harper et al., 2007). Some studies indicate that anxious parents may be less sensitive or responsive (Ierardi et al., 2019; Nicol-Harper et al., 2007; Stein et al., 2012) though other studies find no such evidence for this and instead indicate lower levels of encouraging behaviour (in parents with social anxiety; Murray et al., 2007). Overall, the evidence seems to suggest that anxious parents are characterised by additive rather than absent behaviours in interactive contexts.

By contrast, studies of infants of anxious parents have found evidence of a more inhibited set of behaviours, consistent with understandings about the role of inhibited temperament in the aetiology of

anxiety (see section 2.1.6). Evidence suggests that these infants show less involvement during interactions (e.g., alertness and initiatory behaviour; Feldman, 2007; Feldman et al., 2009), though this is unstable over time (Feldman et al., 1997). They also show lower variability in positive engagement with their parent (Reck et al., 2018) and are less 'emotional' during social challenges (Kaitz et al., 2010). This is consistent with findings that infants of anxious parents actively avoid interaction (e.g. protesting, rejecting, distancing; Kaitz & Maytal, 2005; Murray et al., 2008). Research also shows that infants increase their own self-regulatory behaviours during 'joy' episodes with their mothers (perhaps to cope with the parent 'trying too hard' to generate positive affect; Granat et al., 2017). This largely withdrawn set of infant behaviours complements the high levels of stimulation apparently generated by the parent.

In addition to behaviours observed in the parent and infant as individuals, there is a small body of evidence that examines the temporal relatedness of both partners' behaviour, i.e., their moment-by-moment coordination ('synchrony'). For instance, among dyads where the parent has anxiety, low affect synchrony has been observed (indexed by facial expression; Beebe et al., 2011). In addition, high levels of synchrony between partners in touch and gaze modalities have been identified (Beebe et al., 2011; Granat et al., 2017). Speculatively, these higher levels of synchronisation are thought to relate to the highly stimulating behaviour of the parent, and impede the likelihood of transitioning between states of mismatch and reparation. Such transitions are considered necessary for the development of typical regulatory function in the infant; the absence of these may therefore lead to the development of early dysregulatory processes (Granat et al., 2017; Tronick, 1998).

The evidence presented above represents a range of periods in the postpartum period, raising the question of how anxiety-related parent and child behaviour fluctuates during early development. The most frequently identified parental behaviours have been observed across the postpartum period. Intrusive parental behaviour in the context of perinatal anxiety has been observed early in development (3-4 months; Feldman et al., 1997; Kaitz & Maytal, 2005; Ierardi et al., 2019), towards the end of the first year of life (8-10 months; Stein et al., 2012; Hakanen et al., 2019) as well as in the intervening period (6 months; Wijnroks, 1999). Consistent with this is evidence showing that highly stimulating or high intensity parental behaviour associates with parental anxiety throughout the child's first year of life, including at 4 months (Beebe et al., 2011), 6 months (Kaitz et al., 2010) and 10-14 months (Murray et al., 2008). Less sensitive or responsive parental behaviour has similarly been observed in anxious parents in both the early (3 months; Ierardi et al., 2019) and later (10-14 months; Nicol-Harper et al., 2007; Stein et al., 2012) postpartum period.

While some anxiety-related parental behaviours remain relatively under-researched in the context of parent-infant interaction, making their developmental course hard to evaluate (e.g., unpredictability; Holmberg et al., 2020), it appears that the profile of more intrusive, higher intensity and less responsive parental behaviour emerges early, but is not uniquely tied to the immediate postpartum

period involving adjustment to parenthood. Feldman and colleagues' (1997) work showing that a decrease in parental anxiety from 3 to 9 months postpartum relates to increased parental sensitivity and decreased intrusiveness has also suggested that perinatal anxiety fluctuates and may – at any given point during the first year of life – have an impact on parent-infant interactive behaviour.

Common child behaviours observed during interaction with an anxious parent (avoidance; low involvement) have also been demonstrated across the first year of life; early on (3-5 months; Kaitz & Maytal, 2005; Feldman, 2007) as well as later (9-14 months; Murray et al., 2008; Feldman et al., 2009). This perhaps represents the development of an ongoing, functional adaptation to the over-stimulation and intrusion experienced in parental interaction. Unresponsiveness to a stranger in infants of socially anxious parents has also been observed as early as 10 weeks, indicating that perturbations in infant social behaviour emerge early in the context of parental anxiety; before, even, the development of more sophisticated face-to-face social exchanges during the third month of life (Feldman et al., 2009).[7]

[7]High levels of parent-infant synchrony in the context of parental anxiety have also been demonstrated in early infancy (4 months; Beebe et al., 2011) and later infancy (9 months; Granat et al., 2017), coherent with our understanding of the developmental course of synchrony more broadly (see section 2.2.4).

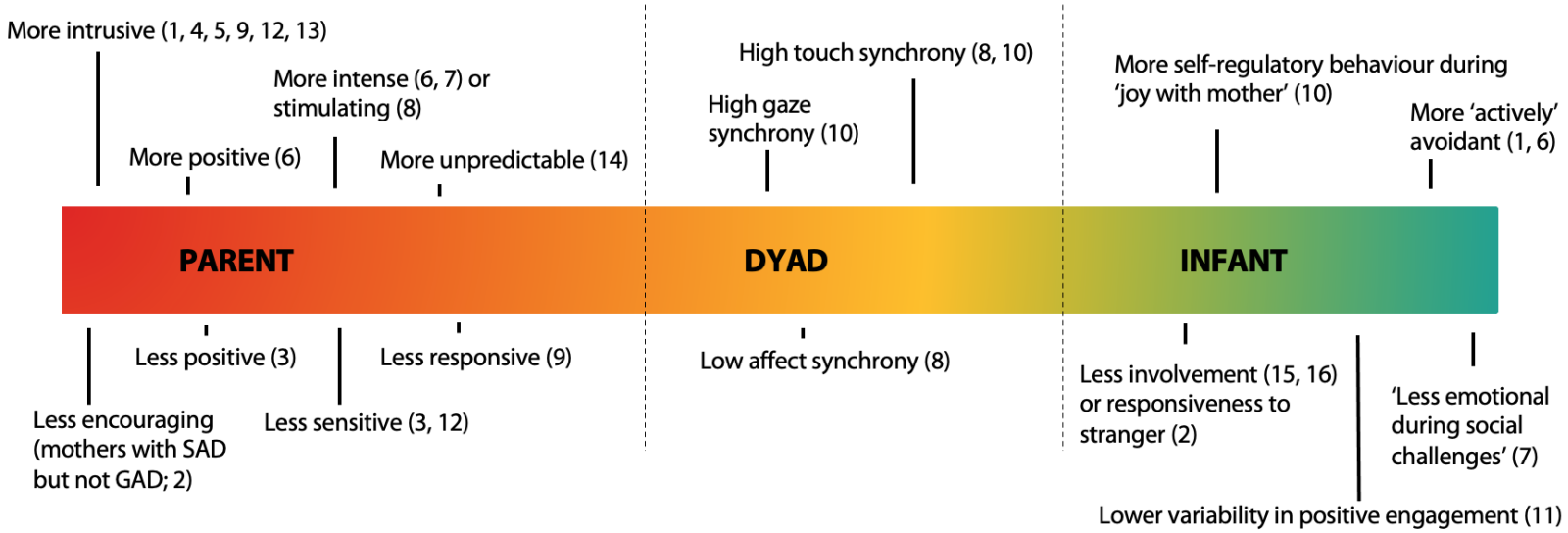

Fig. 2.2 Schematic showing micro-behavioural parent-infant patterns of relating in the context of perinatal anxiety. 1 - Kaitz & Maytal, (2005); 2 - Murray et al., (2007); 3 - Nicol-Harper et al., (2007); 4 – Wijnroks, (1999); 5 - Feldman et al., (1997); 6 - Murray et al., (2008); 7 - Kaitz et al., (2010); 8 - Beebe et al., (2011); 9 - Stein et al., (2012); 10 - Granat et al., (2017); 11 - Reck et al., (2018); 12 - Ierardi et al., (2019); 13 - Hakanen et al., (2019); 14 - Holmberg et al., (2020); 15 – Feldman, (2007); 16 – Feldman et al., (2009). GAD = generalised anxiety disorder; SAD = social anxiety disorder. Of note, this schematic is purely illustrative and does not denote a continuum whereby endpoints indicate more extreme levels of behaviour. Also, in practice, parent-infant interaction is inter-dependent and not neatly categorised by individual attributes. However, to visually summarise the available evidence, categories have been drawn based on coding schemes that divide interaction by parent, infant, and dyad codes (e.g. Feldman, 1998; Biringen & Easterbrooks, 2012) and descriptions provided by each study (e.g., 'maternal behaviour' versus 'infant behaviour' in Murray et al., 2007, 2008).

2.2.3 Transactional relations

The emotional developmental risk for infants of parents with anxiety is well established (Leis et al., 2014; Loomans et al., 2011; Rees et al., 2019), and might be partly mediated by alterations in parent-infant interaction. However, there is a body of evidence indicating that child outcomes are determined by transactional relations; in this context, this refers to interactions between infant exposure to parental anxiety, and both parent and child characteristics (Aktar & Bögels, 2017; Goodman & Gotlib, 1999; Murray et al., 2009). To identify key variables on the pathway from perinatal anxiety to later dysregulatory processes in the child, it is necessary to review findings from longitudinal studies.

Investigations of whether parent-infant interaction mediates the relationship between perinatal anxiety and later child emotional development are limited. Available evidence suggests that certain parental behaviours, such as maternal sensitivity, do not mediate the link between trait anxiety among pregnant mothers and their infants' later behavioural problems (Frigerio & Nazzari, 2021). A similar pattern of results has been found in an examination of prenatal anxiety exposure and later internalising or externalising behaviour in toddlers. In this example, an aggregate parenting measure (averaging parental sensitivity, intrusiveness, hostility and structuring capacity) was not found mediate the relation between prenatal anxiety and toddler socio-emotional difficulties (Endendijk et al., 2017). This evidence base, while small and inconclusive, suggests that anxious parents' behaviour does not uniquely mediate the relationship between perinatal anxiety and child regulatory processes in early development.

Studies examining the risk factors for childhood anxiety disorder strongly suggest that individual differences in infant temperament, in addition to parenting behaviour, play an important role in determining children's regulatory processes. Two temperamental domains appear to be particularly salient. A self-regulatory child temperament trait, effortful control (Rothbart et al., 2003) is negatively predicted by intrusive parenting (Graziano et al., 2010). Effortful control also has bidirectional relations with intrusive parenting (Eisenberg et al., 2015), and is positively related to child resilience over time (Taylor et al., 2013).[8] In addition, an avoidant temperamental trait, behavioural inhibition, predicts later childhood anxiety symptoms, and this relationship is strengthened in the presence of intrusive parental behaviour (Lewis-Morrarty et al., 2012; Prinzie et al., 2014; Rubin et al., 2002). These studies have generally used convenience sampling. However, it is likely that the effects identified would be amplified in infant samples recruited on the basis of parental anxiety, given the

[8]Bidirectional relations refer to the 'relative impact of child behaviour on parent behaviour, and of parent behaviour on child behaviour' (Pettit & Arsiwalla, 2008, p. 713). This term is used somewhat interchangeably with 'reciprocal relations' (Pettit & Loulis, 1997), which describe an 'ongoing concept of adjustment as environments are influenced by individuals and individuals are influenced by environments' (Wille et al., 2012, p. 307).

evidence demonstrating a relationship between perinatal anxiety and intrusive parenting (Fig 2.2), as well as between perinatal anxiety and impaired socio-emotional development (Polte et al., 2019).

It is also likely that young children's own symptomatic anxiety has a role in shaping their parents' behaviour, potentially leading to greater atypicalities in child socio-emotional development. Evidence shows that higher levels of child anxiety in early development associates with subsequent reductions in autonomy-granting behaviours among parents, as well as increased parental hostility and decreased parental sensitivity (Gouze et al., 2017; Yirmiya et al., 2021). These parental behaviours are unlikely to provide the necessary scaffolding for the child to develop self-regulatory capacities (Gueron-Sela, Bedford, et al., 2018; Gueron-Sela, Camerota, et al., 2018; Morris et al., 2002). In addition, bidirectional relations between parent and child anxiety have been identified, suggesting cross-generational influences of parent and child on one another's anxiety levels (Yirmiya et al., 2021). Such findings raise questions over the optimal strategy for mitigating psychopathological or socio-emotional difficulties in childhood, particularly in the early stages of development. Specifically, there is interest in whether interventions focused exlusively on only one member of the parent-child dyad are sufficient (e.g., Stein et al., 2018).

2.2.4 Physiological synchrony

The longitudinal study of transactional relations between parent and infant behaviour represents one, trait-level approach for examining joint mechanisms of emotion dysregulation in young children. An alternative approach, alluded to previously, is to investigate the extent to which infants synchronously match, or mimic, the behavioural and biological states of their parent.

The term 'synchrony' relates to a construct identified by a range of names, and describes the 'coordination of biological and social processes during social contact' (Feldman, 2015, p. 369). It is variously referred to as coordination (Feldman et al., 2011; Feldman, 2015; Granat et al., 2017), coupling or 'relatedness' (Jaffe et al., 2001), reciprocity (Anderson et al., 1977), mutuality (Boomen et al., 2021), attunement (Ostlund et al., 2017; Woltering et al., 2015), and entrainment (Wass et al., 2020), among others. More specifically, synchrony between two members of a dyad may be operationalised as 'concurrent' ('when A is high, B is high') or 'sequential' (or lagged; 'changes in A forward-predict changes in B'; Helm et al., 2018; Wass et al., 2020).

The developmental course of parent-child synchrony is difficult to ascertain, given how synchrony varies by context and level of analysis (e.g., behaviour *vs*. physiology). Behavioural synchrony in its typical form (as defined above; Feldman, 2015) emerges early in infancy, around 3-4 months, and continues across early childhood (Harrist & Waugh, 2002; Feldman et al., 2012). Throughout the first year of life, as children develop greater intentionality, intersubjectivity and joint attention, face-to-face synchronous exchanges start to become mutually agentic, with each partner playing a more equal role in sustaining coordinated engagement; this continues progressively throughout early childhood

(Harrist & Waugh, 2002). The long-term stability of behavioural synchrony, however, remains unclear.

There is some evidence that synchrony remains stable from early to middle childhood, and into adolescence. However, in older children this has only been observed to date during structured social tasks (Motsan et al., 2021) or behavioural paradigms eliciting positive or negative affect (Bureau et al., 2021; Levy et al., 2019; Roman-Juan et al., 2020), as opposed to free-play paradigms commonly used in early childhood (Leclère et al., 2014). These findings raise the question of whether parent-child synchrony declines over time as children develop greater independence, with synchrony retained only during high arousal events associated with affective or socio-cognitive processing. This view appears consistent with evidence on physiological synchrony in late childhood and adolescence, which indicates sensitivity to emotional context (e.g., Lougheed & Hollenstein, 2018; Woltering et al., 2015), though there is relatively little data in this area (DePasquale, 2020). In addition, there remain numerous, broad questions about the developmental course of parent-child synchrony, including what the trajectories might be for potentially different causes of synchrony (e.g., parent responding to the child, and/or child responding to the parent); why, when, and in what contexts physiological and behavioural synchrony become negatively related (Motsan et al., 2021), and whether synchronous exchanges become progressively lagged over time, as children develop more top-down metacognitive processes (Heyes, 2018).

One area of greater clarity is the relationship between parent-child synchrony and child adjustment outcomes. There is much evidence to suggest that higher levels of behavioural synchrony between parents and infants associate with more positive socio-emotional functioning in children (Feldman et al., 1997, 1999; Harrist & Waugh, 2002; Yaniv et al., 2021). It has also been shown that depressed parents exhibit low levels of gaze synchrony with their infants, while ‘healthy control’ parents exhibit higher levels. However, anxious parents exhibit the highest levels of synchrony with their infants, over and above healthy controls (Granat et al., 2017). This is consistent with evidence showing that parents with greater anxiety show more synchrony in the touch modality with their infants, compared to parents with mid-range anxiety (Beebe et al., 2011). These increased levels of behavioural synchrony have been interpreted as a signal of the anxious parent’s vigilant interactive style, and as an obstacle to dyadic regulation via the restriction of autonomy-promoting moments of miscoordination (Granat et al., 2017). Taken together, these results suggest that emotional development is shaped by behavioural synchrony, and that behavioural synchrony is altered in the presence of parental psychopathology.

To build on these results, and to expand our understanding of how synchrony relates to later development, research attention has turned to the investigation of physiological processes. When referring to physiological synchrony, the term has been defined broadly as: ‘any interdependent or associated activity identified in the physiological processes of two or more individuals’ (Palumbo et

al., 2017). Measures of autonomic activity are often selected when designing studies examining physiological synchrony, including but not limited to indices of sympathetic activity (e.g., heart rate, skin conductance) or parasympathetic activity (e.g., respiratory sinus arrhythmia, RSA; heart rate variability, HRV; Cacioppo et al., 2007; Mendes, 2009). This may be due to the relative acceptability of equipment application, as well as specialised analytical techniques capable of measuring high-frequency, fast-acting influences on autonomic activity (de Barbaro et al., 2017; Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019).

Physiological synchrony between parent-infant dyads is likely to be an important factor explaining both the intergenerational transmission of anxiety states and the development of emotion dysregulation. This is because arousal dysregulation is a known pathophysiological mechanism underlying anxiety disorders (see section 2.1.5, and, e.g., Ottaviani et al., 2016; Thayer et al., 1996); these arousal dynamics, if shared by infants, may become entrenched, becoming strongly encoded as a default. Subsequently, these dynamics may precipitate and perpetuate maladaptive regulatory processes in later life. While the field of physiological synchrony is nascent, there are increasing efforts to understand how this interaction between parents and infants relates to emotional development, and how this is impacted by parental psychopathology (Davis, West, et al., 2018; DePasquale, 2020).

Research on the relationship between perinatal anxiety and physiological synchrony is scant. Available evidence suggests that parents and teenage children with anxiety-related conditions, such as posttraumatic stress disorder (PTSD), are more likely to display high levels of RSA synchrony; by contrast, those exhibiting more signs of resilience display low levels, while a control group exhibits a mid-level (Motsan et al., 2021). These findings, presented in Figure 2.3, potentially indicate that low levels of physiological synchrony in parent-child dyads have some adaptive capacity. However, there is little other formal analysis of this construct among parents with anxiety-related conditions and their children (with one exception that found no association between perinatal anxiety and autonomic synchrony during a brief interaction: Ostlund et al., 2017). Previous studies have identified increased rates of skin conductance in dysregulated infants, as well as ‘high physiologic anxiety’, in their mothers (Ham & Tronick, 2006). However, these analyses are limited; they only tell us whether two individuals’ physiological activity tends to be higher than others, precluding interpretations of the data as synchronous.

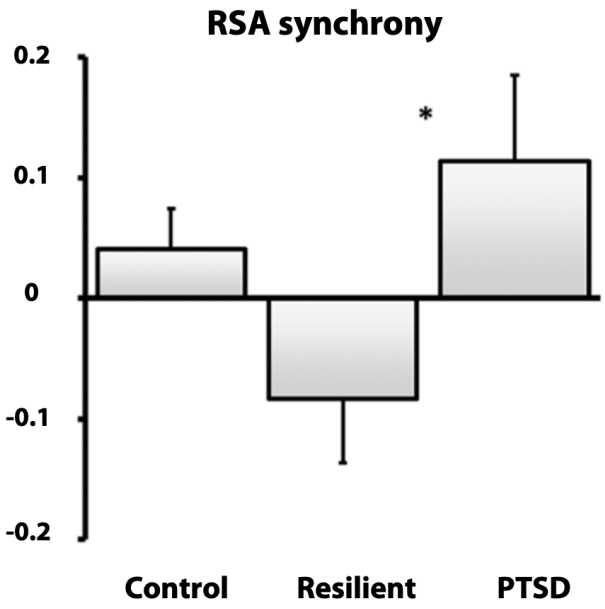

Fig. 2.3 Group differences in autonomic synchrony during a social interaction episode (Mean ± SE). PTSD, posttraumatic stress disorder; RSA, respiratory sinus arrhythmia; * $p < .05$. Republished with permission of John Wiley & Sons, from *Physiological and social synchrony as markers of PTSD and resilience following chronic early trauma.* Motsan et al. © 2021; permission conveyed through Copyright Clearance Center, Inc.

While higher levels of behavioural synchrony have typically been associated with greater socio-emotional functioning in children, the same relationship is not observed with physiological synchrony. The association between physiological synchrony and child functioning appears to differ depending on environmental context. For instance, in low-risk samples with young children, elevated parent-child autonomic synchrony is associated with fewer child externalising problems (Lunkenheimer et al., 2015), greater behavioural synchrony (Feldman et al., 2011), faster infant quieting (Wass, Smith, Clackson, et al., 2019), and non-maltreatment (Lunkenheimer et al., 2018). By contrast, in high-risk samples, elevated autonomic synchrony is associated with low child self-regulation (high socio-economic risk; Suveg et al., 2016) and insecure attachment (child safeguarding risk; Smith et al., 2016).

Though there is insufficient evidence available to draw firm conclusions about the relationship between physiological synchrony and the development of emotion dysregulation in children, a general pattern has been identified: in low-risk contexts, parents may be able to facilitate better emotion regulation in their children via elevated autonomic synchrony, while in high-risk contexts, synchrony may act as an additional risk factor with respect to the intergenerational transmission of stress from parent to child (DePasquale, 2020). It is therefore important to understand how physiological

synchrony manifests in the context of anxious parents and their infants, and how this might relate to child outcomes.

Another perspective on how physiological synchrony relates to child outcomes is informed by differential and biological sensitivity theory. Under this conceptualisation, elevated physiological synchrony acts as a susceptibility factor. That is, a biological marker that explains why some children are more susceptible than others to both 'risk-augmenting' and 'development-enhancing' contexts (Ellis et al., 2011). Recent research has shown that elevated RSA synchrony strengthens the relation between intrusive, coercive parenting and adolescent internalising difficulties, while also strengthening the relation between engaged, autonomy-granting parenting and positive adolescent adjustment outcomes (Oshri et al., 2021). If elevated physiological synchrony acts as a marker of biological sensitivity to context, detecting this in anxious parents and infants may help to inform future interventions for children with or at risk of emotion dysregulation difficulties (e.g., by focusing on the caregiving environment, as has been suggested in earlier studies; Gueron-Sela et al., 2017).

Investigations of physiological synchrony in young children and their parents commonly use one of two procedures. In the first procedure, physiological activity is measured during a free-play episode of parent-infant interaction, which is then interrupted by a brief stressor for the child. After this, free-play is resumed. Such methods are common in studies using the still face paradigm, involving a stressor in which the adult is instructed to stop responding to the child for a period of time (see Fig 2.4a; Tronick et al., 2009; Ham & Tronick, 2006; Moore et al., 2009). In the second procedure, the parent and infant's resting physiological activity is measured. The parent then undergoes an experimental manipulation intended to increase physiological arousal, and is subsequently united with the infant. After this there may be further interaction with a novel experimenter, or participants proceed directly to a free-play episode. The physiological activity of both partners is recorded throughout. These methods are common in studies examining 'arousal contagion' – a construct closely related to synchrony - whereby elevated arousal is induced in one partner and then observed subsequently in their partner (see Fig 2.4b; Waters et al., 2014, 2017). There are also variations in which the infant, rather than the parent, undergoes the arousal manipulation (Ebisch et al., 2012; Manini et al., 2013), or in which both partners are induced at the same time (Shih et al., 2019). This apparent transfer of physiological states has been linked to affect sharing between partners (Chauhan et al., 2008; Critchley, 2009; Heyes, 2018). Crucially, assessments of arousal contagion can help identify processes by which dyadic arousal states become altered or amplified during interaction (Butler, 2011).

It is worth highlighting that, while synchrony refers to coordination or covariation between two or more partners' biobehavioural processes during social contact (Feldman, 2015), contagion refers more directly to 'an exchange or transfer of some aspect of emotion from one person to another' (Butler, 2011, p. 375). The two terms are often used interchangeably, and share many technical similarities;

however, they are associated with distinct bodies of literature. The work on contagion is more emphatic of leader-follower dynamics, and of behavioural or cognitive mechanisms that serve to increase arousal transmission between partners (see differences between Feldman, 2007; Feldman & Eidelman, 2004; Feldman & Greenbaum, 1997, and Waters et al., 2014, 2017, 2020).[9]

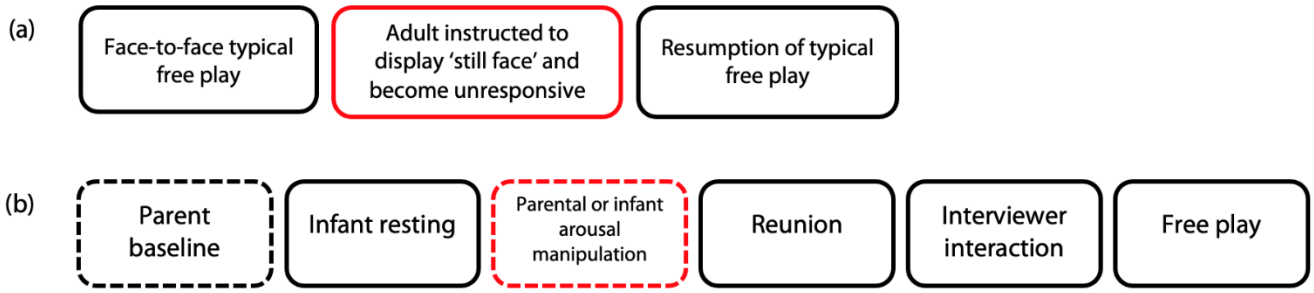

Fig. 2.4 Schematic outlining two experimental procedures traditionally used to examine joint physiological processes in young children and their parents: (a) free-play episodes with an intermediary stressor, e.g., the still face paradigm; (b) an arousal manipulation of one member of the dyad, usually undertaken alone after a baseline period, followed by reunion with partner, interaction with a novel experimenter, and free play (modified from: Waters et al., 2014, p. 936, Fig 1). Hatched lines indicate separation of the dyad. Red lines indicate introduction of stressor.

2.3 Limitations of stimulus-response models and research on physiology

There is now a body of evidence suggesting that, among parents and their infants, joint physiological processes may potentially help explain the process by which young children come to regulate their affect and arousal states. Further, it appears that in certain risk conditions, elevated physiological synchrony between partners is associated with worse self-regulation and adjustment outcomes for children. However, there remain multiple aspects of this relationship in need of further inquiry.

Physiological synchrony, while investigated in a broad range of contexts among parents and young children, has yet to be studied among populations with anxiety symptoms (DePasquale, 2020; with exception: Ostlund et al., 2017). In addition, the vast majority of research on physiological synchrony is conducted according to stimulus-response models. In these procedures, infants' regulatory responses to a random stressor, experienced either directly or indirectly, are recorded. These approaches are limited for two principal reasons. Firstly, they preclude the study of self-generated arousal in the infant. And secondly, experimentally controlled events are fundamentally different to

[9]While it would not be unreasonable to conflate the terms synchrony and contagion, feedback from researchers outside the field have indicated that the distinction is helpful here.

how arousal acts in the real world. To illustrate this, we can think about the difference between standard laboratory paradigms – such as those described above, involving infant exposure to a discrete stressor – and a real-world scenario, such as a child tantrumming in a shop. The real-world version has been described previously by Wass (2021a, p. 8):

> 'A child might pick up a toy, and announce that they want it; their parent, tired and in a hurry, might abruptly say 'no', and attempt to take the toy off them, leading to a physical tug of war. The child might lose this, sit down with a bump, and burst out crying. Or, they might start bashing the toy on the floor and break it; others in the shop might turn around to look at the noise.'

In this example, there is a chain of events: the parent's 'no'; the physical tussle; the sudden bump on the floor; other customers turning round to stare. These events are all separate from each other, but share causal relations. Importantly, they also take place through interactions between the child and the social environment. As it is not possible for lab-based studies to adequately capture these interactive dysregulatory cascades, it would be beneficial to study regulation among anxious parents and their infants using more naturalistic research methods.

There are also practical, technical limitations inherent in lab-based studies of physiological synchrony and arousal regulation. Measures of autonomic arousal, such as heart rate, have typically been collected using stationary equipment (e.g., de Barbaro et al., 2016; Waters et al., 2014; Woody et al., 2016) and, increasingly, smaller portable systems specialised for acquisition of electrocardiogram signals (e.g., Amole et al., 2017; Lunkenheimer et al., 2015; Oshri et al., 2021; Skoranski et al., 2017). Portable systems have the advantage of allowing greater freedom of movement than fixed apparatus. However, even these portable systems require surface electrodes to be placed on the body, and then connected by wires to a data acquisition system - creating a 'tethering' effect (Maitha et al., 2020). These wired electrodes are commonly attached to a sizeable transponder, which has to be hidden in clothing or attached to the participant's body. This presents an issue when conducting studies with very young children, such as infants. Large units mounted on the body are typically not well tolerated by this age group, leading to protest and technical interference, both of which compromise data acquisition and confound the study of arousal. Solutions to these problems have come in the form of wearable technologies, which have the potential to provide both accuracy and flexibility when measuring arousal in developmental populations (Lourenço et al., 2021; Maitha et al., 2020; Ragot et al., 2018). Wearable technologies can also be used for long periods of time, without researcher supervision, in participants' home environments. This methodology may therefore help to address both the theoretical and practical limitations posed by studying parent-infant physiology in a laboratory setting.

2.4 Longitudinal accounts with elevated likelihood samples

A further limitation of the current literature on emotion dysregulation relates to longitudinal studies. Relatively few studies have examined the way in which parental behaviours and infant regulatory characteristics interact over time to shape the pathway to anxiety precursors in young children (e.g., internalising behaviour, associated with the later development of depressive and anxious symptoms; Broeren et al., 2013; Toumbourou et al., 2011; Winsper et al., 2020). The paucity of longitudinal research during the early developmental stage leaves a gap in our understanding of the mechanisms by which early regulatory problems develop and shape consequent psychopathology early in life (Cole et al., 2019, 2020). Where studies have been conducted, these have not typically involved participants with a family history of psychopathology (e.g., Rubin et al., 2002; Taylor et al., 2013). Such samples prevent the generalisability of findings to clinical or subclinical populations. Studying transactional relationships in cohorts at elevated likelihood of developing emotion dysregulation and internalising behaviour – e.g., infant siblings of children with existing psychiatric conditions - may therefore provide greater external validity. This approach may also help translational researchers to develop interventions for prodromal anxiety that more precisely target underlying mechanisms.

2.5 Interventions for mitigating effects of perinatal anxiety on parent and infant

A final gap in the current literature pertains to intervention research. While there is evidence to suggest that the early parent-infant relationship is perturbed in the context of perinatal anxiety, it is unclear how – or if – interventions might help to mitigate this. It is also unclear which perinatal interventions are most effective for reducing parental anxiety (Loughnan et al., 2018). As parents and infants constitute a coregulatory unit (Tronick, 1998), and since there are cross-generational influences on both parent and young children's anxiety states (Yirmiya et al., 2021), it is likely that interventions involving both partners are necessary for reducing anxiety and increasing socio-emotional competency. A review of the effects of perinatal anxiety interventions on both parent and infant outcomes is therefore warranted.

2.6 Chapter summary

The intergenerational transmission of anxiety from parent to infant is multifaceted, as is the complex aetiology of anxiety. Developmental psychopathologists suggest that anxiety arises in part due to: (i) multiple interactions between environmental factors, such as parenting behaviour and child characteristics, and (ii) the early establishment of emotion dysregulation in young children. There is evidence to suggest that transactional relations between parent and child characteristics result in poor child self-regulation, and increased anxiety levels across both members of the dyad. However, studies of infants at elevated likelihood of emotion dysregulation are lacking, and it is not known whether treatments for perinatal anxiety address the interaction between parent behaviour and infant characteristics.

In addition, developmental theories suggest that infants' early regulatory systems are fostered through interaction with their parent. Recent research suggests that physiological synchrony between parent and infant may serve as a precursor to emotion regulation, with higher levels of physiological synchrony relating to improved child socio-emotional functioning in low- but not elevated-risk contexts. Arousal dysregulation is a core feature of anxiety, yet at present the physiological processes underlying naturalistic interaction between anxious parents and their infants have not been researched.

CHAPTER 3 - Overall Project Aims

In this section, the principal and secondary aims of the present thesis are set out. This is followed by a summary of the novel contributions this work will bring to the field.

3.1 Aims and research questions

The principal aim of this project is to examine differences in arousal regulation among infants with a parent with higher anxiety levels, versus those with a parent with lower anxiety levels. There are also two secondary aims. Firstly, to examine whether early self-regulatory difficulties are shaped by both parent and infant characteristics in a sample at elevated likelihood of psychiatric conditions. And secondly, to examine whether infant socio-emotional functioning and the parent-infant relationship can be improved by clinical treatments for perinatal anxiety. The main research questions of this thesis are as follows:

1. Do infants with a parent with higher anxiety levels display elevated levels of physiological synchrony with their parents versus infants of parents with lower anxiety levels?

2. Does spontaneously generated, stimulating parenting behaviour yield differential arousal responsivity among infants in high versus low anxiety groups?

3. In samples including families at elevated likelihood of psychiatric conditions, how does parenting behaviour associate with infant behavioural inhibition and effortful control in relation to early dysregulatory behaviour?

4. Are perinatal interventions effective in improving parental anxiety symptoms, as well as infant socio-emotional functioning and the parent-infant relationship?

3.2 Novel contributions

This project is novel in that it will be the first to examine physiological and behavioural processes among parents and infants using wearable technologies in the home environment, in the context of anxiety. This work will enhance our understanding of how dynamic changes in infant arousal correspond to patterns of physiological and behavioural activity in their parent, without the confounding influence of a controlled laboratory environment. A further benefit of using wearable technologies is that they facilitate the measurement of longer time courses, providing greater opportunity to measure cascades of arousal events. Two empirical studies addressing the principal aim of this thesis are reported in chapters 4 and 5.

This work will also be innovative in two other respects. Firstly, it will longitudinally examine associations between parental behaviour and infant temperament in a sample including infants at elevated likelihood of developing self-regulation problems, shedding light on early developmental pathways to multiple psychiatric conditions (chapter 6). Secondly, this work will fill a gap in the

literature by reviewing the effects of perinatal interventions on both parent anxiety and infant development outcomes (chapter 7).

II. EMPIRICAL STUDIES

CHAPTER 4 – Anxious parents show higher physiological synchrony with their infants

The following chapter is a publication of an original article investigating physiological processes in parents with higher or lower levels of anxiety, and their infants (Smith, Jones, Charman, et al., 2021). Subheadings, figure placement, figure and table numbers, and citation style have been adapted to conform to the general thesis format. The supplementary materials (SM) for this chapter are available in Appendix A.

Abstract

Background

Interpersonal processes influence our physiological states and associated affect. Physiological arousal dysregulation, a core feature of anxiety disorders, has been identified in children of parents with elevated anxiety. However, little is understood about how parent–infant interpersonal regulatory processes differ when the dyad includes a more anxious parent.

Methods

We investigated moment-to-moment fluctuations in arousal within parent-infant dyads using miniaturised microphones and autonomic monitors. We continually recorded arousal and vocalisations in infants and parents in naturalistic home settings across day-long data segments.

Results

Our results indicated that physiological synchrony across the day was stronger in dyads including more rather than less anxious mothers. Across the whole recording epoch, less anxious mothers showed responsivity that was limited to 'peak' moments in their child's arousal. In contrast, more anxious mothers showed greater reactivity to small-scale fluctuations. Less anxious mothers also showed behaviours akin to 'stress buffering' – downregulating their arousal when the overall arousal level of the dyad was high. These behaviours were absent in more anxious mothers.

Conclusion

Our findings have implications for understanding the differential processes of physiological coregulation in partnerships where a partner is anxious, and for the use of this understanding in informing intervention strategies for dyads needing support for elevated levels of anxiety.

4.1 Introduction

Research has shown continuity of lifetime anxiety disorders from parents to children: multiple anxiety disorders pose a significant risk of anxiety in offspring (Lawrence et al., 2019). However, while anxiety disorders aggregate in families, the reasons for this are still not yet understood (Murray et al., 2009). Genes associated with an underlying liability towards current anxiety symptoms across the population are largely shared with those predisposing individuals to professionally-diagnosed lifetime anxiety disorder (Purves et al., 2020), yet evidence acknowledges the key role of environmental influences in the development of anxiety (Eley et al., 2015). Early childhood has been found to be a crucial period for identifying environmental risk factors for anxiety disorder (Möller et al., 2016), including the potential for early identification of high-risk individuals, and for preventative, early interventions. The present study examines, therefore, how anxious symptoms in parents relate to affect coregulation in parent-infant dyads.

In both anxious and non-anxious families, there is considerable evidence that parents play a positive role in regulating children's physiological, behavioural and affective states (Bridgett et al., 2015; Reddy et al., 1997). Behavioural studies have, for example, identified sensitive parenting behaviours that mediate the relationship between household chaos and infant self-regulatory skills (Vernon-Feagans et al., 2016), and parental encouragement mediates the relationship between parent anxiety and anxiety symptoms in early childhood (Murray et al., 2008, 2009). Physiological studies examining how autonomic arousal co-fluctuates in parent-infant dyads have traditionally concentrated on physiological synchrony, referring to a range of temporally interdependent or associated activities in the physiological processes of two partners (Davis, West, et al., 2018; McFarland et al., 2020). Previous research has suggested that the benefits of synchrony are bidirectional (Feldman, 2007): the parent, by adapting to the child, helps by responding contingently to the child's needs (Feldman, 2009); the child, by adapting to the parent, gains both self-control, and self-awareness (Feldman et al., 1999). Previous research has identified synchronous patterns of change in physiological arousal in the lab following the administration of experimental stressors (Ham & Tronick, 2009). Recent research that recorded naturalistic arousal co-fluctuations in parent-infant dyads found that synchronous patterns of co-fluctuating arousal were not observed across all arousal states: rather, that short-term increases in parent-child synchrony were triggered in response to ‘peak’ instances of physiological arousal in the infant, but that synchrony at other times was not observed (Wass, Smith, Daubney, et al., 2019; Wass, Smith, Clackson, et al., 2019).

There is also substantive evidence that anxious parenting can associate with the dysregulation of behavioural and physiological states in children (Nikolić et al., 2016). Behavioural studies examining tabletop play between anxious parents and their infants found evidence for an ‘overloaded, highly stimulating’ behavioural profile in anxious mothers (Feldman, 2007), along with higher levels of behavioural synchrony (Beebe et al., 2011; Granat et al., 2017). Anxiety in these studies was

measured via self-report questionnaire. Experimental investigations have also shown overactive regulatory responses from infants of anxious mothers, particularly following the onset of positive social stimuli (Granat et al., 2017). Lab-based physiological studies have found evidence for 'stress contagion', whereby increases in autonomic activity in the mother are reflected in increases in the infant following emotionally-valenced experimental tasks (Waters et al., 2014, 2017). However, naturalistic investigations of physiological synchrony between infants and parents with anxiety are minimal.

Overall, studies of maternal anxiety and physiological dysregulation in early childhood remain scant. Arousal dysregulation (often defined as increased autonomic changes in response to an experimentally administered challenge, along with longer recovery times; e.g., Beauchaine & Thayer, 2015) is a core feature of anxiety in adulthood (Ottaviani et al., 2016; Thayer et al., 1996) and middle childhood (Dieleman et al., 2015; Koszycki et al., 2019), but the majority of research on this topic focuses on children aged 6 or over (Siess et al., 2014). In addition, these findings examine change relative to a stressor, with a discrete and experimenter-defined start and end period, administered during short periods (~<10 min) of lab-based interaction. No previous research has examined whether spontaneous fluctuations in a child and parent's biological and behavioural systems associate with one another in naturalistic, day-to-day settings, assessing how these relationships differ between more or less anxious parents. Additionally, while emotion dysregulation is also characteristic of anxiety disorders (Amstadter, 2008; Hofmann et al., 2012), there has been little study into the relationship between affect states and physiological dysregulation in mother–infant pairs where the mother has anxiety. One issue with measuring hyperarousal alone is that its valence cannot be determined; to resolve this, vocal signals of positive or negative affect may be used to identify valence (as in previous work showing that extremes of valence are more likely at elevated levels of arousal; see Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019) To our knowledge, no previous research has disaggregated infant recovery from an instance of physiological hyperarousal with positive or negative valence and examined whether the relationship between infant recovery and maternal reactivity to positive or negative hyperarousal events varies by maternal anxiety.

To address this, we developed new techniques, including miniaturised microphones, video cameras, electrocardiograms, and actigraphs that could be worn concurrently by infants and parents for a day at a time at home (Maitha et al., 2020; Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019). We recorded both partners' autonomic fluctuations during the day, by measuring heart rate (RR intervals, where R is the peak of the QRS complex of the ECG wave), heart rate variability, and movement (via actigraphy). According to previous research, elevated heart rate, decreased heart rate variability and increased movement are associated with increased physiological stress, i.e. a higher ratio of sympathetic to parasympathetic nervous system activity (Cacioppo et al., 2007). We also

recorded the auditory environment and coded the vocalisations spoken by the infant, and those directed to the infant by the parent.

The goal of the current study was to examine associations between the physiological profiles for parent-infant dyads with higher or lower measures of maternal anxiety. In the analyses of two partners' time series data, a well-established distinction has been drawn between 'concurrent' synchrony ('when A is high, B is high') and 'sequential' synchrony ('changes in A forward-predict changes in B' – see Wass et al., 2020). Given previous evidence, we asked a set of four interlinked questions from around 4 hours per dyad of continuously measured parent and child arousal data:

First (hypothesis 1), we examined the degree of concurrent and sequential parent-infant arousal synchrony across the full time series of home-based data from each dyadic pair. We predicted that both forms of synchrony would be greater in dyads with more anxious parents.

Second, across the next three analyses, we examined how overall levels of dyadic synchrony relate to structured variation in the degree of synchrony across the time series. In hypothesis (2), we asked how sequential synchrony varies in relation to the current levels of arousal in both dyadic partners, considered at the same time – and we examined how this differs by parental anxiety level. We predicted that arousal changes in each partner considered independently would be influenced by the overall level of arousal of the dyad and that this relationship would differ contingent on parental anxiety.

Third, since previous research (Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019) has shown that synchronous responses may be constrained to highly stressful events, we went on to focus the analysis on moments when the infant showed a peak in their arousal (hypothesis 3). We predicted that more anxious parents would show greater event-related physiological hyperarousal.

Finally, peak arousal events in the infant could be positive or negative in affect. In hypothesis (4) we predicted that parents' event-related hyperarousal would associate with infants' hyperarousal across different emotionally valenced events.

4.2 Method

4.2.1 Experimental participant details

The project was approved by the Research Ethics Committee at the University of East London. Participants were recruited from the London, Essex, Hertfordshire and Cambridge regions of the UK. In total, 91 parent-infant dyads were recruited to participate in the study, of whom usable autonomic data were recorded from 82. Of these, usable paired autonomic data (from both parent and child) were obtained from 74 participants. Of these, 68 of these participants also completed the full anxiety screening questionnaire. A consistent outlier-detection strategy was applied equally for all analyses, by excluding outliers that were >2 inter-quartile range (IQR) from the mean, to avoid violating the

assumptions of the statistical tests being conducted. Outliers were only found for the analyses presented under hypotheses 1 and 2, reported below in the Results. Further details, including exclusion criteria, and extra demographic details on the sample, are given in Table 4.1 and SM, section 1.1. Of note, we excluded families in which the primary day-time care was performed by the male parent because the numbers were insufficient to provide an adequately gender-matched sample. All participating parents were, therefore, female. Participants received £30 in Love2Shop gift vouchers as a token of gratitude for participation, split over two visits.

	Low anxiety	High anxiety
Infant age (days) – mean (s.d.)	349 (39)	370 (41)
Gender (*N* (%) male)	14 (42)	13 (39)
Infant ethnicity *N* (%)		
White British	17 (51)	16 (47)
Other white	1 (4)	1 (4)
Afro-Caribbean	4 (11)	3 (9)
Asian, Indian and Pakistani	2 (7)	5 (16)
Mixed – White/Afro-Caribbean	1 (4)	1 (4)
Mixed – White/Asian	0 (0)	4 (11)
Other mixed	3 (9)	4 (11)
Household income (%)		
Under £16k	9 (27)	10 (31)
£16–£25k	8 (24)	10 (31)
£26–£35k	7 (20)	3 (9)
£36–£50k	4 (11)	4 (11)
£51–£80k	4 (11)	2 (7)
>£80k	1 (4)	3 (9)
Maternal education (%)		
Postgraduate	12 (36)	9 (27)
Undergraduate	19 (56)	16 (47)
FE qualification	0	1 (4)
A-level	0	2 (7)
GCSE	3 (9)	1 (4)
No formal qualifications	0	2 (7)
Other	0	2 (7)

Table 4.1. Demographic data split by low/high parental GAD-7 score.

4.2.2 Parent screening

To screen parents for maternal anxiety, participants filled out the Generalized Anxiety Disorder 7-item screener (GAD-7), which assesses anxiety symptoms over the past 2 weeks (Spitzer et al., 2006). Responses were given on a 4-point scale ranging from 0 (not at all) to 3 (nearly every day). Validity for this questionnaire has been provided by studies with clinical and non-clinical populations, with scores above 6 representing mild to moderate anxiety (Löwe et al., 2008). The internal consistency of the scale was $\alpha = 0.89$.

The mean (SD) (range) of scores obtained on the GAD-7 was 3.4 (3.9) (0–17). A median split was performed to differentiate between high and low anxiety groups. The dichotomisation of this variable was necessary due to our statistical analysis plan (in particular, our use of time series analyses), though additional analyses based on a quintile split were used to explore the consistency of associations (see SM 2.1). The mean (SD) (range) GAD-7 score was 0.76 (0.85) (0–2) for the low anxiety group and 6.16 (3.96) (3–17) for the high anxiety group, indicating mild to moderate anxiety.

4.2.3 Experimental method details

Participating parents were invited to select a day during which they would be spending the entire day with their child but which was otherwise, as far as possible, typical for them and their child. The researcher visited the participants' homes in the morning (c. 7.30–10 am) to fit the equipment, and returned later (c. 4–7 pm) to pick it up. The mean (SD) recording time per day was 7.3 (1.4) hours.

The equipment consisted of two wearable layers, for both infant and parent (see Fig. 4.1). For the infant, a specially designed baby-grow was worn next to the skin, which contained a built-in electrocardiogram (ECG) recording device (recording at 250Hz), accelerometer (30Hz), Global Positioning System (1Hz), and microphone (11.6kHz). A T-shirt, worn on top of the device, contained a pocket to hold the microphone and a miniature video camera (a commercially available Narrative Clip 2 camera). For the parent, a specially designed chest strap was also worn next to the skin, containing the same equipment. A cardigan, worn as a top layer, contained the microphone and video camera. The clothes were comfortable when worn and, other than a request to keep the equipment dry, participants were encouraged to behave exactly as they would do on a normal day. To ensure good quality recordings, the ECG device was attached using standard Ag-Cl electrodes, placed in a modified lead II position.

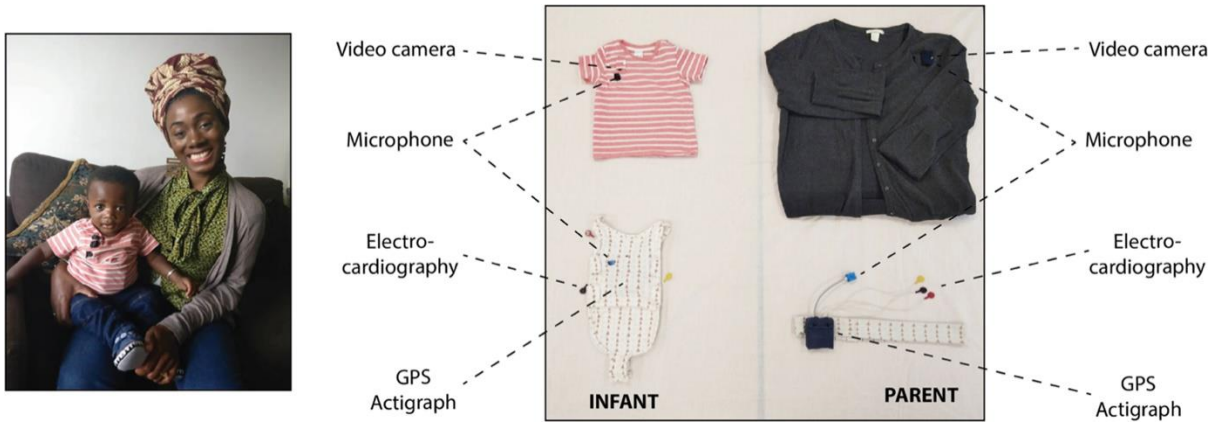

Fig. 4.1 Left – illustration of parent and child wearing the equipment; right – the equipment used for home monitoring.

4.2.4 Quantification and statistical analysis

4.2.4.1 Autonomic data parsing and calculation of the autonomic composite measure

Further details on the parsing of the heart rate, heart rate variability, and actigraphy are given in the SM (section 1.2). To ensure the accuracy of these recording devices, they were cross-validated by recording heart rate and heart rate variability using both the new devices at home and established recording devices (a Biopac MP150 amp recording at 2000Hz) in lab settings. High reliability was observed both for heart rate (rho = 0.57, $p < 0.001$) and heart rate variability (rho = 0.70, $p = 0.01$). In the SM (section 1.3), we also present further details on our motivation for collapsing these three measures into a single composite measure of autonomic arousal.

4.2.4.2 Affect coding

The microphone recorded a 5-s snapshot of the auditory environment every 60 s. Post hoc, coders identified samples in which the infant was vocalising, and coded them for vocal affect on a scale from 1 (fussy and difficult) to 9 (happy and engaged). In order to assess inter-rater reliability, 24% of the sample was double coded; Cohen's kappa was 0.60, which is considered acceptable (McHugh, 2012). All coders were blind to intended analyses. Negative affect vocalisations were defined as all vocalisations coded as 4 or less; positive affect vocalisations included all vocalisations coded on 6 or more; neutral affect vocalisations include vocalisations coded 5.

4.2.4.3 Home/awake coding

Our analyses only examine segments of the data in which the dyad was at home, and the infant was awake. This is because our preliminary analyses suggested that infants tended to be strapped in to either a buggy or car seat for much of the time that they were outdoors, which strongly influenced their autonomic data. Further details for how these home/awake segments were identified are given in

the SM, section 1.4. Following these exclusions, the mean (SD) total amount of data available per dyad was 3.7 (1.7) hours, corresponding to 221.5 (102.4) 60-second epochs per dyad.

4.2.4.4 Cross-correlation analyses

To test hypothesis 1, we used cross-correlation to examine relations between concurrently measured epochs of parent and infant arousal. Infant and adult arousal data were synchronised, 60-s epoched and linear de-trended. Spearman's rank order correlations were conducted across all pairs of time-locked (i.e., simultaneously occurring) epochs for infant and parent and plotted as time '0' ($t = 0$). Correlations between non-simultaneous pairs were then computed and plotted against time lag and direction on the *x*-axis (adult's arousal forward-predicting infant arousal on the positive axis, infant arousal forward-predicting adult arousal on the negative). Figures present data for a selected epoch of 600 s before to 600 s after an event to fully contextualise profiles of change around the focal point (see Thorson et al., 2018). Permutation-based temporal clustering analyses were applied to correct for multiple comparisons across time bins (see below, and SM, section 1.6 for more details).

4.2.4.5 Vector plots

To test hypothesis 2, we computed vector plots. To do this, all infant and adult arousal data were downsampled into 60-s epochs and collated into six equally sized bins, individually for each participant (infant and adult). Each epoch was then classified according to what bin it fell into for both infant arousal and parent arousal. This is represented as a two-dimensional matrix – so all epochs that were bin 3 for infant arousal and bin 4 for adult arousal are drawn at location (x −3, y −4). The size of each dot within the matrix indicates what proportion of the total available samples was located within each bin. For each bin, we then calculated the average change from all epochs in that bin, to the epochs immediately following. This change score is drawn on the vector plot as a red line. Thus, for the point located at (6, 6) on the vector plot, which represents all epochs that were classified as in bin 6 for both infant arousal and parent arousal, the vector extends −0.8 on the *x*-axis (representing a change in infant arousal), and −1 on the *y*-axis (representing a change in adult arousal). This indicates that across all epochs starting from (6, 6), the average change to the next epoch was a reduction of 0.8 bins in infant arousal, and 1 bin in adult arousal.

These plots, therefore, allow us to examine how the parent's present arousal level *interacts with* the child's present arousal level in predicting the change in parent arousal – i.e., how the change in one partner's arousal is influenced by both partners' arousal, considered in combination. To quantify this, we compared the change in adult arousal between the bottom right (high infant-low adult arousal) and bottom left (low infant-low adult arousal) quadrants of the Vector plot; and between the top right (high infant-high adult arousal) and top left (low infant-high adult arousal) quadrants of the Vector plot. The observed results are compared to a chance value of 0 using a *t* test.

4.2.4.6 Permutation-based temporal clustering analyses

To estimate the significance of time series relationships, a permutation-based temporal clustering approach was used for the analyses presented under hypotheses 1, 3, and 4. This procedure, which is adapted from neuroimaging (Maris, 2012; Maris & Oostenveld, 2007), allows us to estimate the probability of temporally contiguous relationships being observed in our results, a fact that standard approaches to correcting for multiple comparisons fail to account for (Maris & Oostenveld, 2007; see also Oakes et al., 2013). For further details, see SM, section 1.5.

4.3 Results

4.3.1 Raw data and descriptives

Prior to testing our four main hypotheses, we first present raw data and descriptive analyses. Figure 4.2 shows a raw data sample of the home data, and Table 4.1 shows demographic data for the sample, subdivided by low/high GAD-7 scores. Independent samples *t* tests were conducted for all demographic variables (i.e., with the exception of ethnicity) to assess whether significant group differences were observed. No significant differences were identified (all *ps* > 0.15).

As a preliminary analysis, we examined how the low/high GAD-7 groups differed on mean arousal levels across the day. This analysis was based on the raw autonomic data included in the arousal composite, prior to the calculation of *z* scores on a per-participant basis for the composite measure. When considering just samples in which the dyad was at home, and the infant was awake, *t* tests indicated no differences between the lower/higher anxiety groups on any of the heart rate variables included in the *z*-scored composite, namely mean waking heart rate, sleeping heart rate, waking or sleeping heart rate variability, for either infants or parents (all *ps* > 0.27). Hence, arousal levels did not differ significantly between the groups. Waking movement levels were, however, significantly lower in the high GAD-7 group $t(69) = 2.17$, $p = 0.03$.

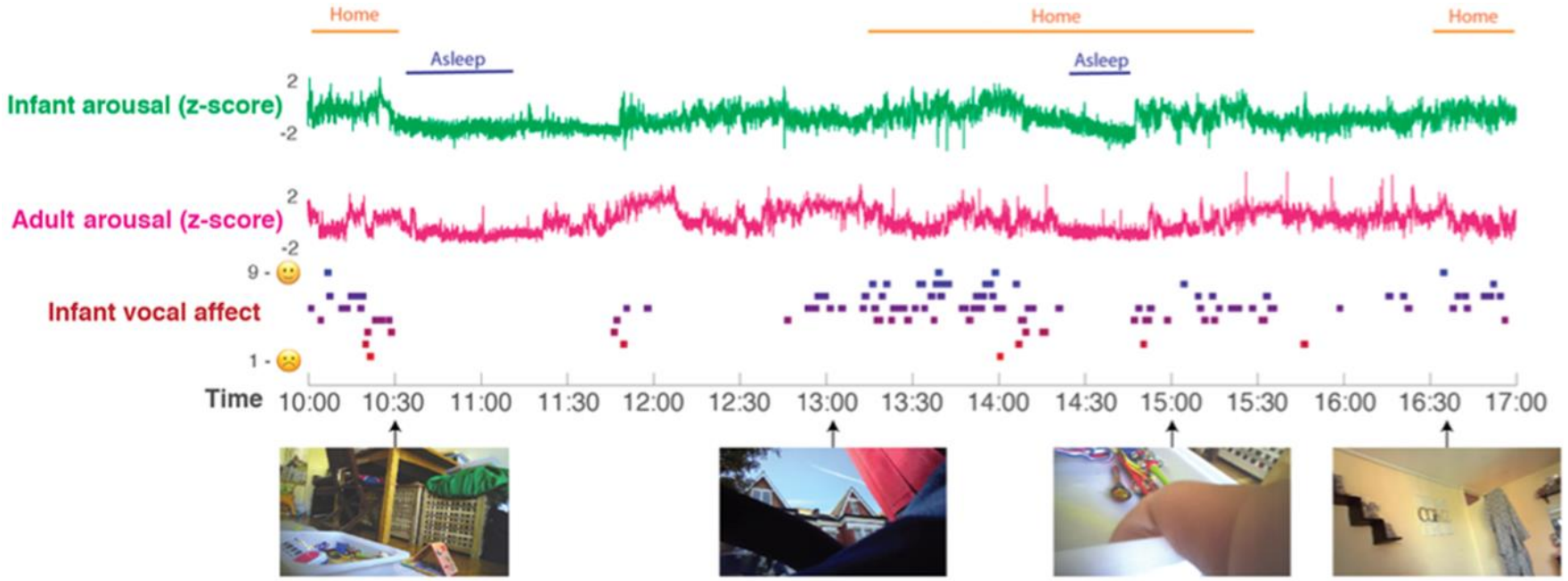

Fig. 4.2 Raw data sample. A sample day's data from a single dyad is shown. Time (from 10 am to 5 pm) is shown on the *x*-axis. From top to bottom: the home/awake coding; the infant and parent arousal composites (see SM, section 1.1); infant vocal affect; sample frames from the data recorded from the camera. All measures are calculated as described in the Methods section.

4.3.2 Hypothesis 1: concurrent and sequential parent-infant synchrony in physiological arousal is greater in dyads with more anxious parents

To test this hypothesis, we examined the cross-correlation between infant and parental arousal. Prior to conducting the *t* test group comparisons described below, two outliers (one from each group) were excluded using the >2 inter-quartile range (IQR) criterion.

In previous research, we used an identical analysis to show that, across all parents, no significant temporal co-fluctuation in infant and parental autonomic arousal levels is observed (Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019). When results are subdivided by parental anxiety, however, a significant zero-lagged cross-correlation between infant and parent arousal is observed in the anxious group [*t* test *v.* chance value of 0 ($t(32) = 4.2$, $p < 0.001$)] but not the non-anxious group [$t(32) = 1.03$, $p = 0.32$ (Fig. 4.3a)]. Group comparisons indicated higher zero-lagged cross-correlations in Group 1 *v.* Group 2: $t(64) = 2.16$, $p = 0.035$. In sum, when considering all home-awake segments of the day, there is significant co-fluctuation in autonomic arousal between parent and child arousal in the high GAD-7 but not the low GAD-7 group.

Further details and interpretation of the cross-correlation function are given in the SM, section 2.1. In this section, we also provide a further analysis subdividing our groups using a quintile split by GAD-7 score (see SM, Fig. S2). This shows the relationship between arousal cross-correlation and GAD-7 is distributed uniformly across the sample and is highest in participants with the most elevated levels of anxiety.

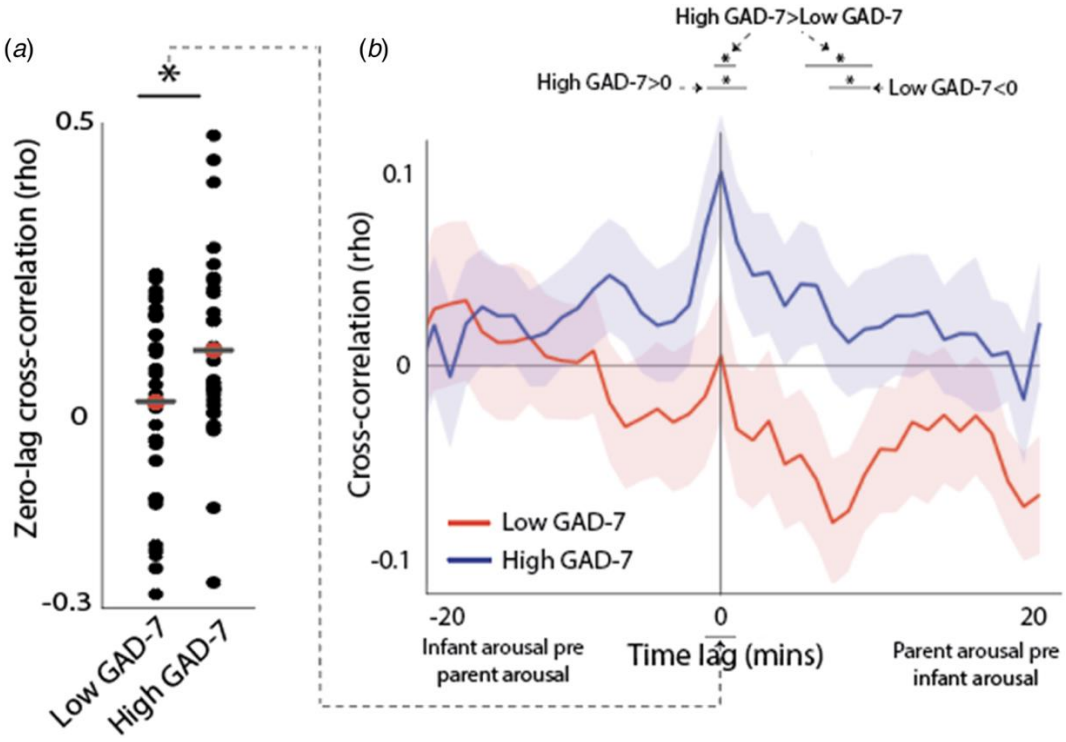

Fig. 4.3 (a) Scatterplot showing the zero-lagged cross-correlation between parent and child arousal, subdivided by maternal anxiety (i.e., low and high GAD-7). * indicates the results of the *t* tests conducted as described in the main text $p < 0.05$. (b) Cross-correlation function between parent and child arousal, subdivided by low and high parental anxiety. The peak at time 0 indicates that when parent and infant arousal synchrony are compared, they significantly associate and this is greater in high anxiety dyads than low anxiety dyads. Shaded areas indicate the standard error of the means. * $p < 0.05$ following correction for multiple comparisons using permutation-based temporal clustering analyses (see SM, section 1.5).

4.3.3 Hypothesis 2: arousal changes in each partner will be influenced by the overall arousal level of the dyad; this relationship will differ contingent on parental anxiety

Hypothesis 1 examined differences in arousal synchrony across all data collected while the dyad was at home and the infant was awake. In addition, we also wished to examine how intra-dyadic influences in arousal would vary contingent on the arousal level of parent and child, considered separately. To examine this, we calculated a vector plot (see the Methods section).

The parent-infant arousal change score is drawn on the vector plot as a red line. For example, for the point located at (1, 1) on the vector plot (Fig. 4.4a), the vector extends +0.3 on the *x*-axis (representing a change in infant arousal), and +0.7 on the *y*-axis (representing a change in adult arousal). Hence, across all epochs starting from (1, 1), the average change to the next epoch was a gain of +0.3 bins in infant arousal, and +0.7 bins in adult arousal (see Fig. 4.4a, b). Across all data, the vectors tend to point towards the centre of the plot. This indicates regression to the mean: in an epoch where infants' and parents' arousal starts low, an increase is expected to the next epoch; whereas for an epoch that starts high, a decrease is expected. The centre point of the vectors appears to be around bin 4 (out of 6), consistent with the lightly positively skewed distribution observed across all data (see Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019).

In order to examine how the change in one partner's arousal is influenced by both partners' arousal considered in combination, we can examine, for example, the bottom rows of each vector plot (Fig. 4.4a, b), which show instances in which the adult's arousal is low. The bottom left quadrant (shaded yellow on Fig. 4.4c) shows instances in which both parent and infant arousal is low; the bottom right quadrant (shaded red) shows instances in which the parent arousal is low but infant arousal is high. To estimate whether, in both groups, the change (increase) in adult arousal is greater where the infant arousal is high than when it is low, we calculated the change in adult arousal between the bottom right and bottom left quadrants of the vector plot (Fig. 4.4c), and compared the observed results to a chance value of 0 using a *t* test. Results from four participants were excluded (three low/one high) using the ±2IQR rule. For both the low [$t(30) = 2.03$, $p = 0.05$] and high [$t(32) = 2.39$, $p = 0.02$] GAD-7 groups, marked differences from zero were observed. Hence, when adults' arousal is low and infants' arousal is high, then adults show upregulation in their arousal in response – a feature which is present in both the low and high GAD-7 groups.

The top rows of the vector plot (Fig. 4.4c, d) show instances in which the adult's arousal is high. In the non-anxious group, it appears that the negative vertical displacement of the lines is greater in the top right quadrant (shaded green on Fig. 4.4c), compared to the top left quadrant (shaded brown). If true, this would indicate that, when the adult's arousal starts high, their arousal *decreases* more in instances where the infant's arousal is high than when it is low. To estimate this, we calculated the change between quadrants and compared the observed results to a chance value of 0 using a *t* test. Results

from three participants were excluded (one low/two high) using the ±2IQR rule. For the lower anxiety [$t(32) = 2.16$, $p = 0.04$] but not the higher anxiety [$t(31 = 0.75$, $p = 0.46$] groups, a significant difference was observed. An independent samples *t* test also identified a significant difference between groups on this measure [$t(63) = 2.05$, $p = 0.045$]. Hence, when the overall arousal level of the dyad is high, then adults show downregulation in their arousal in response – but this feature is only present in the low GAD-7 group.

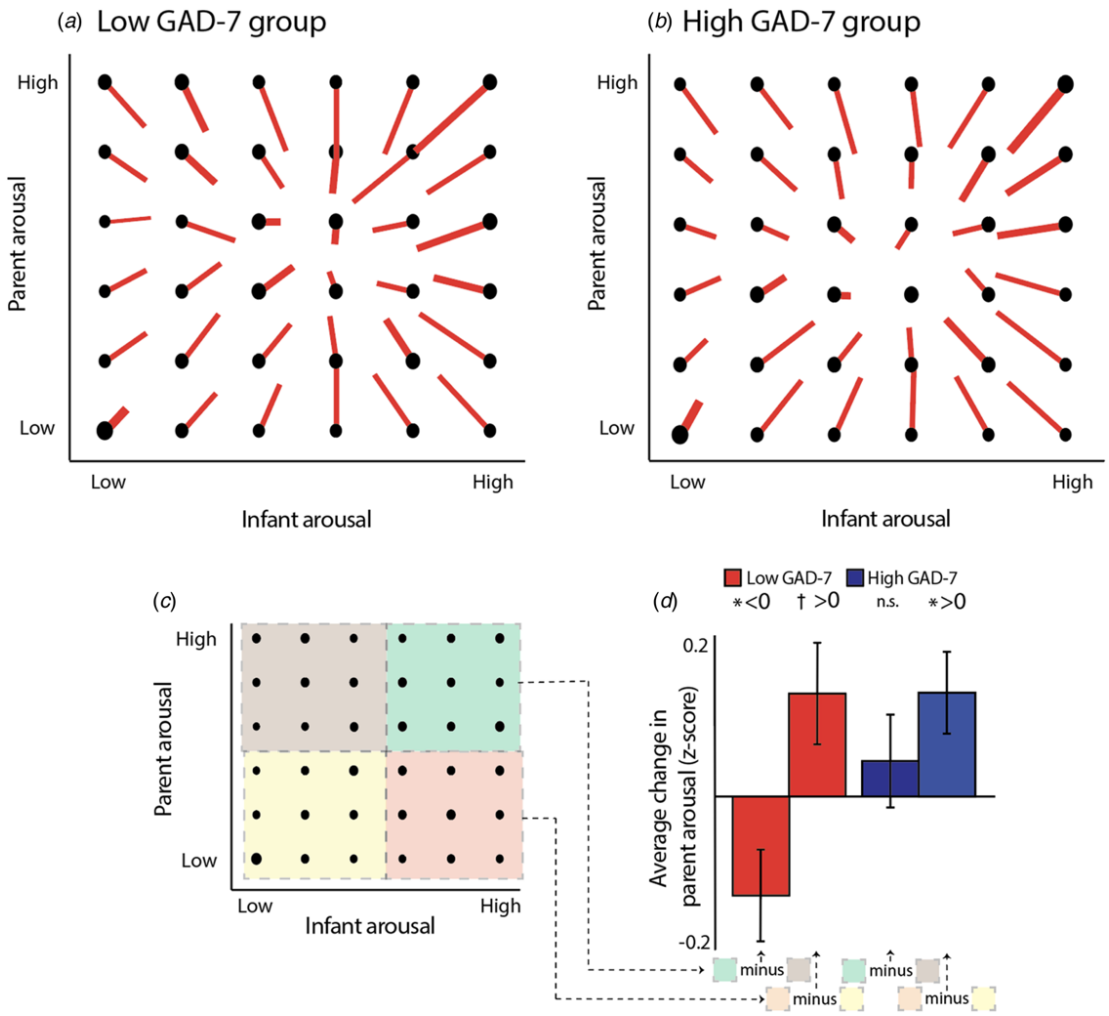

Fig. 4.4 (a)–(b) Vector plot illustrating transitions between arousal bins, contingent on starting arousal state. (a) Shows non-anxious (low GAD-7) group; (b) shows anxious (high GAD-7) group. Data were averaged into 60-s epochs and binned from 1 (low) to 6 (high), for infant and parent separately. Thus, an epoch classified as (1, 1) indicates an epoch in which both infant and parent were in a low arousal state. The red line indicates the average direction of travel between that and the subsequent epoch, averaged across all epochs in that bin. Thus, for the position (1, 1) on plot (a), the red line shows a displacement of +0.3 on the *x*-axis and +0.4 on the *y*-axis, indicating that the average epoch starting at (1, 1) showed an increase of +0.3 in infant arousal and +0.7 in adult arousal to the subsequent

epoch. (c) Schematic illustrating the analysis whose results are shown in panel d. Each vector plot was divided into four quadrants: Parent low/Infant low (yellow, *1*), Parent low/Infant high (red, *2*), Parent high/Infant low (brown, *3*), and Parent high/Infant high (green, *4*). In order to investigate how infant arousal and adult arousal interacted to predict the change in adult arousal, we subtracted the average adult change scores in quadrant *4* from quadrant *3*, and quadrant *2* minus quadrant *1*. This was performed separately for the two groups. (d) Bar chart showing the results of the analysis: when the adult's arousal starts high, their arousal decreases more in instances where the infant's arousal is high, than when it is low (low GAD-7 group only). * indicates the significance of the analyses comparing the observed values to a chance level of 0. * $p < 0.05$, † $p = 0.05$.

4.3.4 Hypothesis 3: more anxious parents will show greater event-related physiological hyperarousal

Hypothesis 1 examines parent-infant synchrony, i.e., the continuous association between parent and infant arousal across all data. In addition and motivated by previous findings (Wass, Smith, Clackson, et al., 2019; Wass, Smith, Daubney, et al., 2019), we also examined adult reactivity to 'peak' arousal events from the infant. Figure 4.5a shows a schematic illustrating this analysis. First, the adult's arousal data were *z*-scored, participant-by-participant. Next, instances, where the infant's arousal crossed a centile threshold (e.g., exceeded the 97th centile of samples for that infant in that day) were identified. Then, for each instance, the average change in adult arousal from 600 s before to 600 s after the infant peak arousal moment was excerpted (see Fig. 4.5b). This allows us to examine how the adult's arousal changes on average around the top 3% most elevated arousal moments for that infant on that day. Then, we repeated the analysis using different values for the centile threshold (Fig. 4.5b), to examine instances where the infant's arousal exceeded the 95th centile of samples for that infant on that day, the 90th centile, and so on, down to the 75th centile.

We were interested to examine whether a significant peak in parent arousal was observed relative to the peak arousal moment in the infant, and whether peaks in parent arousal were only observed for the most extreme instances of elevated infant arousal (i.e., the top 3% of samples for that infant in that day), or whether they were also observed for less extreme, yet still relatively high, arousal instances (i.e., the top 25% of the sample for that infant that day). To quantify whether a significant peak in parent arousal was observed relative to the peak arousal moment in the infant, we performed a permutation-based clustering analysis (see SM, section 1.6, Method 1). Instances where a significant peak was observed are drawn as coloured datapoints on Fig. 4.5c (blue/red for high/low GAD-7 groups); instances where no significant peak was observed are drawn as black datapoints. It can be seen that, after correction for multiple comparisons, the low GAD-7 group only show peaks in parent arousal relative to the 3% and 5% most extreme instances of elevated infant arousal. In contrast, the high GAD-7 group show significant peaks in parent arousal relative to the 25%, 15%, 10%, 5%, and 3% most elevated instances. Overall, these results show that both groups showed maternal reactivity

to extremes of infant arousal, but that high GAD-7 parents also showed greater autonomic reactivity to less extreme arousal fluctuations in the infant.

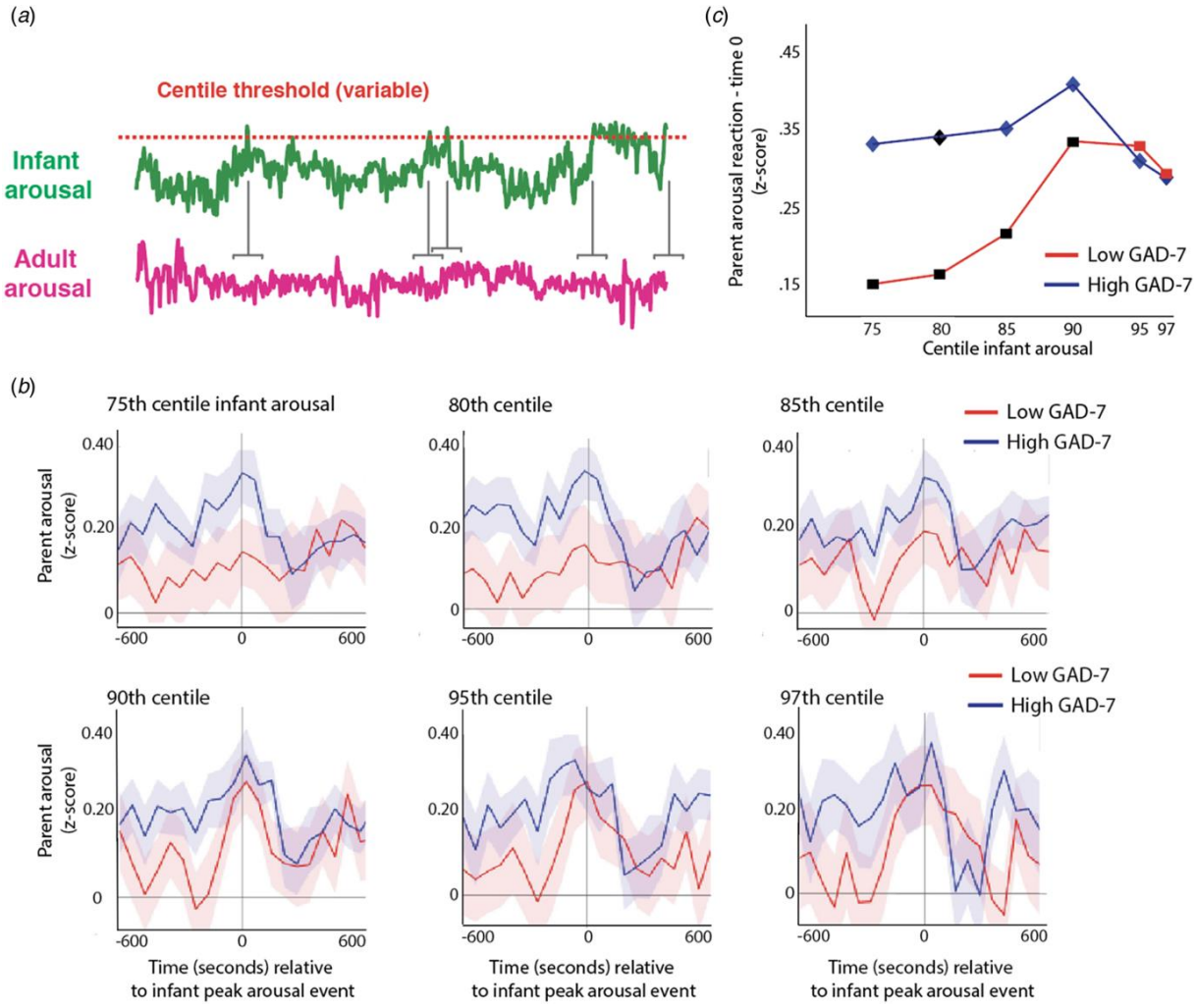

Fig. 4.5 (a) Schematic illustrating the analysis shown in (b)–(c). First, the adult's arousal data were *z*-scored, participant by participant. Next, instances where the infant's arousal crossed a centile threshold (e.g., exceeded the 95th centile of samples for that infant in that day) were identified. Then, for each instance, the change in adult arousal from 600 s before to 600 s after the infant peak arousal moment was excerpted. Individual instances were averaged to index how the adult's arousal level changed relative to the 'peak' arousal moment of the infant. The analysis was repeated using different values for the centile threshold. (b) Change in parent arousal relative to 'peak' arousal moments of the infant, defined using variable centile thresholds. (c) Summary plot showing just the time 0 parent arousal levels from the plots in panel b. Both groups showed maternal reactivity to extremes of infant arousal, but high GAD-7 parents showed greater autonomic reactivity to small-scale fluctuations in infant arousal. Where the permutation-based temporal clustering analyses indicated that a significant peak in adult arousal was observed relative to the infant 'peak' arousal event, the datapoint has been

drawn in colour (blue/red for anxious/non-anxious group, i.e., high/low GAD-7 groups). Where no significant peak in adult arousal was observed, the datapoint has been drawn black. It can be seen that the lower anxiety group only show significant peaks in parent arousal relative to the 3% and 5% most extreme instances of elevated infant arousal; but the higher anxiety group show significant peaks in parent arousal relative to the 25%, 15%, 10%, 5%, and 3% most extreme instances.

4.3.5 Hypothesis 4: parents' event-related hyperarousal associates with infants' hyperarousal across different emotionally valenced events

Hypothesis 3 examines how adults react to naturally occurring 'peak' moments in infant arousal during the day. However, high arousal levels can be positive or negative, and differently valenced infant arousal may make a difference to parent responsivity. To examine this, we also studied hyperarousal relative to vocalisations, which signal whether infants are experiencing positive or negative emotional valence. We examined how parents' event-related hyperarousal associates with infants' hyperarousal across different emotionally valenced events.

First, we identified all infant vocalisations that occurred during the day; for each vocalisation, we examined the rate of change of infant physiological arousal relative to these vocalisations (Fig. 4.6a-c). The significance of group differences was calculated by first conducting *t* tests separately for each individual time bin, and then correcting for multiple comparisons using a permutation-based clustering analysis (see SM, section 1.6, Method 2). As expected, all vocalisations showed a significant peak in infant autonomic arousal at time 0 – i.e., the time of the infant vocalisation (all permutation-based clustering *p*s < 0.001). The infants with more anxious mothers showed significantly higher infant physiological arousal at the time of the negative affect vocalisation, along with significantly higher infant arousal during the period 8–12 min after the vocalisation, indicating slower recovery (Fig. 4.6a, $p = 0.023$). A similar pattern was evident following positive affect vocalisations (Fig. 4.6b, $p < 0.001$), but not following neutral affect vocalisations. These differences were not attributable to differences in the frequency of vocalisations as these did not differ significantly between groups ($z = 0.31/1.50/0.97$, $p = 0.75/0.30/0.33$ for negative/positive/neutral affect vocalisations, respectively).

We also wished to assess how infant recovery following a positive or negative vocalisation related to the differences in parental reactivity to moments of peak infant arousal examined in hypothesis 3, above. To do this, we measured the degree to which maternal autonomic reactivity is specific to 'peak' infant arousal moments, using the following method. For each participant, the maternal arousal response to >97th centile infant arousal moments was calculated (see Fig. 4.5b). This was done by averaging the *z*-scored maternal arousal values from 3 min before and after the peak infant arousal moment (corresponding to the peaks visible on Fig. 4.5b; as seen in Fig. 4.5, analyses were also repeated using other time windows with similar results). For each participant, the maternal arousal

response to >75th centile arousal moments was also calculated (see Fig. 4.5b). The degree to which maternal autonomic reactivity is specific to 'peak' infant arousal moments was calculated by subtracting the >97th centile arousal responses from the >75th centile responses so that a larger value indicates that maternal autonomic reactivity is more specific to 'peak' infant arousal moments.

Infant recovery was assessed by calculating the average infant arousal during the period from 1200 s before and after the positive and negative affect vocalisations (corresponding to the time periods shown in Fig. 4.6), and subtracting the average arousal during the period after the vocalisation from the average arousal during the period before. In order to assess how infant recovery related to parental reactivity, we calculated the bivariate correlation between the two measures. Infant recovery following negative affect related to more selective parental reactivity (i.e., a bigger difference between >97th centile and >75th centile arousal responses): rho = −0.33 p = 0.045. This finding was observed consistently in the lower (rho = −0.31) and higher (rho = −0.50) parental anxiety groups. No relationship was observed between the same variable and infant recovery following positive affect (rho = −0.07). These results show that more selective parental autonomic reactivity is associated with faster infant recovery following naturally occurring peaks of negative affect – a finding which is observed independently in both the low and high GAD-7 groups.

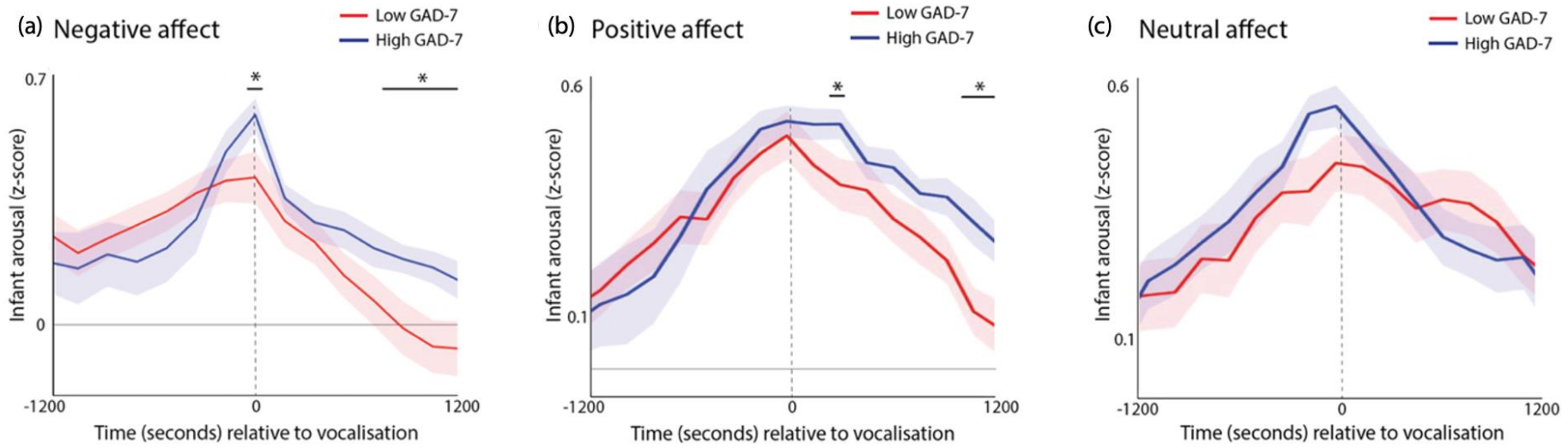

Fig. 4.6 Change in infant autonomic arousal relative to (a) negative affect vocalisations; (b) positive affect vocalisations; (c) neutral affect vocalisations. For each plot, the blue line shows the anxious group (high GAD-7), and the red line the non-anxious group (low GAD-7). The high GAD-7 group show significantly higher infant physiological arousal at the time of the negative and positive (but not neutral) vocalisation at time 0, along with significantly high arousal 8–12 min afterwards. Shaded area shows standard errors. Areas identified as showing above-chance group differences following correction for multiple comparisons using the permutation-based clustering analysis are highlighted with *.

4.4 Discussion

The present study aimed to examine how anxious symptoms in parents relate to arousal coregulation in parent-infant dyads. Primarily, we investigated whether concurrent and sequential synchrony in physiological arousal would be greater in dyads with more anxious parents (Hypothesis 1). We also examined how intra-dyadic influences in arousal vary contingent on the starting arousal level of parent and child, considered separately (Hypothesis 2). In addition, we examined patterns of event-related change (sequential synchrony). We examined whether more anxious parents show greater event-related changes in their own physiological arousal, relative to 'peak' moments of arousal in the child (Hypothesis 3). And we examined whether parents' event-related hyperarousal associates with infants' hyperarousal across different emotionally valenced events (Hypothesis 4). To address these questions, we used miniaturised microphones and cameras, and wearable physiological monitors, to record vocalisations and day-long physiological fluctuations in 12-month-old infants and their parents. Participating parents completed a self-rating scale of current anxiety symptoms (the GAD-7).

Our preliminary analyses indicated that mean heart rate and heart rate variability did not differ between the more or less anxious groups for either parent or infants in home settings. This is informative, because no previous research has, to our knowledge, examined baseline (resting) physiology in an infant proband sample. We did however, find differences in how arousal levels in dyads associated with each other throughout the day. Overall, dyads in the more anxious group showed higher concurrent synchrony in physiological arousal (Hypothesis 1). Conversely, in the less anxious group, mothers' arousal levels were less tightly coupled with infant levels (Fig. 4.3b and SM, section 2.1).

Recent research has reported correlated neural activity between socially interacting animals (Kingsbury et al., 2019; Zhang & Yartsev, 2019) consistent with previous neuroimaging findings in adults (Hari et al., 2013; Hasson et al., 2012). Our results extend this by identifying, for the first time, *higher* physiological synchrony in anxious parent-child dyads. Although our finding is consistent with some previous evidence on behavioural synchrony in anxious dyads (Beebe et al., 2011; Granat et al., 2017), the finding of greater physiological synchrony is novel. This finding contributes to a growing evidence base suggesting that 'sustained intervals of synchrony may be too demanding from a resource allocation perspective' (McFarland et al., 2020, p. 58), and that a mid-range of synchrony whereby partners are neither over- nor under-coordinated is optimal (Beebe et al., 2011; Granat et al., 2017; Jaffe et al., 2001). This is important for understanding mechanisms for direct transfer of physiological stress across parent-child dyads.

Also novel is our finding examining how parents react to small- *v.* large-scale arousal fluctuations in their child (Hypothesis 3). Our results showed that, for the non-anxious group, significant peaks in adult arousal were observed only relative to the top 5% and top 3% most elevated instances of infant

arousal, whereas, anxious parents show peaks in arousal also relative to the top 25%, 15%, and 10% most elevated instances of infant arousal (key to this finding is that anxious parents exhibited a significant *change in arousal* – rather than greater arousal overall). This suggests that, whereas non-anxious parents upregulate their own arousal only relative to 'peak' arousal moments in their infant, more anxious parents show greater reactivity to small-scale fluctuations in their child. Thus, non-anxious mothers were 'there when you need me' – showing reactivity to peak child arousal events, but not otherwise. But anxious mothers were 'always on' – showing reactivity to small-scale child arousal fluctuations as well. In Hypothesis 4, we found that more selective parental reactivity is associated with faster infant recovery following naturally occurring peaks of negative affect – a finding which is observed independently in both the low and high anxiety groups. These findings support evidence for an 'overloaded, highly stimulating' behavioural profile in anxious mothers (Feldman, 2007), that leaves insufficient time for infants to experience neutral affect, or 'time off', thereby losing opportunities to practice self-regulation.

Finally, our results provide new evidence on how anxious parents' arousal levels change depending on their own and their infant's starting arousal level (Hypothesis 2). Our results suggested that, when adults' arousal is low and infants' arousal is high, then adults tend to upregulate their arousal in response – a feature which is present in both the low and high anxiety groups. But, when the overall arousal level of the dyad is high, then adults tend to downregulate their arousal in response – a feature which is only present in the lower anxiety group. This latter feature potentially indicates behaviours akin to 'stress buffering' (Hennessy et al., 2009); this behaviour was absent among more anxious mothers. Our findings suggest that the mechanism by which affective and arousal states are transmitted from one partner to another does not operate consistently across more anxious and less anxious dyads, and may therefore be a fruitful target for further research.

Our research is limited by several factors. Firstly, our sample was sourced from the community. Subgroup analyses (see SM, section 2.1, Fig. S2) suggested that the relationship between arousal cross-correlation and GAD-7 was distributed uniformly across the sample, and highest in participants with most severe anxiety, although the elevated levels of anxiety found in clinical samples were relatively under-represented in our sample. Of note, there is genetic evidence that total GAD-7 scores have the same genetic underpinnings as professionally diagnosed anxiety disorders (Purves et al., 2020). Though trait scores of anxiety may be more pertinent to the general population than clinical diagnosis and have broader relevance in terms of effects, further research with a clinical sample would be needed to investigate the effects of moderately severe and severe levels of anxiety in mothers.

A second limitation of our study is that we investigated biobehavioural relations between mother-infant dyads and not father-infant dyads; research has suggested that gender differences in parents are relevant for childhood anxiety disorders and should be a focus in the future (Majdandžić et al., 2014;

Möller et al., 2015). A third limitation is that, though we requested participants select a typical day for the home recording session, we had no way of confirming the typicality of the day chosen; as such, there was no way to know if state anxiety, as well as trait anxiety, could be exerting an effect on parent or infant arousal. Finally, our research did not differentiate anxiety subtypes, for example general anxiety disorder *v.* panic disorder or social anxiety disorder; evidence suggests children respond differentially to parents on these bases, and therefore these subtypes should be incorporated into future research among mother-infant dyads (de Rosnay et al., 2006; Murray et al., 2007).

Our research provides new information on how the regulatory profiles of anxious mother-infant dyads are inter-dependent on one another. It also contributes to the evidence-base on the intergenerational transmission of anxiety from parent to infant, building on our understanding of how parent–child interactions differ in anxious parents during the first year of life. The research also provides evidence that even in mothers without a professional diagnosis of anxiety, there are apparent effects of maternal anxiety on physiological processes in both mother and infant. This information is helpful for developing our knowledge of the environmental mechanisms underlying the development of anxiety disorders, and provides a basis for future investigations into *how* an individual partner might downregulate another's arousal levels. It may also inform future intervention studies focused on reducing overall levels of anxiety in the dyad, whether or not the parent has a clinical diagnosis; for example, targeting interoceptive capacities in the parent.

4.5 Supplementary material

The supplementary material for this article can be found at:
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4.6 Acknowledgements

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4.7 Conflicts of interest

None.

[10]Supplementary materials are also reproduced for convenience in Appendix A.

CHAPTER 5 – Vocalisation and physiological hyperarousal in parent-infant dyads where the parent has elevated anxiety

The previous chapter showed that levels of physiological synchrony are elevated among parent-infant dyads where the parent has higher levels of anxiety. In addition, parents with higher levels of anxiety did not show physiological evidence of downregulating the overall arousal level of the dyad, whereas parents with lower levels of anxiety did. The current chapter reports the findings of a second empirical study, in which stimulating parental behaviour was investigated in the context of parent and infant physiological activity. The study was intended to highlight the difference in parental vocal behaviour, and corresponding changes in dyadic arousal, among those in the high and low anxiety groups. The supplementary materials (SM) for this chapter are available in Appendix B.

Abstract

Background

Coregulation of physiological arousal within the parent-child dyad precedes later self-regulation within the individual. Despite the importance of unimpaired self-regulatory development for later adjustment outcomes, little is understood about how early coregulatory processes can become dysregulated during early life. Aspects of parental behaviour, such as patterns of anxious speech, may be one factor influencing infant arousal dysregulation.

Methods

We made day-long, naturalistic biobehavioural recordings in home settings in parent-infant dyads using wearable autonomic devices and miniature microphones. We examined the association between arousal, vocalisation intensity and parent anxiety.

Results

Moments of high physiological arousal in infants were more likely to be accompanied by high parental arousal when parents had high self-reported anxiety symptoms. Anxious parents were more likely to vocalise intensely at states of high arousal, and produce intense vocalisations that occurred in clusters. High intensity vocalisations were associated with more sustained increases in autonomic arousal for both anxious parents and their infants.

Conclusion

Parental vocal behaviour differs in anxious parents, co-occurs with dyadic arousal dysregulation and could contribute to physiological arousal transmission. Implications for parental vocalisation as an intervention target are discussed.

5.1 Introduction

Though our experience of stress seems personally situated and internally regulated, these sensations can originate from the socio-emotional states of those around us. Evidence that stress can be transmitted among individuals has been found in rodents who have witnessed the social defeat of a conspecific (Carnevali et al., 2017), in adult humans who have observed video-taped adults in high-pressure conditions (Dimitroff et al., 2017), and in parent-child human pairs following maternal participation in a stress test (Waters et al., 2014). Given parent-infant dynamics are core to early socio-emotional development, it is important to understand how stress might be transmitted from parent to infant (Feldman, 2015). However, a virtually unlimited range of human experiences can be subsumed under the umbrella term 'stress' (Epel et al., 2018). Stress may be quotidian or clinical; it may be biological, affective, or cognitive; its course may be acute or chronic; it may describe circumstance (a 'stressor') or a reaction (a 'stress response'). Scientists examining stress among infants are unable to elicit verbal report, and so are forced to concentrate on the biological correlates of stress – focusing on the autonomic nervous system (ANS), the fast-acting neural substrate of the body's stress response (Cacioppo et al., 2007). Elevated levels of arousal within the ANS are characterised by increased activity in the sympathetic ('fight or flight') nervous system compared to the parasympathetic ('rest or digest') nervous system (although the two also operate non-additively; Berntson et al., 1994; Lacey, 1967). Hyperarousal is also accompanied in adults by increased psychological reports of stress (McCall et al., 2015; Ottaviani et al., 2016). Consequently, we consider physiological indicators of arousal within the autonomic nervous system as proxies for stress states, such that increased states of arousal index increased states of stress (Wass, 2021b).

5.1.1 Physiological synchrony in clinical populations

The sharing of arousal states between parent and infant is thought to aid the socio-emotional stability of the developing infant (Fogel, 1993; Lobo & Lunkenheimer, 2020; Sameroff, 1983). Parent-infant dyads – particularly in the early developmental period - are thus thought to operate to some degree as single regulatory units of arousal (Bridgett et al., 2015; Kopp, 1982; Tronick, 1982; Wass, Smith, Clackson, et al., 2019). As such, researchers have queried how shared arousal states within dyads are impacted by parental mental health conditions (Davis, West, et al., 2018). If infants are sharing their parents' disrupted arousal states, we might expect to see different patterns of arousal within at-risk and low-risk dyads. One potential risk factor for the dyadic relationship is parental mood disorder. Parental anxiety, in particular, is likely to lead to greater change or increase in arousal states within the dyadic relationship, given that arousal dysregulation is a core feature of many adult anxiety disorders (Craske et al., 2017; Ottaviani et al., 2016; Thayer et al., 1996), and that children of anxious parents show signs of event-related physiological hyperarousal from a very young age (Nikolić et al., 2016, Nikolić, Aktar, et al., 2018). If infants share their anxious parents' dysregulated arousal dynamics, these may become strongly encoded, subsequently precipitating or perpetuating

maladaptive emotion regulation strategies later in life.

A small number of recent studies have looked at physiological synchrony and anxiety-related risk within parent-child dyads (Roman-Juan et al., 2020). Physiological synchrony refers to coordination between two or more partners' autonomic processes during social contact (Butler, 2011; Feldman, 2015). One study investigated parent-child dyads where the child either had posttraumatic stress disorder (PTSD) or resilient characteristics (Motsan et al., 2021). The study found that the dyads with a parent and a child with PTSD exhibited the highest synchrony in respiratory sinus arrhythmia (RSA), whereas resilient dyads displayed the lowest. These findings are also consistent with behavioural evidence suggesting that dyadic pairs in which one partner has anxiety display higher synchrony in gaze and touch, while healthy dyadic pairs or dyadic pairs with a depressed partner show moderate or low levels of synchrony respectively (Beebe et al., 2011; Granat et al., 2017). This small evidence base suggests that, through physiological synchrony, anxious parents' atypical arousal regulation patterns may influence their children's own arousal dynamics.

While these studies explore physiological synchrony among parent-child dyads with PTSD or anxiety-risk (Motsan et al., 2021; Roman-Juan et al., 2020), they are limited to later-stage development. In addition, they do not explore parental anxiety specifically. This is despite robust evidence showing that anxiety conditions pass from generation to generation (Aktar et al., 2019), and that prodromal anxiety states are observed early in childhood (Möller et al., 2016).

Recent research from our group has examined the relationship between parental anxiety and parent-infant physiological reactivity. In a separate analyses of the same sample, we found that synchrony between parents and their 11-month old infants' arousal (measured as a composite of heart rate, heart rate variability, and actigraphy) was higher among dyads where the parents were more anxious (Smith, Jones, Charman, et al., 2021). We also found that less anxious parents showed behaviours akin to 'stress buffering', downregulating their arousal when the overall arousal level of the dyad was high. These behaviours were absent in more anxious parents (Smith, Jones, Charman, et al., 2021; Wass, Smith, Clackson, et al., 2019). These findings suggest that atypical patterns of physiological synchrony and coregulation between children and parents with elevated psychological distress emerge early in development.

5.1.2 Arousal contagion

Closely related to the concept of physiological synchrony is arousal contagion, defined by the transfer of affective states from one partner to another (highlighting 'leader-follower' dynamics; Butler, 2011; Engert et al., 2019). Developmental studies of arousal contagion have typically been conducted in controlled laboratory conditions following an experimental stress induction task, during and after which indices of physiological arousal are measured in both 'target' (leader) and 'observer' (follower) members of a dyad. Findings include: increased skin temperature covariation in parents and

preschool-aged children following a stress induction task for the child (Ebisch et al., 2012; Manini et al., 2013); increased preejection period and heart rate covariation in parents and infants following a negative evaluation condition for the parent (Waters et al., 2014); and increased interbeat interval reactivity covariation in parent-infant dyads following a maternal stress task (Waters et al., 2017). While several studies have examined arousal contagion in adult populations (usually from a neuroendocrinal perspective; see: Buchanan et al., 2012; Engert et al., 2014, 2018), the subject of arousal contagion is of particular interest to developmental scientists seeking to understand early pathways to both typical and atypical emotion regulation (Feldman, 2012; Waters et al., 2020).

5.1.3 Mechanisms of arousal contagion

In recent years, research attention has focused on elucidating the mechanisms through which arousal contagion operates. Arousal contagion, like other neurobiological state-matching phenomena such as neural entrainment, can occur when one partner's autonomic activity causes a subsequent social behaviour, such as a facial expression or vocalisation, which is then perceived by the second partner, leading to a change in that partner's physiology (Feldman et al., 2011; Wass et al., 2020). In parent-infant studies of arousal contagion, several behaviours have been explored. For example, infants sitting on their parents' laps were found to show increasingly stronger covariation of changes in heart rate following a stress test with their parents than infants in a no-touch condition, suggesting touch may play a crucial role in arousal contagion (Waters et al., 2017). This is consistent with findings from adult literature on arousal contagion between attachment partners, in which the touch condition was isolated from the potentially confounding variables of proximity or motion (Chatel-Goldman et al., 2014). In addition, an experiment in which parents were asked to use maladaptive social cognitive behaviours (e.g., 'suppression'; hiding or masking emotion) following a stressor showed that suppression increased the covariation in sympathetic nervous system activity between parents and their infants (Waters et al., 2020). However, little is known about how social behaviours influence physiological reactivity in parent-infant dyads where the parent has symptoms of an affective disorder.

One behavioural modality that has received less attention in the literature is vocalisation. The role of voice is important in the early dyadic relationship as it can be used more widely than other modalities; vocalisation requires neither close proximity nor eye contact, as is the case in touch and gaze modalities. It also has a role in situations where greater vigilance might be required (for example, raising one's voice to stop a child from stepping into a road with oncoming traffic).

In atypical parent-infant interaction episodes, anxious parents express higher levels of vocal behaviour compared to controls, including child-directed speech (Murray et al., 2008). Anxious parents also display higher intensity vocal profiles than depressed parents or controls (Feldman, 2007), in accordance with acoustic evidence showing that fear-related emotional states are commonly

associated with high vocal intensity (i.e. vocal amplitude, or 'loudness'; Juslin & Laukka, 2001, 2003). While we know that a more intense vocal style is typical of anxious parents, we do not know how this social behaviour relates to arousal contagion between parents and children.

Evidence on the rhythm of adult vocalisations also suggests that adaptive interpersonal communication is marked by a paced, periodic structure (Abney et al., 2018; Jaffe et al., 2001). By contrast, less periodic vocalisations are thought to associate with anxiety states (e.g., speech dysfluency; Laukka et al., 2008) or increased information transfer (e.g., 'burstiness,' temporally clustered behaviours followed by lulls of inactivity; Abney et al., 2018), such as that seen in the overstimulating behaviours of anxious parents (Feldman, 2007; Granat et al., 2017). Empirical studies on the temporal structure and periodicity of vocal behaviour in anxious parents in the context of childrearing, are, however, scant, despite aperiodic vocalisations being an atypical behaviour that could influence arousal levels within the dyad.

Taken together, results from arousal contagion studies with parent-infant dyads suggest that ostensive cues, such as touch and gaze, can facilitate the transmission of physiological arousal from one partner to another during social interaction (Waters et al., 2017). Very little, however, is known about the role of speech in arousal contagion, despite the importance of the auditory modality in communication between parent and infant (Ghazanfar & Zhang, 2016; Wass, Phillips, Smith, et al., 2021; Zhang & Ghazanfar, 2020). This is particularly true when the infant is out of reach and not directly controllable, a potentially stress-inducing context that becomes increasingly common as the infant develops. In addition, there is little available evidence on arousal contagion within at-risk dyads, even though this is likely to be critical for understanding patterns of dysregulated emotion in very early childhood. The present study therefore examines how parental vocalisations and mood disorder-related distress relate to parent-infant arousal contagion.

5.1.4 The present study

Evidence suggests that vocal behaviour is altered in anxious adults and thus could play a role in parent-infant arousal contagion within the context of elevated parent anxiety. Understanding these parent-infant dynamics is a necessary step towards understanding aspects of dyadic coregulation, the foundational stage preceding the infant's development of their own self-regulation skills.

To address this, we used miniaturised autonomic- and audio-recording devices, worn by parents and infants at home throughout the day, to examine how parental vocalisations relate to arousal contagion among anxious parents and their infants. Specifically, we tested four primary hypotheses. Firstly, on the basis that anxiety-related distress is associated with high parent-child physiological synchrony (Motsan et al., 2021), we predicted that infants of anxious parents would show elevated physiological arousal in response to high points in parental physiological arousal. Secondly, on the basis that anxious parental behaviour is associated with a highly stimulating, intense vocal profile (Granat et al.,

2017; Juslin & Laukka, 2003; Murray et al., 2008), we predicted that greater parental arousal would associate with higher intensity parental vocalisations in anxious parents. Thirdly, given links between aperiodic vocal behaviour and overloaded communicational styles of anxious parents (Abney et al., 2018; Feldman, 2007), we predicted that anxious parents would be more likely to repetitively vocalise in clusters. Finally, since vocal sequences are tightly linked to respiratory patterns modulated by the autonomic nervous system (Zhang & Ghazanfar, 2016), we predicted that high intensity parental vocalisations in anxious parents would associate with subsequently sustained increases in both parent and child physiological arousal; a pattern consistent with a role in arousal contagion.

5.2 Methods

5.2.1 Participant details

Approval for this project was given by the Research Ethics Committee at the University of East London. Participants were recruited from London, Essex, Hertfordshire and Cambridge in the UK. Overall, 91 parent-infant dyads were recruited to the study, of which usable paired autonomic data were available from 74 dyads, and full parental anxiety data were available from 68. Further details, including exclusion criteria, outlier-detection strategy, and extra demographic details on the sample are given in Table 5.1 and SM sections 1-2. Of note, we could not include families in which the primary day-time care was performed by a man or non-binary person, as the numbers were insufficient to deliver an adequately gender-matched sample. Subsequently all participating parents identified as women. We did not explicitly ask participants to identify their genetic relationship to the infant, and all participants identified themselves as mothers. As a token of appreciation for participating, dyads received £30 gift vouchers split over two visits.

5.2.2 Parental screening

Parents were screened for anxiety using the Generalized Anxiety Disorder 7-item (GAD-7) screening tool, which assesses generalised anxiety symptoms over the preceding fortnight (Spitzer et al., 2006)**.** While acknowledging the multiplicity of individual anxiety disorders, the GAD-7 tool was selected as a global 'catch-all' measure of anxiety for the present community sample, in line with transdiagnostic perspectives (Norton & Paulus, 2017). Studies of both clinical and non-clinical populations have validated this questionnaire, with scores above 6 representing mild to moderate anxiety (Löwe et al., 2008). Parents were asked to rate the frequencies of particular thoughts and behaviours on a 4-point scale ranging from 0 (not at all) to 3 (nearly every day). Cronbach's alpha for the internal consistency of the scale was .89. The GAD-7 scores ranged between 0 and 17 ($M = 3.4$, $SD = 3.9$). Where possible we have analysed GAD-7 scores as a continuous variable. Where necessary for presenting time series analyses, we have dichotomised our group using a median split to differentiate high and low anxiety groups, and performed follow-up analyses based on a quartile split to explore the associations' consistency (see SM, section 6). For the median split, the low anxiety group's GAD-7

scores ranged between 0 and 2 (M = 0.76, SD = 0.85); the high anxiety group's scores ranged between 3 and 17 (M = 6.16, SD = 3.96), indicating mild to moderate anxiety.

5.2.3 Procedure

Participants were invited to choose a day during which they would be spending the whole day with their child but which was, in every other respect, as far as possible, typical for them and their infant. A researcher made a home visit to the participant in the morning (c. 7.30-10 am) to fit the equipment before returning later (c. 4-7 pm) to collect it. The mean (SD) recording time per day was 7.3 (1.4) hours.

The equipment comprised two wearable layers for both parent and infant (see Figure 5.1). For the infant, a custom designed baby-vest was worn next to the skin, within which was embedded an electrocardiogram (ECG) recording device (recording at 250Hz), accelerometer (30Hz), global positioning system (GPS; 1Hz), and microphone (11.6kHz). A T-shirt worn over the top of the vest contained a pocket to hold the microphone and a miniaturised, commercially available video camera (Narrative Clip 2). The parent wore the same equipment: a custom-built chest strap containing the main recording device as the base layer, and a cardigan containing the microphone and video camera as a secondary layer. The garments were unobtrusive and comfortable to wear and, other than a request to keep the equipment dry, participants were encouraged to behave as they would on a typical day. To optimise recording quality, the ECG device was attached using standard AgCl electrodes placed in a modified lead II position.

5.2.4 Quantification and data analysis plan

5.2.4.1 Autonomic data parsing and calculation of the autonomic composite measure

A full description of how the autonomic data were parsed is given in the SM sections 3.1-3.2. The accuracy of the ECG recording devices was ensured through a cross-validation procedure by which heart rate (HR) and heart rate variability (HRV) were recorded using both the devices developed for home use and established, lab-based recording devices (a Biopac MP150 amp recording at 2000Hz). High reliability was observed both for HR (rho = .57, $p < .001$) and HRV (rho = .70, $p = .01$). In the SM we also described the high tonic and phasic correlations we observed between HR, HRV and actigraphy, which were our primary motivation for collapsing the three measures into a single composite measure of autonomic arousal (see SM, section 3.3). Prior to all analyses, the autocorrelation was also removed from the arousal data. The procedure for this is given in SM (section 3.4).

5.2.4.2 Vocal coding

The microphone recorded a 5-second snapshot of the auditory environment every 60 seconds. Post hoc, coders identified samples in which the parent was vocalising and coded them for vocal intensity

on a scale from 1 (least intense) to 9 (more intense). Coders were blind to the parents' anxiety status. In order to ensure an even distribution, for all analyses presented low intensity vocalisations were defined as all vocalisations coded ≤4; mid-level intensity vocalisations were coded as 5; high intensity vocalisations ≥6. In total, 42% of vocalisations were coded as low intensity; 20% as medium intensity; 38% as high intensity. In order to assess inter-rater reliability, 24% of the sample was double-coded; Cohen's kappa was .60, which is considered acceptable (McHugh, 2012). All coders were blind to intended analyses.

5.2.4.3 Home/Awake coding

Due to preliminary analyses indicating that infants tended to be strapped into a buggy or car seat for much of the time they were outdoors, which strongly influenced their autonomic data, our analyses only examine segments of the data in which the dyad was at home and the infant was awake. Further details on how home/awake segments were identified are given in the SM (section 4). Following these exclusions, the mean (SD) total amount of data available per dyad was 3.7 (1.7) hours, corresponding to 221.5 (102.4) 60-second epochs per dyad.

5.2.4.4 Permutation-based temporal clustering analyses

To estimate the significance of time-series relationships, a permutation-based temporal clustering approach was used for the analyses presented below. Two different analytical approaches were used. One analysis looked at whether 'peak' physiological reactions were observed relative to a known 'Time=0' moment (such as relative to a particular event). This method was used to test Hypotheses 1-3. The other analysis examined temporally contiguous patterns of physiological change in instances where the centre-point of the expected response window was unknown or unimportant (Maris & Oostenveld, 2007). This method was used to test Hypothesis 4. These permutation-based temporal clustering analyses, adapted from neuroimaging (Maris & Oostenveld, 2007; Maris, 2012), allow us to estimate the probability of temporally contiguous relationships being observed in our results, a fact that standard approaches to correcting for multiple comparisons fail to account for (Maris & Oostenveld, 2007; Oakes et al., 2013). Of note, this analytical technique is best adapted for use with categorical data. See further details in SM (section 5).

5.3 Results

5.3.1 Raw data and descriptives

Before tests of our three main hypotheses, raw data and descriptive analyses are presented. Figure 5.1 shows the recording equipment worn by participants as well as a raw data sample of the home visit. Demographic data for the sample is shown in Table 5.1, subdivided by low/high GAD-7 score. Independent samples *t*-tests were conducted for the demographic variables (excepting ethnicity) to assess group differences. None were identified (all *ps* > .15). In addition, previous subgroup analyses

on the present sample found that arousal levels, measured from the raw autonomic data including in the arousal composite, did not differ significantly between the groups (Smith, Jones, Charman, et al., 2021). In addition, we examined whether the frequency of parent vocalisations, or the mean intensity of the vocalisations, differed contingent on parent anxiety. No significant correlations were observed between GAD-7 scores and either parent vocalisation frequency (rho = -.12, p = .38) or intensity (rho = .19, p = .16).

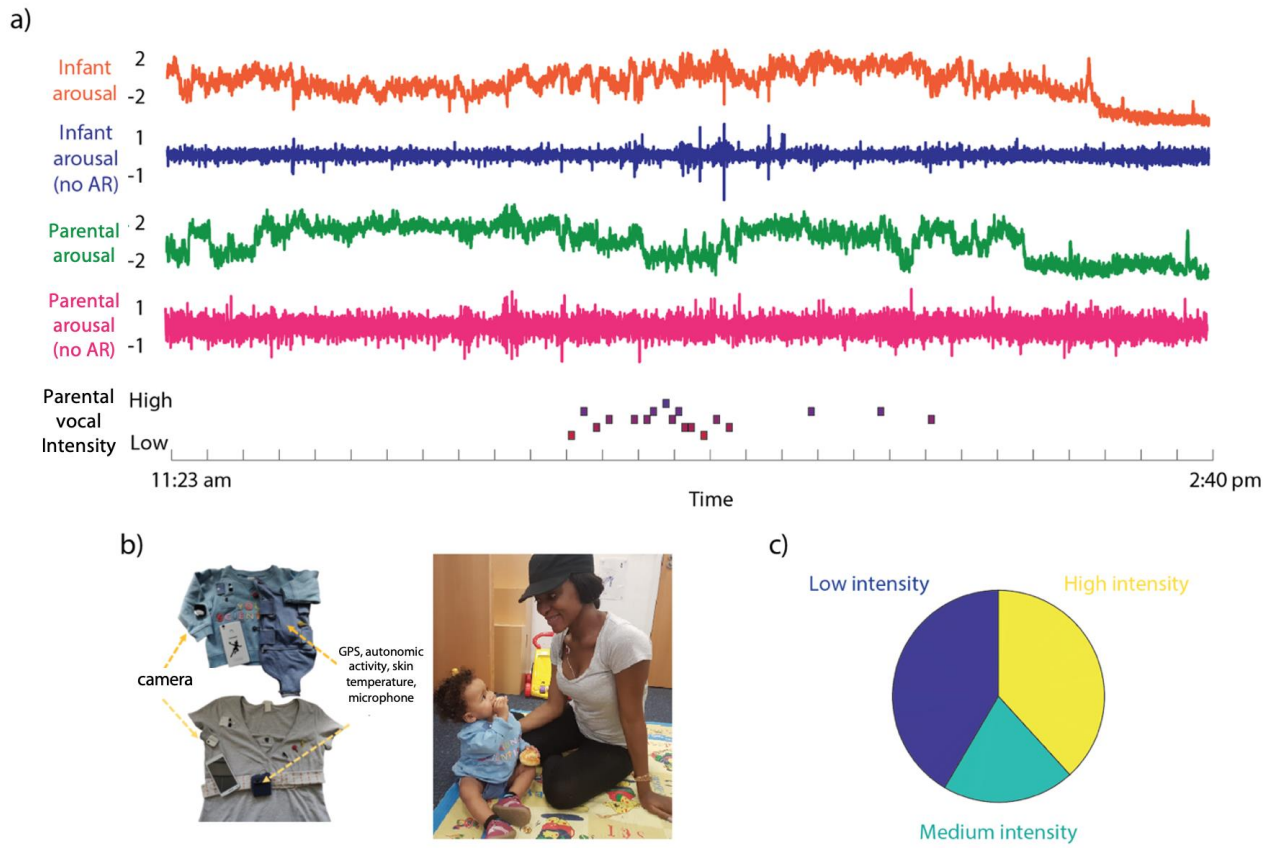

Fig. 5.1 (a) Illustration of raw data from the parent and child wearing the equipment. From top to bottom: infant arousal composite (see SM sections 3.1-3.3 for details of how this was calculated); infant arousal (no AR) – after removal of autocorrelation from the arousal data (see SM section 3.4); parental arousal composite; parental arousal (no AR); parental vocal intensity; (b) illustration of the equipment used for home monitoring; (c) pie chart showing the distribution of parental vocal intensity codes after splitting into low/medium/high intensity values.

	Low anxiety	High anxiety
Infant age (days) – mean (s.d.)	349 (39)	370 (41)
Gender (*N* (%) male)	14 (42)	13 (39)
Infant ethnicity *N* (%)		
White British	17 (51)	16 (47)
Other white	1 (4)	1 (4)
Afro-Caribbean	4 (11)	3 (9)
Asian, Indian and Pakistani	2 (7)	5 (16)
Mixed – White/Afro-Caribbean	1 (4)	1 (4)
Mixed – White/Asian	0 (0)	4 (11)
Other mixed	3 (9)	4 (11)
Household income (%)		
Under £16k	9 (27)	10 (31)
£16–£25k	8 (24)	10 (31)
£26–£35k	7 (20)	3 (9)
£36–£50k	4 (11)	4 (11)
£51–£80k	4 (11)	2 (7)
>£80k	1 (4)	3 (9)
Maternal education (%)		
Postgraduate	12 (36)	9 (27)
Undergraduate	19 (56)	16 (47)
FE qualification	0	1 (4)
A-level	0	2 (7)
GCSE	3 (9)	1 (4)
No formal qualifications	0	2 (7)
Other	0	2 (7)

Table 5.1 Demographic data split by low/high parent GAD-7 score.

5.3.2 Hypothesis 1: elevated physiological arousal in anxious parents associates with increased infant arousal

To investigate the moment-by-moment sequelae of parental arousal for infant reactivity, we examined infant reactivity to 'peak' arousal events from the parent. A schematic illustrating this approach is shown in Figure 5.2a. Initially, we identified instances where the parent's *z*-scored arousal crossed a centile threshold (e.g., exceeded 97% of samples for the parent for that day). For each instance, we then excerpted the average change in infant arousal from 600 seconds before to 600 seconds after the parental peak arousal moment. Doing so allowed us to examine how the infant arousal changed, on average, around the top 3% most elevated arousal moments for the parent's arousal in that day. The time interval was selected to fully contextualise profiles of change around the focal point (see Thorson et al., 2018). Finally, to examine instances where the parent's arousal exceeded incrementally lower centile thresholds of samples for that day, we repeated the analysis using different values for the centile threshold (e.g., 95th centile, 90th centile, and so on, down to the 75th centile; Fig 5.2b).

Primarily, we investigated two questions: (i) whether a significant peak in infant arousal was observed relative to the peak arousal moment in the parent, and (ii) whether peaks in infant arousal were selective (i.e., only observed for the most extreme instances of elevated parental arousal, e.g., the top 3% of samples for the parent that day) or whether they were also observable at less extreme yet relatively high arousal instances (e.g., the top 25% of samples for the parent that day). Fig 5.2b shows the changes in peak relative to the 0-horizontal line (which indexes infant average arousal); the further away from this line, the more change in infant arousal. It can be seen that, in the low anxiety group, there are no systematic changes in infant arousal around the peaks in parental arousal. But, in the high anxiety group, there appear to be systematic increases in infant arousal around the peaks in parental arousal. Fig 5.2c is a summary figure showing just the Time 0 scores from Fig 5.2b. To quantify whether the observed changes in infant arousal relative to the peak moment of parental arousal differed significantly from chance we performed a permutation-based clustering analysis (see SM section 5, Method 1). Instances where a significant peak in infant arousal was observed are drawn yellow on Fig 5.2c. The low GAD-7 group showed no significant peaks in infant arousal relative to instances of elevated parental arousal. By contrast, the high GAD-7 group showed a significant (p = .019) peak in infant arousal relative to the top 3% most elevated instances. In sum, these results show that, in parents with elevated anxiety, peaks in their own autonomic arousal tend to co-occur with peaks in infant autonomic arousal; but this relationship is only present when the most elevated instances of parental arousal are considered. This relationship is not present in parents with lower anxiety.

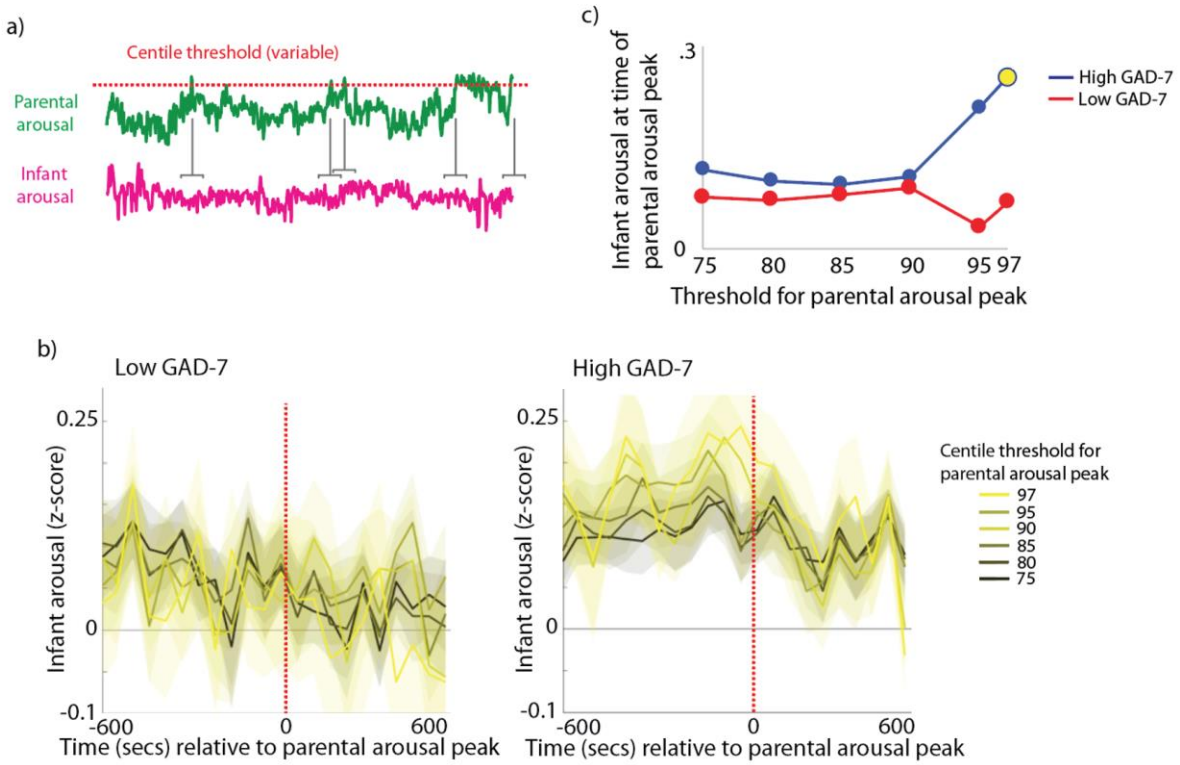

Fig. 5.2 (a) Schematic illustrating the analysis shown in panels b-c. (b) Change in infant arousal relative to 'peak' arousal moments of the parent, defined using variable centile thresholds. (c) Summary plot indicating group differences in change of infant reactivity to parental arousal peaks, showing infant arousal relative to the time 0 threshold values from panel b. Where the permutation-based temporal clustering analyses indicated that a significant peak in infant arousal was observed relative to the parental 'peak' arousal event, the datapoint has been drawn in yellow.

5.3.3 Hypothesis 2: high arousal associates with high intensity vocalisations in anxious parents

Next, we examined how parental vocalisations differed contingent on the presence of elevated parental arousal, split by group. As with the above analyses, we began by *z*-scoring parental arousal data on a participant-by-participant basis. Next, we identified instances where the parent's arousal crossed the 97th centile (i.e., exceeded 97% of samples for the parent for that day). We then, for each group, calculated the proportion of low/high intensity vocalisations out of all vocalisations occurring immediately around each arousal peak (defined as the period from one minute before to one minute after). To examine whether the proportion of high/low intensity vocalisations around arousal peaks differed significantly from the overall baseline rate of vocalisations, we also performed a control analysis in which we randomly selected an equal number of timepoints in our data that were not associated with arousal peaks, and used identical analyses to examine the proportion of high/low intensity vocalisations around these control datapoints. Observed and control data were compared using Mann Whitney U tests. As with Hypothesis 1, the same analysis was then repeated using different thresholds for identifying parental arousal peaks (see SM, section 5).

The results, shown in Figure 5.3a, indicated that, in parents with increased anxiety, a significant increase in the likelihood of high intensity parental vocalisations was observed around elevated peaks in parental arousal (≥90th centile threshold). That is, in parents with increased anxiety, high intensity parental vocalisations were more clustered around arousal peaks than would be expected by chance. The same effect was not observed in the low anxiety group. The same effect was also not observed when the same analysis was repeated to examine low intensity vocalisations (Figure S4).

In order to verify whether this pattern was attributable to an increased prevalence of high intensity parental vocalisations (as a proportion of all vocalisations) in the elevated anxiety group overall, we also examined the overall proportion of high intensity parental vocalisations observed, independent of arousal (Fig 5.3b). No significant difference between the groups was observed. This suggests that our findings are specific to an increase in the proportion of high intensity parental vocalisations around parental arousal peaks.

Taken together, these results suggest that, in parents with elevated anxiety, peaks in parental arousal are associated with an increased likelihood of high intensity parental vocalisations. The same effect is not observed in the low anxiety group. These differences are not attributable to an overall increase in the proportion of high intensity vocalisations in parents with elevated anxiety. Hence, high intensity vocalisations are more common around arousal peaks only in parents from the high anxiety group.

5.3.4 Hypothesis 3: high intensity vocalisations are more likely to occur in clusters in anxious parents

In addition to examining how the rate of parental vocalisations varied contingent on fluctuations in arousal we also wished to examine whether parental vocalisations varied contingent on whether a vocalisation had occurred previously. In other words, we examined the degree to which vocalisations occurred in clusters.

To examine this, we examined how parental vocalisations were clustered in time using the following procedure. First, we examined the likelihood of a high intensity vocalisation in the time window 10 minutes prior to a high intensity vocalisation. To examine whether the observed rate differed from the overall baseline rate of high intensity vocalisations, we performed a control analysis by randomly inserting an equal number of control 'nonvocalisation' timepoints into our data, and using an identical procedure to examine the rate of high intensity vocalisations around these control datapoints. We then used a Mann Whitney U test to examine the effect size of the observed *v.* control comparison for the high and low GAD-7 groups separately. These two effect sizes are drawn as the first two datapoints onto the line plot in Figure 5.3d. Then, we repeated the analysis based on the next time window (i.e., examining the likelihood of a high intensity vocalisation in the time window 9 minutes prior to a high intensity vocalisation, and so on). In this way, we examined how the vocalisation rate varied across the time window from 10 minutes before to 10 minutes after each vocalisation. Figure 5.3d shows the results for high intensity vocalisations; Figure 5.3e shows the same plot for low intensity vocalisations.

For the elevated anxiety group, a significant increase in the likelihood of a high intensity vocalisation is observed for all time windows up to 10 minutes before and after each high intensity vocalisation. For the lower anxiety group, a significant increase is also observed, but only up to 5 minutes before and after each vocalisation. For low intensity vocalisations, an increase in vocalisation likelihood is observed for all time windows up to 5 minutes before and after each low intensity vocalisation, for both the higher and the lower anxiety groups. Overall, these results suggest that high intensity vocalisations are likely to occur in longer lasting clusters for parents with elevated anxiety. The same effect is not observed for low intensity vocalisations.

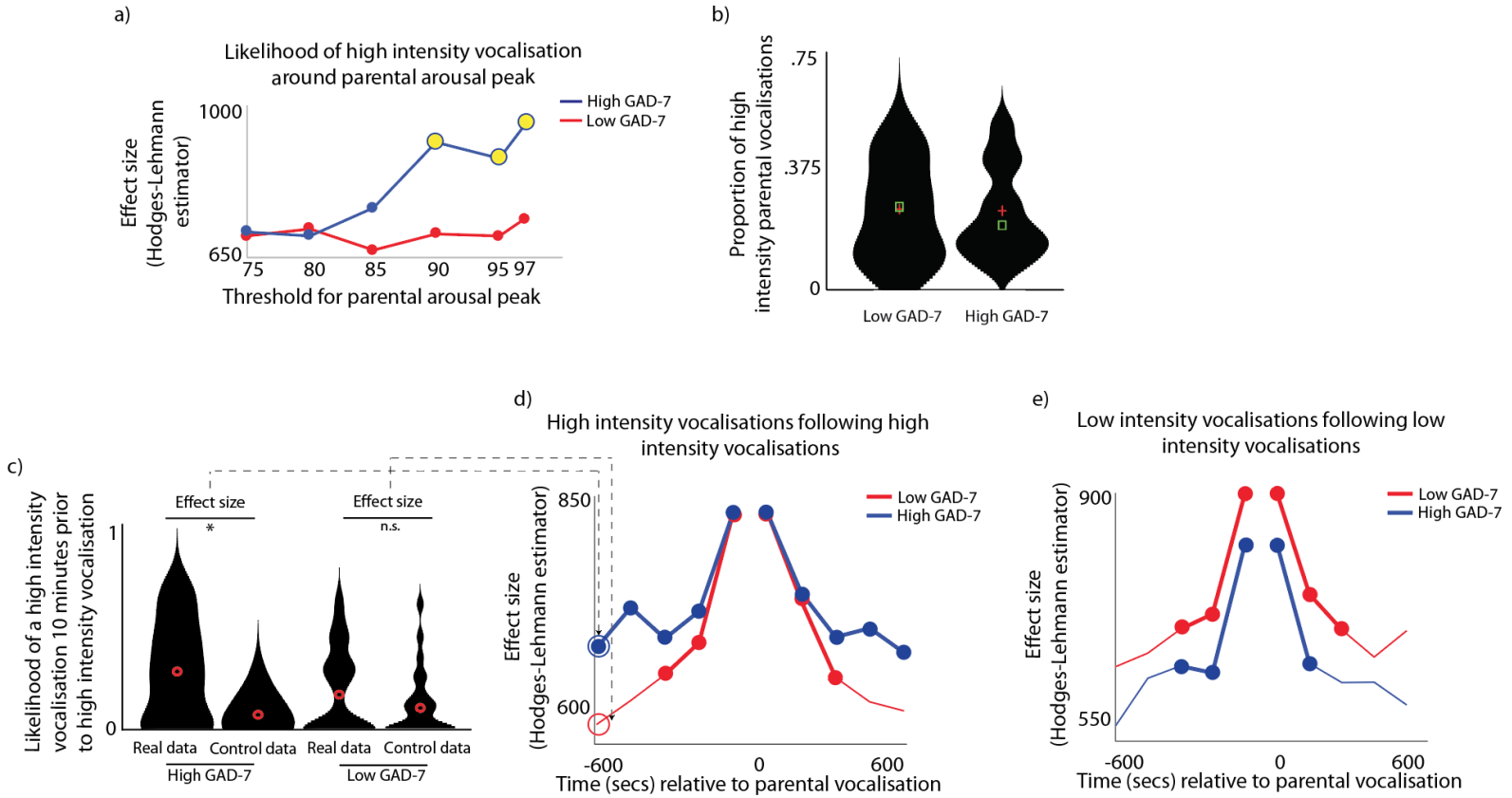

Fig. 5.3 (a) Likelihood of high intensity parental vocalisations around parental arousal peaks. *Y*-axis shows the effect size of the difference between the observed and the control data for the low GAD-7 (red) and the high GAD-7 (blue) groups, calculated as described in the Methods. Yellow circles indicate results showing a significant difference between the observed and the control data. (b) Violin plot showing the proportion of high intensity parental vocalisations. No significant difference was observed between groups. (c) Violin plot showing one sample time-window of the analysis iterated across multiple time windows in 5.3d and 5.3e. The plot shows the likelihood of a high intensity vocalisation in the time window 10 minutes prior to a high intensity vocalisation. The effect size of the real *v.* control comparison has been drawn separately for the high and low GAD-7 groups in Figure 5.3d. (d) Line plot

showing the same comparison as shown in 5.3c, but iterated across multiple time windows (i.e., examining the likelihood of the high intensity vocalisation in the time window 9 minutes prior to a high intensity vocalisation, and so on). Where a circle has been drawn, this indicates a timepoint where a significant difference was observed between the real and control data, following the statistical steps described in the Methods. (e) The same plot examining low intensity vocalisations. For both groups, significant increases are only observed for the time window up to 5 minutes before and after each vocalisation.

5.3.5 Hypothesis 4: high intensity parental vocalisations predict increased parent-child arousal if parent has anxiety

Finally, we wished to examine the rate of change of parent and infant physiological arousal relative to high intensity parental vocalisations. First, we examined the low anxiety group (Figure 5.4a). To start, we identified all instances of high intensity parental vocalisations that occurred during the day. Then, for each vocalisation, we examined how the parent's arousal level changed across the time interval from 600 seconds before that moment to 600 seconds afterwards. As a control comparison, for each vocalisation we randomly selected a moment during the day when the parent was at an equivalent arousal level as immediately prior to the vocalisation, but did not vocalise. To compare the observed and the control data we conducted Mann-Whitney U tests separately for each individual time bin. We then repeated the same analysis with the higher anxiety group (Figure 5.4b). In addition, we also performed an identical analysis to examine the change in infant arousal relative to high intensity parental vocalisations in the lower (Figure 5.4c) and higher (Figure 5.4d) anxiety groups.

In the higher anxiety group, both parents and infants showed significant sustained increases in physiological arousal in the 600 second window following the high intensity parental vocalisation (all *ps* < .02). This response was absent in the low anxiety group (*ps* >.12). Overall, our results suggest that, in anxious parents with elevated arousal, high intensity vocalisations are associated with sustained increases in physiological arousal in both the parent (Fig 5.4b), and the infant (Fig 5.4d). The same pattern was not observed in the low anxiety group (Figs 5.4a, c). This finding was probed for consistency by repeating the analyses of the observed data according to a quartile, rather than median, split. Results indicated that the higher the parental anxiety, the higher both parent and infant arousal relative to high intensity parental vocalisation (see SM 6, Figure S4).

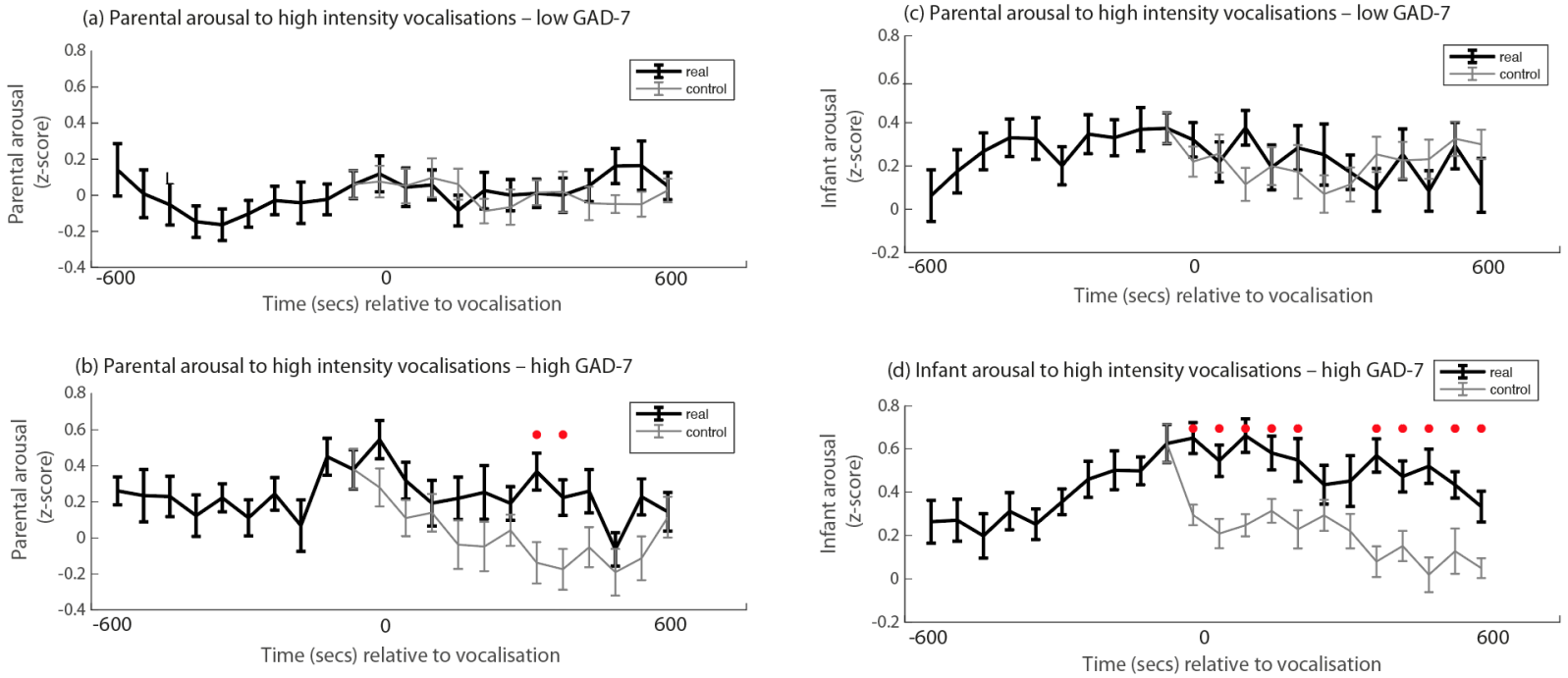

Fig. 5.4 (a) Parental arousal relative to high intensity parental vocalisation in the low GAD-7 group; (b) parental arousal relative to high intensity parental vocalisation in the high GAD-7 group; (c) infant arousal relative to high intensity parental vocalisation in the low GAD-7 group; (d) infant arousal relative to high intensity parental vocalisation in the high GAD-7 group. High GAD-7 parents and their infants show more sustained arousal increases around intense parental vocalisations. Lines coloured black indicate index data (time series following a high intensity parental vocalisation) while grey coloured lines indicate control data (time series following a moment where the parent was at an equivalent arousal level but did not vocalise intensely). Dots marked red indicate areas of significant ($p < .05$) event-related change.

5.4 Discussion

In the present study, we examined the relationship between parental anxiety, parental vocalisations, and physiological arousal in parents and their infants. Our results showed that peaks in parental arousal were associated with increases in infant autonomic activity in the high but not the low anxiety group (Hypothesis 1, Figure 5.2). We also found that high arousal was more likely to associate with high intensity vocalisations in anxious parents (Hypothesis 2, Figure 5.3a), and that anxious parents tended to produce high intensity vocalisations in clusters (Hypothesis 3, Figure 5.3c-d). Finally, we found that high intensity parental vocalisations were succeeded by sustained increases in physiological arousal in both parents and infants in the high (not the low) anxiety group (Hypothesis 4, Figure 5.4). Taken together, these findings indicate a role for parental vocal behaviour in sustaining arousal transmission in the context of parental anxiety, through altered parent-infant interaction dynamics.

5.4.1 Infants of anxious parents show hypersensitivity to parental arousal

In a previous analysis of the same sample we found that anxious parents show heightened autonomic reactivity to naturally occurring peak infant arousal, along with greater co-fluctuation of physiological arousal overall (Smith, Jones, Charman, et al., 2021). In the present article, we extend this by showing that moments of elevated physiological arousal in anxious parents were more likely to be accompanied by elevated infant arousal in the high, but not the low, anxiety group. This is consistent with evidence suggesting that infants of parents with anxiety conditions are more reactive to external stimuli generally (Möller et al., 2016); however, our finding that both infants and parents are hyper-reactive to changes in the other partner *within* the parent-infant dyad is novel, to our knowledge. These findings provide new insight into the mechanisms through which atypical patterns of infant arousal can be both dynamic and reciprocal; they develop through interactions with others, rather than purely in response to isolated stimuli (Fogel, 1993; Granat et al., 2017; Ham & Tronick, 2009; Murray et al., 2009; Wass, 2021a).

5.4.2 High arousal associates with high intensity vocalisations in anxious parents

When we examined how parental vocalisations differed contingent on the presence of elevated parental arousal, we found that parents with elevated anxiety were more likely to produce high intensity vocalisations around peaks in their own arousal. These associations were not found in less anxious parents, and differences were not attributable to an overall increase in the proportion of high intensity vocalisations in parents with elevated anxiety. Our results build on previous studies showing that psychiatric conditions in adults and children are generally associated with vocal loading – i.e., higher than typical vocal intensity (Garcia-Real & Díaz-Román, 2016; Hamdan et al., 2009; Hunter et al., 2020). This may be due to intense vocal behaviour mimicking the function of the infant cry. Lay opinion and survey data has suggested that crying is a cathartic behaviour that relieves stress and

reduces arousal; however, laboratory data has shown that it exacerbates distress and increases autonomic arousal (Rottenberg et al., 2008). If intense parental vocal behaviour is understood as resembling the functionality of infant crying, this could notionally lead to further cycles of arousal in the parent.

5.4.3 High intensity vocalisations are more likely to occur in clusters in anxious parents

Our results also suggest that parents with elevated anxiety are likely to produce high intensity vocalisations in longer-lasting clusters. In psychiatry more broadly, clustered high intensity speech is associated with cognitive symptoms such as racing thoughts, characterised by an elevated number of thoughts that are experienced rapidly and without a sense of control (Keizer et al., 2014; Piguet et al., 2010). While chiefly associated with mania and depressive symptoms, racing thoughts have also been implicated in state anxiety (Weiner et al., 2019). In cognitive behavioural theory, cognitive disturbances are thought to perpetuate elevated arousal states, and vice versa (Maguth Nezu & Nezu, 2015; Salkovskis et al., 1996). For researchers seeking to devise interventions that break cycles of distress within individuals from perinatal populations, it may be useful to empirically investigate whether rapid thought patterns lead to clustered high intensity speech, and how this in turn leads to a chain of physiological and behavioural responses.

An alternative explanation for the finding of clustered, high intensity vocalisations in anxious parents could relate to cognitive load theory and related cognitive deficits observed within anxiety. Cognitive load theory assumes that working memory resources used for processing information are limited; when information inputs are high and working memory resources are diminished, this results in heavy cognitive load (Debue & van de Leemput, 2014; Sweller, 1988). Heavy cognitive load has been associated with reduced self-regulatory control (Hofmann et al., 2008). In addition, meta-analyses have shown that anxiety restricts the capacity of working memory, raising propensity for heavy cognitive load, potentially due to task-interfering cognitive processes such as uncontrollable worry and active threat monitoring (Gústavsson et al., 2021; Moran, 2016). In the acoustic literature, heavy cognitive load has been found to affect speech prosody, increasing vocal intensity and ‘jitter’; an index of vocal aperiodicity (Huttunen et al., 2011; Mendoza & Carballo, 1998; Murphy, 2000). While direct studies on high intensity and clustered infant-directed speech have not been conducted, we speculate that young children of parents tending towards this vocal behaviour might find such communication cognitively taxing, leading to increased arousal lability and distress within interaction.

5.4.4 High intensity vocalisations in anxious parents and autonomic hyperarousal in the dyad

Our results also showed that, in the high anxiety group, both parents and infants showed physiological hyperarousal following high intensity parental vocalisations. This may be due to a combination of factors: first, because maternal vocal intensity directly influences infant autonomic reactivity (as has been shown in other populations; Kolacz et al., 2019); second, because intense vocalisations are more

likely to overlap and occur in clusters, as we showed in Hypothesis 3; third because the semantic content of vocalisations from anxious parents may differ (as has already been shown in other studies; Nikolić, Brummelman, et al., 2018).

Overall, then, do our results suggest that intense vocalisations among anxious parents are a *consequence* of heightened arousal, or a *cause* of it? Chains of causation are hard to untangle in naturalistic studies, as the events are overlapping. However, one possibility consistent with our findings is that events take place in dynamic, self-sustaining interactive cascades (Wass, 2021a). For example, an increase in child arousal might be more likely to trigger an increase in adult arousal in a parent with elevated anxiety; which in turn triggers an intense vocalisation, which in turn triggers a further increase in child arousal. Or, an external cause might trigger an increase in adult arousal, which triggers an intense vocalisation, which triggers an increase in child arousal, which triggers a further increase in adult arousal; and so on. This bidirectional transfer of arousal states might be understood as a form of 'mutual arousal contagion,' a process by which arousal states in partner A cause behaviours that amplify arousal states in partner B, which in turn cause behaviours that further amplify arousal states in partner A, and so on. These interactive dysregulatory cascades are under-researched in developmental psychopathology (Cole et al., 2019; Wass, 2021a). In attention deficit hyperactivity disorder (ADHD), for example, there is evidence that parental expressed emotions (e.g., hostility, criticism, low warmth) can operate both as causes, and as consequences, of oppositional child behaviour (Christiansen et al., 2010; Harold et al., 2013), but these studies have been conducted at the trait-level (i.e., 'do parents of children with ADHD tend to show more expressed emotions on average?') rather than at the state-level (i.e., 'how do parenting strategies, child/parent arousal, and child oppositional behaviour dynamically influence each other during the day?').

5.4.5 Limitations

There are several limitations to the present study. Firstly, time series analyses only allow for an inference of statistical, granger-causality (whereby changes in time series A forward-predict changes in time series B); as such we are not able to impute a causal chain of events between parental reactivity, parental vocal behaviour, and parent-infant reactivity. Future studies incorporating single model approaches, e.g., dynamic-causal modelling, would allow for greater investigation of causative pathways between partner variables. Secondly, parents in our sample were not assessed diagnostically for anxiety disorders, but were grouped according to GAD-7 scores; the heterogeneity of different anxiety disorders and high severity levels typically found in clinical samples are therefore under-represented in the present study. Of note, total GAD-7 scores have been shown to have the same genetic underpinnings as clinically diagnosed anxiety disorders (Purves et al., 2019), and the milder symptomatology of anxiety represented by the current sample may have broad relevance to the general public in terms of effects. Further research with a clinical population representing multiple different anxiety disorders and a range of severity levels would, however, be needed to investigate

more specific effects. Finally, our sample consisted of mothers and thus may not necessarily be representative of parent-child relations more generally (though the demographic spread was balanced in other respects, e.g., the sample was well-matched with the ethnicity distribution in multi-cultural cities such as London). We also did not record whether the mothers were genetically related to their infants, limiting a consideration of the potential for genetics to impact the strength of associations. Future studies seeking to investigate arousal contagion in the context of perinatal mental health and infant development should incorporate more diverse families; this would help shed light on any potential group differences, and ensure stronger external validity for the full community of parents accessing perinatal services.

5.4.6 Clinical implications and conclusions

These results showing the role of parental vocal behaviour in parent-infant arousal contagion may be clinically useful for understanding and breaking chains of arousal transmission in families where the parent is experiencing anxiety. Currently, although there is evidence that parent-targeted interventions can improve infant outcomes, these interventions are generally heterogeneous and not informed by an in-depth understanding of how parent-infant interactions are atypical in parents with elevated anxiety (see chapter 7). For example, a parent-mediated, cognitive-behaviour based intervention might focus on raising awareness that intense vocalisations are more likely to be triggered at times when the parent's arousal is high. It might also raise awareness that intense vocalisations are more likely to occur in clusters, and that intense parental vocalisations trigger increases both in child and in parent arousal. Consequently, it might focus on diverting arousal-triggering vocalisations. Finally, interventions might also raise awareness that both infants and parents are hyper-responsive to one another in dyads where the parent has elevated anxiety, and discuss mechanisms to cope with this (Smith, Jones, Charman, et al., 2021).

However, future intervention development requires us to consider the extent to which atypical patterns of parent-infant coordination fit within a deficit model. Disrupted parent-infant coregulation, for instance, may be related to infant development of maladaptive coping as a functional adaptation (Wadsworth, 2015). For example, responding to facial or vocal cues of impending parental anger or frustration may increase early onset of self-regulatory processes in these infants, as the need for these are potentially higher than offspring of parents without mental distress. These complexities of parental behaviour may lead to unintuitive parent-infant patterns of relating; tight coregulation or covariation of regulatory indices may index elevated likelihood of parental distress. Those investigating interventions for such dyads may therefore need to take into account the potential threat to the infant's functional adaptation.

CHAPTER 6 – Infant effortful control mediates relations between nondirective parenting and internalising-related child behaviours in an autism-enriched infant cohort

The following chapter is a publication of an original article investigating associations between parenting behaviour, infant temperament, and subsequent child internalising behaviours in an autism-enriched cohort (Smith, Jones, Wass, et al., 2021). The analyses are based on a prospective longitudinal study of infant siblings of autistic children, and controls.[11] Autism commonly co-occurs with anxiety conditions among children (Lai et al., 2019; White et al., 2009). There are also high rates of psychological disorders among parents of autistic children, including 33% with anxiety disorders (20-48% CI; Schnabel et al. 2020). The relations between parent and infant characteristics in this sample are therefore pertinent to understanding parent anxiety and the early emergence of emotion dysregulation. Additionally, by examining infant siblings of autistic children, the following study allows for a consideration of infants of comparable age to the other studies of this thesis. This would not have been possible by directly examining autistic children, who tend to receive diagnoses later in childhood. Subheadings, figures, table numbers, and citations style have been adapted to conform to the general thesis format. The supplementary materials (SM) for this chapter are available in Appendix C.

Abstract

Internalising problems are common within autism spectrum disorder (ASD); early intervention to support those with emerging signs may be warranted. One promising signal lies in how individual differences in temperament are shaped by parenting. Our longitudinal study of infants with and without an older sibling with ASD investigated how parenting associates with infant behavioural inhibition (8-14 months) and later effortful control (24 months) in relation to 3-year internalising symptoms. Mediation analyses suggest nondirective parenting (8 months) was related to fewer internalising problems through an increase in effortful control. Parenting did not moderate the stable predictive relation of behavioural inhibition on later internalising. We discuss the potential for parenting to strengthen protective factors against internalising in infants from an autism-enriched cohort.

[11]A note on terminology: the terms 'autism' and 'autism spectrum disorder' (ASD) are both preferred terms among members of the autistic community, with the latter term being preferred to a lesser extent (Kenny et al., 2016). The terms 'ASD' and 'children with ASD' (denoting 'person-first' language) are associated with medicalised accounts considered to be stigmatising (Botha et al., 2021; Woods, 2017). However, others find such diagnostic labels to accurately represent the profound challenges they or their children face (Humphrey & Lewis, 2008; Kenny et al., 2016). This chapter is a reproduction of an article that was accepted for publication before I had learned about different community preferences for terminology. It also represents a study designed within a medical framework, with reference to diagnoses, symptoms and official nosologies. For these reasons, the text of Chapter 6 (and its SM) refers to 'ASD' and 'children with ASD,' while the rest of the thesis refers to 'autism' and 'autistic children.'

6.1. Introduction

ASD is a neurodevelopmental condition associated with two core symptom domains: social interaction and communication difficulties, and restricted and repetitive behaviours in tandem with sensory processing atypicalities (DSM-5; American Psychiatric Association, 2013). These core symptoms are often accompanied by additional mental health conditions (Salazar et al., 2015; Simonoff et al., 2008); in particular, internalising-related disorders such as anxiety (van Steensel et al., 2011).

Internalising disorders – in particular, anxiety - affect approximately 40% of individuals with ASD, and are often clinically identified in mid-childhood (Davis et al., 2011). 'Internalising' is a broad dimension of psychopathological variation comprising anxiety and mood disturbances, and is commonly used to indicate prodromal symptoms of affective disorders (Kostyrka-Allchorne et al., 2020; Krueger & Markon, 2006; Rueter et al., 1999). The co-occurrence of internalising symptoms and ASD is thought to interact to amplify core difficulties; for example, difficulties in social interaction can increase for those with ASD and anxiety difficulties, as contexts involving social evaluation trigger both anxious and autistic symptoms (Chang et al., 2012). As such, investigation into internalising-related distress within ASD has been identified as a research priority of the autism community (Lord et al., 2020).

Controversy remains about the co-occurrence of internalising disorders and ASD, with varying interpretations available: (a) internalising constitutes a part of ASD; (b) ASD symptoms cause internalising disorders, or (c) internalising disorders and ASD are phenotypically distinct but overlap with regard to early risk factors (Kerns & Kendall, 2012; Wood & Gadow, 2010). Research into the overlapping risk factors for internalising disorders and ASD has increased in recent years (Yarger & Redcay, 2020). To investigate internalising within ASD in early development necessarily involves prospective study of infant cohorts, before the emergence of ASD. The advantages of investigating internalising within ASD from an early developmental perspective are twofold. Early prediction of risk for internalising within ASD could eventually enable intervention that may attenuate emerging affective disorders, reducing the potential for positive feedback between overlapping symptoms and thus having cascading benefits for individuals with ASD. Further, identifying early markers of internalising disorders in infants, before ASD emerges, could help us understand the aetiology of the two conditions' concurrence.

6.1.2 Infant temperamental predictors of subsequent internalising disorders

Temperament, emerging early in life and defined broadly as 'the extent to which individuals respond to their environment, and their ability to modulate and control these responses' is thought to be an early marker for later psychopathology (Kostyrka-Allchorne et al., 2019, p. 401). Several prospective studies of infants with a family history of ASD have investigated temperament, showing early

differences in domains such as surgency (indexing active, approach behaviours and positive affect) and effortful control (indexing self-regulatory processes) in infants with a family history of ASD (Clifford et al., 2013) and in those who later develop ASD (Pijl et al., 2019). The extent to which these differences relate to later core symptoms of ASD or whether they could instead relate to co-occurring internalising problems remains largely unclear. However, two recent studies of infant siblings of children with ASD - investigating the same sample as the present study - have examined temperament associations to later ASD symptoms versus the internalising-related symptoms of anxiety. Behavioural inhibition and effortful control were shown to correlate with anxiety and ASD symptoms (Ersoy et al., 2020), while other differences, such as activity levels and inhibitory control, were not (Shephard et al., 2018). This work suggests these two former temperament domains may be particularly important for explaining the development of internalising disorders such as anxiety: (1) behavioural inhibition, and (2) effortful control.

6.1.2.1 Behavioural Inhibition

In normative populations, behaviourally inhibited temperament has been shown to predict later childhood internalising problems; in particular, anxiety (Muris et al., 2011; Murray et al., 2009). Early behavioural inhibition is defined as 'a tendency of some children to withdraw and/or exhibit negative affect in response to novel stimuli (people, places, events, and objects)' (Gartstein et al., 2010, p. 652) and is broadly characterised as a form of avoidance and distress towards novelty (Fox et al., 2020). These behaviours emerge early, and individual differences are stable from 4 months (Rothbart, 1988; Schmidt et al., 2020). Although not true of all children with a history of behavioural inhibition, those displaying the temperament in infancy are at elevated likelihood of developing anxiety in adulthood (Frenkel et al., 2015). In addition, studies of children with community-referred ASD symptoms show that infants who have inhibited temperaments (as well as other temperament domains, such as negative emotionality) are more likely to have co-occurring internalising symptoms compared to infants with stronger self-regulatory capacities (Chetcuti, Uljarević, Varcin, Boutrus, Wan, Green, et al., 2020; Chetcuti, Uljarević, Varcin, Boutrus, Wan, Slonims, et al., 2020).

6.1.2.2 Effortful Control

Self-regulatory temperamental traits in infancy, such as effortful control, are also thought to relate to later internalising problems, such as anxiety. Effortful control reflects an individual's ability to activate or inhibit responses and voluntarily control attention (Rothbart et al., 2003) and has a long developmental time course that becomes clear over the second year of life (Putnam et al., 2001). In normative populations, reduced levels of effortful control during middle childhood have been associated with greater likelihood of developing anxiety in later life (Muris et al., 2008). In research examining children with neurodevelopmental conditions, studies have shown that children with ASD tend to have reduced levels of effortful control, as compared with typically developing children and

children with developmental delay or Fragile X syndrome, who have relatively higher levels (Bailey et al., 2000; Burrows et al., 2016; Macari et al., 2017). Effortful control has also been associated with internalising problems in children with ASD (de Pauw et al., 2011). Notably, low effortful control has also been identified among infants at elevated likelihood of developing ASD, compared to controls (Clifford et al., 2013; Pijl et al., 2019).

Greater behavioural inhibition and reduced effortful control may therefore represent underlying risk factors for developing internalising-related conditions such as anxiety among infants at elevated likelihood of ASD. While the above studies indicate concurrent associations between temperament, anxiety and ASD, prospective longitudinal cohort studies are needed to establish whether temperament traits precede psychopathology symptoms.

6.1.3 Parenting-temperament associations and the development of internalising disorders

Growing demand for early intervention strategies has motivated a research focus on early environmental factors that may combine with temperamental predispositions to modify trajectories towards affective problems. In particular, parenting has received substantial attention because it is a tractable target for early holistic intervention (Yap et al., 2016). Two parenting variables are especially relevant to interventions focused on attenuating the development of internalising-related symptoms in childhood. Firstly, nondirective parenting, which refers to low levels of intrusive parenting (an overinvolved behavioural style that places demands on the child while limiting autonomy, associated with the development of anxiety; Möller et al., 2016). And, secondly, sensitive parenting, defined as parental responsivity to age-appropriate growth needs in the infant (Feldman et al., 2004), and generally associated with positive socio-emotional child outcomes (Bigelow et al., 2010; Leerkes et al., 2009).

To design effective early interventions, we need to know how parenting interacts with temperament to shape later outcomes. Two statistical approaches facilitate this process: moderation and mediation. Moderation analyses indicate the conditions under which the direction or strength of an effect varies (Holmbeck, 1997); if a predictor variable is related to an outcome variable, but only under certain conditions (‘M’), then M is a moderator variable (Kraemer, 2016). By contrast, mediation analyses can be used to test hypotheses about the mechanism through which a given effect occurs; an independent variable influences the mediator variable which in turn influences the outcome (MacKinnon et al., 2007). This technique allows for the examination of potential causal chains, such as the influence of parenting on child temperament and subsequent developmental outcomes. Identifying moderators and mediators can help investigators better target their early intervention designs; understanding moderating variables may tell us what intervention is most effective for which individuals with what specific difficulty, under which set of circumstances, whilst identifying a

mediating path can help investigators more closely target underpinning mechanisms or identify appropriate proxy outcome measures (Breitborde et al., 2010).

6.1.3.1 Moderation relationships

In the general population, parenting behaviours are thought to moderate the relationship between individual differences in infant temperament and the likelihood of developing internalising disorders in later childhood (Ryan & Ollendick, 2018). Nondirective and sensitive parenting behaviours become established early on in the first year of life and remain stable over time (Wan et al., 2013). Several studies have indicated that these dimensions of parenting could have a moderating effect on the relation between infant behavioural inhibition and later affective disorders. For example, Rubin and colleagues (2002) show that low levels of nondirective parental behaviour increase the likelihood for infants with greater behavioural inhibition to develop symptoms consistent with anxiety. Other studies have shown a similar pattern in mid-to-late childhood, such that the predictive relation between earlier inhibition and later anxiety states is increased by low nondirective parenting (Lewis-Morrarty et al., 2012; Prinzie et al., 2014).

Very little is known about how parental behaviour might moderate the relationship between temperament and internalising/anxiety states in young children at risk of developing neurodevelopmental conditions; however, several studies have identified early differences in nondirective and sensitive parenting in infants with later ASD. Among infants who have an older sibling with ASD, parents of infants who later receive ASD diagnoses show lower nondirectiveness and lower sensitive parenting between 9 and 15 months (Campbell et al., 2015; Srinivasan & Bhat, 2020; Wan et al., 2012). A number of intervention studies have shown that parenting behaviour can also be shifted in elevated-likelihood samples to produce a moderate amelioration in core symptom trajectories (see, e.g., Green et al., 2015, 2017; Ventola et al., 2017) though not in all instances (e.g., Whitehouse et al., 2019); indicating that this is a promising domain to explore in relation to later internalising-related distress within ASD.

6.1.3.2 Mediation relationships

While moderation models can examine how different parenting styles might influence the predictive relation between infant temperament and later psychopathology, mediation models can be used to examine the mechanisms and potential causal chains through which parent behaviour shapes and conditions child behaviour and subsequent outcomes (Kasari & Sigman, 1997; Totsika et al., 2011). Mediation models can be useful to unpick the reciprocal transactions between environmental factors and infant characteristics that occur over development (Beauchaine & Hinshaw, 2010; Kiff et al., 2011). One particularly important domain to consider is effortful control, since it has a much longer developmental time course than other domains of temperament (Putnam et al., 2001; Rothbart, 1988), has a hierarchical relationship to other domains of function (Nigg, 2017), and is predicted over time

by parenting in early childhood (Karreman et al., 2008; Kochanska et al., 2000; Lengua et al., 2007, 2019). Indeed, mediation analyses have shown that, in typically developing populations, greater nondirective parenting associates with higher child resilience through the mediating effect of increased infant effortful control (Taylor et al., 2013). This evidence, combined with the findings from infant sibling cohorts regarding temperamental risk factors for anxiety and ASD, suggest that it may be fruitful to examine whether changes in effortful control mediates any relation between parenting and internalising outcomes in children with a family history of ASD.

6.1.4 The present study

We used a prospective longitudinal design to examine how early parenting behaviour moderates the relation between early-emerging behavioural inhibition and later internalising-related problems; and whether relations between early parental behaviour and later child internalising difficulties are mediated by changes in the later-emerging temperament domain of effortful control. Such study designs allow observations of broad phenotypic characteristics expressed in very young relatives of children who have already received a specific developmental disorder diagnosis (Jones et al., 2014; Szatmari et al., 2016). We included infants with an elevated likelihood of developing ASD (who had an older sibling with ASD) and a typical likelihood control group who were infants with an older sibling with typical development. Our primary models included infant behavioural inhibition and parenting behaviour at 8 and 14 months; toddler effortful control at 24 months, and child internalising behaviour at 36 months. We measured parent-report scores of infant temperament and behaviour, as well as observed parent-infant interaction.

In line with the existing literature, we expected that infant behavioural inhibition would associate with later internalising symptoms. We also hypothesised that: (1) early nondirective parenting would moderate the effects of early infant behavioural inhibition on later child internalising problems; (2) early sensitive parenting behaviour would moderate the effects of early infant behavioural inhibition on later child internalising problems, and (3) the relationship between early nondirective parenting and later reductions in child internalising problems would be mediated by changes in toddler effortful control. Two sets of exploratory analyses were conducted to probe for the influence of: (i) child age and (ii) interactions between child inhibition and effortful control (SM).

6.2 Methods

6.2.1 Participants

As part of the British Autism Study of Infant Siblings (BASIS; www.basisnetwork.org), 133 infants took part in research assessments at 8, 14, 24 and 36 months (hypotheses 1-2 examined 133 participants while hypothesis 3 examined a subset of 123 participants due to missing data; see data analysis plan for more detail). At enrolment, each elevated likelihood (EL) infant (N = 89) had an older sibling with a community clinical ASD diagnosis, confirmed using the Development and Well-

Being Assessment (DAWBA; Goodman et al., 2000) and the Social Communication Questionnaire (SCQ; Rutter et al., 2003) by expert clinicians in the team (TC). For further information on the diagnostic status of participants' older siblings, see SM (section 1).

A control group of 44 infants (which we refer to as TL, due to their typical likelihood of ASD) were full-term infants recruited from a volunteer database at the Birkbeck Centre for Brain and Cognitive Development. At enrolment, all control infants had at least one older sibling with typical development and no first-degree relatives with a diagnosis of ASD; the SCQ was used to confirm absence of ASD in older siblings, with no child scoring above instrument cut-off (≥15). Ethical approval was obtained from the NHS National Research Ethics Service (NHS RES London REC 08/H0718/76; 14/LO/0170). Parental written consent was obtained at all visits. A subset of the participants described above also participated in a separate randomised control trial that examined a parenting intervention; to ensure the robustness of our results and in the interests of transparency, we address this potentially confounding factor in the data analysis plan and Results below.

Exclusion criteria for both groups, based on parent report, included significant prematurity (gestational age ≤ 32 weeks), medical conditions such as epilepsy, heart conditions, vision and hearing impairments, cerebral palsy, and genetic conditions such as Down's syndrome or Fragile X. None of the infants had any known medical or developmental condition at the time of enrolment.

6.2.2 Measures

6.2.2.1 Infant temperament

Temperament was captured using the Infant Behavior Questionnaire-Revised (IBQ-R; Gartstein & Rothbart, 2003) at 8 and 14 months, and the Early Childhood Behavior Questionnaire (ECBQ; Putnam, Gartstein, & Rothbart, 2006) at 24 months. These parent-report questionnaires ask to rate the frequency of specific offspring behaviours during the previous two weeks.

Behavioural Inhibition was measured using the IBQ-R Fear subscale at 8 months for our primary analyses (infant distress or an inhibited approach to novel objects, social stimuli or novelty; 13/16 questions on aversive responses to unfamiliar people or places, while 3 probe startle responses to sudden changes). We selected this subscale as a proxy for behavioural inhibition due to the similarity of the questions to Kagan's original definition ('withdrawal and timidity to the unexpected;' Schmidt et al., 2020, p. 7) and given its explicit definition in the IBQ-R as reflecting behaviour denoting 'inhibition of approach towards novel and/or intense stimuli' (Gartstein & Rothbart, 2003). Other multi-method approach studies have used IBQ-R Fear (Crockenberg & Leerkes, 2006; Gensthaler et al., 2013) and ECBQ Shyness subscales as a proxy of parent-reported behavioural inhibition to complement observed behavioural inhibition (e.g. Geng et al., 2011) and the fear subscale has been linked to later anxiety in other longitudinal studies (Shephard et al., 2018; Tonnsen et al., 2013). For supplementary models, we additionally used the IBQ-R Fear at 14 months and the ECBQ Shyness

subscale at 24 months (discomfort, slow or inhibited approach to novelty and uncertainty in social situations).

For our primary models, effortful control was measured by the ECBQ (Putnam et al., 2006) at 24 months. Effortful control is characterised by the ability of shifting attention, duration of attentional focusing, and low-intensity pleasure. For supplementary analyses we used the related construct of infant regulatory capacity as assessed by the IBQ-R at 14 months (Gartstein & Rothbart, 2003).

6.2.2.2 Parental sensitivity and nondirectiveness

The Manchester Assessment of Caregiver-Infant Interaction (MACI; Wan et al., 2016) was used to rate these parenting behaviours based on 6-minute parent-infant unstructured play interactions, videotaped at the 8- and 14-month laboratory assessment. The parent was instructed to engage in play as they would do at home, using the set of toys provided if they wished (approximately 96% of parents were mothers; mean age 35.7 years [SD = 4.99]). Clips were later independently rated for the first 6 minutes from the point the researchers left the room by a trained coder, blinded to participant information, on 7 (7-point) scales. We focused on the two parent scales: nondirectiveness (a low score [i.e., high directive parenting behaviour] represents demanding, intrusive and negative behaviours, and comments directed at the infant not in the service of promoting infant-initiated behaviour) and sensitivity (a high score represents appropriate, contingent, attentive, supportive and immediate responsivity to infant behaviour and developmental need). Excellent psychometric properties and inter-rater reliability were reported in previous studies (Wan et al., 2013, 2016), where ratings were independent of infant gender, infant nonverbal development, parental age and socioeconomic status. Independently blind-rated clips of a proportion of the current sample (26%) showed reasonable to high agreement: single measures intraclass correlations using a two-way mixed effects model (absolute agreement definition) ranged from r = .68-.83.

6.2.2.3 Internalising symptoms

At the 36 month visit, the Vineland Adaptive Behaviour Scales, second edition (VABS-II; Sparrow et al., 2005) were completed by parents in an interview, including a subscale that measures internalising symptoms, including anxious and withdrawal-type behaviours. Internalising symptoms measured at approximately 3 years have frequently been shown to relate to later childhood internalising difficulties and affective disorders, and as such internalising score at 36 months was chosen for the outcome variable (Tandon et al., 2009; Whalen et al., 2017). The VABS-II internalising scale comprises 11 items, of which 6 probe anxiety-prone behaviour (e.g., 'Is overly anxious or nervous' and 'Refuses to go to school or nursery because of fear, feelings of rejection or isolation'). Cronbach's alpha for the internalising subscale was .82 for the current sample. Raw scores in the internalising domain were used in this analyses, as meaningful variation in psychopathological symptoms in non-clinical

samples is thought to be obscured by the usual translation of raw scores into standardised scores (Hessl et al., 2009).

6.2.2.4 Developmental assessment

At each visit, the Mullen Scales of Early Learning (MSEL; Mullen, 1995) were administered to infants to establish a developmental measure based on task performance. Four scales (visual reception, fine motor, receptive and expressive language) were combined to give an early learning composite score (TL = 116.66 [15.02]; EL = 105.43 [22.19], 36 months).

6.2.2.5 ASD diagnosis

Information available from all visits was triangulated by an independent rating team, combined with expert clinical judgement (TC, GP), to determine an ICD-11 (World Health Organization, 2018) ASD classification. Classification was informed by but not dependent on results from the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1989), a play-based assessment conducted by a trained assessor designed to elicit reciprocal social interaction, language and communication and repetitive stereotyped behaviours.

6.2.3 Timepoint selection

The selection of timepoints for measures of infant temperament and parenting was made on the basis of temporal precedence, which is thought to be theoretically relevant to longitudinal designs (George & Jones, 2000). Given the early emergence of the temperament trait and the stability of the parenting variable, for hypotheses 1-2 behavioural inhibition at 8 months, parenting measures at 14 months, and internalising symptoms at 36 months were selected.

For our third hypotheses, we selected nondirective parenting at 8 months, effortful control at 24 months, and internalising symptoms at 36 months. Effortful control at 24 months was selected given the consensus that this behaviour develops predominantly through the toddler years and upward (Putnam et al., 2001), and as the top-down processes implicated in effortful control are not developed until the second year of life (Hendry et al., 2016; Kochanska et al., 2000).

To explore whether our prespecified hypotheses missed additional information, additional model variants (including different timepoints or switching from mediation to moderation) were examined (sections 3-4, SM). Post-hoc exploratory analyses examining the influence of parental behaviour on infant effortful control where infant behavioural inhibition is also taken into account (section 7, SM).

6.2.4 Data analysis

For our primary models, Pearson's correlation coefficients were calculated to assess the relationships between predictors (temperament traits measured at 8 and 24 months; parent-child interaction domains measured at 8 and 14 months) and internalising measured at 36 months. The reported

significance level was set to $p < .05$, unless otherwise specified (e.g., due to the high number of comparisons, the significance level for bivariate correlations was set to $p < .01$). All predictor and outcome variable correlation coefficients were calculated using SPSS 25. Group differences of temperament and parenting variables were also analysed for our primary models; sample characteristics, including means and standard deviations for measures and risk group comparisons (effect sizes), were calculated.

6.2.4.1 Hypotheses 1-2: nondirective and sensitive parenting as moderators of internalising symptoms

For our first and second hypotheses (Figure 6.1), child internalising scores at 36 months were regressed onto inhibited infant temperament at 8 months, as were two interaction terms: nondirective parenting at 14 months x infant inhibition (Hypothesis 1) and sensitive parenting at 14 months x infant inhibition (Hypothesis 2). Grand-mean centred scores were used to compute the interaction terms. We probed statistically significant interactions at one standard deviation below and one standard deviation above the interaction terms (Aiken et al., 1991).

6.2.4.2 Hypothesis 3: effortful control as a mediator of nondirective parenting and internalising symptoms

In our mediation model (model 3, Figure 6.1), we were specifically interested in measuring: (1) the direct paths from nondirective parenting at 8 months to effortful control at 24 months and internalising symptoms at 36 months; (2) the direct paths from effortful control at 24 months to internalising symptoms at 36 months, and (3) indirect paths from nondirective parenting to internalising symptoms via effortful control. Tests of statistical mediation employed bootstrapping with 10,000 samples to generate bias-corrected confidence intervals for indirect effects (Shrout & Bolger, 2002).

All analyses testing hypotheses were conducted in Mplus 7.13 (Muthén & Muthén, 1998-2015). Maximum Likelihood Robust (MLR) estimation was used to provide robust standard errors to account for the non-normal distribution and skewness in the internalising measure. All parameter estimates were standardised and thus indicate how much the dependent variables would be expected to change for a single standard deviation change in the predictor variable.

Hypotheses were tested using observed (i.e., non-latent) variables only and were estimated using the full sample (n =133) for hypotheses (1-2) and the subset with available parent-child interaction for hypothesis (3), where we assumed data was missing at random (total n = 123). Likelihood group status was treated as a covariate in all models to control for effect and regressed on each predictor and the internalising variable. Group differences in the temperament variables were also tested.

In addition, 17 of the 133 participants in the present sample (12.8%) were assigned an ASD diagnosis at 36 months. To exclude the possibility that the main effects were influenced by ASD outcome, we repeated the analyses in each model after omitting participants with a 36-month ASD diagnosis.

Finally, between the first and second timepoints, 22 infants in the elevated likelihood group participated in the intervention arm of a randomised controlled trial (RCT) of a parent-mediated early intervention programme (Green et al., 2015, 2017). To exclude the possibility of confounding effects, supplementary analyses were conducted (see SM, section 5 for full details).

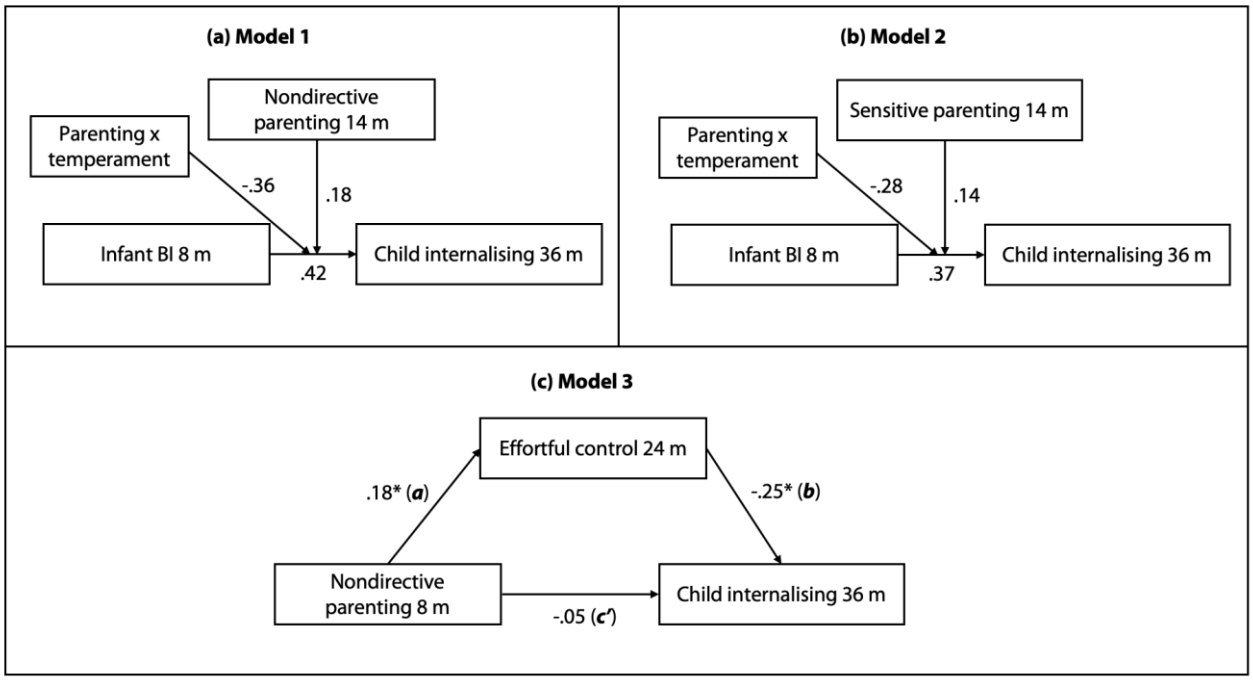

Fig. 6.1 Schematic showing the relationships between variables in the moderation analyses (Hypotheses 1-2) and mediation analysis (Hypothesis 3). Labels a, b and c' are path coefficients representing standardised coefficients; the c-prime path refers to the direct effect**.** * = $p < .01$.

6.3 Results

6.3.1 Sample characteristics

Descriptive statistics of our sample characteristics and our infant and parenting measures are shown in Table 6.1. The groups at typical likelihood (TL) and elevated likelihood (EL) of developing ASD did not differ in the proportion of girls and were the same age at each visit with the exception of the 24-month timepoint.

The EL group scored significantly higher than the typical-likelihood group on the behavioural inhibition scale at 8 months and the effect size was below moderate ($\eta^2 = .07$). The EL group had significantly lower effortful control than the TL group at 24 months; the effect size was also below moderate ($\eta^2 = .06$). Nondirective parenting was higher in the TL group at 8 and 14 months (all $\eta^2 \leq$

.13), as was sensitive parenting at 14 months (all $\eta^2 \leq .09$). Scores on the Mullen Early Learning Composite (Mullen, 1995) were higher in the TL group at 14, 24 and 36 months (all $\eta^2 \leq .1.5$). The EL group scored higher than the TL group on the internalising subscale at 36 months ($\eta^2 = .05$).

	Typical Likelihood M (SD) N	**Elevated Likelihood** M (SD) N	**Group Differences**
Visit 1 (8 months)			
% girls	59.1% $N = 44$	52.3% $N = 88$	*n/s*
Age in months	7.41 (1.23) $N = 44$	7.90 (1.18) $N = 88$	*n/s*
Mullen ELC	104.70 (11.60) $N = 44$	101.56 (13.94) $N = 88$	*n/s*
Behavioural Inhibition	2.50 (.94) $N = 44$	3.11 (1.15) $N = 86$	F (1, 129) = 9.25, p = .003, η^2 = .07
Nondirective parenting	3.98 (1.37) $N = 41$	3.00 (1.18) $N = 37$	F (1, 77) = 11.26, p = .001, η^2 = .13
Visit 2 (14 months)			
% girls	60.5% $N = 43$	(52.8%) $N = 89$	*n/s*
Age in months	13.93 (1.28) $N = 43$	14.15 (1.23) $N = 89$	*n/s*
Mullen ELC	107.60 (15.34) $N = 43$	97.83 (15.15) $N = 89$	F (1, 131) = 11.97, p = .001, η^2 = .09
Nondirective parenting	4.28 (1.39) $N = 43$	3.51 (1.47) $N = 41$	F (1, 83) = 6.06, p = .02, η^2 = .07
Sensitive parenting	4.09 (1.48) $N = 43$	3.46 (1.44) $N = 41$	F (1, 83) = 4.16, p = .04, η^2 = .05
Visit 3 (24 months)			
% girls	62.5% $N = 40$	54.2% $N = 83$	*n/s*
Age in months	23.90 (.71) $N = 40$	25.42 (1.93) $N = 83$	F (1, 122) = 23.21, p = .000, η^2 = .16
Mullen ELC	116.50 (13.72) $N = 40$	100.75 (19.11) $N = 83$	F (1, 122) = 21.73, p = .000, η^2 = .15
ECBQ Effortful Control	4.75 (.45) $N = 40$	4.44 (.61) $N = 77$	F (1, 116) = 7.65, p = .007, η^2 = .06
Visit 4 (36 months)			
% girls	59.1% $N = 44$	53.4% $N = 88$	*n/s*
Age in months	38 (2.61) $N = 44$	38.48 (1.77) $N = 88$	*n/s*
Mullen ELC	116.66 (15.02) $N = 44$	105.43 (22.19) $N = 88$	F (1, 131) = 9.15, p = .003, η^2 = .07
VABS-II Internalising	.77 (1.08) $N = 44$	1.79 (2.34) $N = 89$	F (1, 131) = 7.01, p = .007, η^2 = .05

Table 6.1 Sample characteristics and descriptives by group. Sample characteristics, means and standard deviations for measures and group comparisons (effect sizes); Mullen ELC: Mullen Early Learning Composite, IBQ: Infant Behavior Questionnaire, ECBQ: Early Childhood Behavior Questionnaire, BI; Behavioural Inhibition, EC; Effortful Control, VABS-II Internalising: Vineland Adaptive Behaviour Scale, second edition – Internalising score. Significance threshold set to p = .01.

6.3.2 Bivariate correlations

Table 6.2 shows correlations among the predictor and internalising variables for our primary models in the analysis for the full sample. Higher effortful control at 24 months related to higher nondirective

parenting at 8 months, and lower internalising at 36 months. Nondirective parenting was correlated across timepoints, suggesting stability. Sensitive and nondirective parenting, were inter-correlated. Correlations of key variables at alternative timepoints are recorded in the SM (Table S1, SM).

		1	2	3	4	5	6
1	Infant behavioural inhibition (8 mos)	--	--	--	--	--	--
2	Child Internalising (36 mos)	.13	--	--	--	--	--
3	Infant Effortful control (24 mos)	-.09	-.37**	--	--	--	--
4	Nondirective parenting (8 mos)	.06	-.15	.24**	--	--	--
5	Nondirective parenting (14 mos)	.06	-.08	.08	.28**	--	--
6	Sensitive parenting (14 mos)	.12	-.02	.003	.21*	.60**	--

Table 6.2 Bivariate correlations for primary model variables. Items 1-3 are parent-report measures; items 4-6 are parent-child interaction observations. For significant correlation coefficients, darker cell shading reflects higher values; * = p <. 05, ** = p < .01.

6.3.3 Models 1-2: nondirective and sensitive parenting as moderators of internalising symptoms

In model 1 (see Fig. 6.1, Table 6.3), contrary to hypothesis 1, there were no significant associations between infant behavioural inhibition at 8 months or nondirective parenting at 14 months and internalising symptoms at 36 months, either independently (all $ps \geq .16$) or interactively (β=-.36, p=.45, 95% CI [-1.04, .54]). This remained unchanged after adjustment for the potentially confounding effects of group status (EL *v.* TL). In model 2 (see Fig. 6.1, Table 6.3), we assessed whether an interaction between sensitive parenting at 14 months and infant behavioural inhibition at 8 months was associated with internalising symptoms at 36 months, but the results disconfirmed hypothesis 2 that infants who experienced more sensitive parenting would also have lower internalising scores in toddlerhood (β =-.28, p=.49, 95% CI [-.98, .30]). Additionally, no significant results were found in the model variants in which the same measures taken at different timepoints were entered into the model (Table S2, SM). Excluding children with an ASD diagnosis at 36 months led to no changes to the null findings of the moderation model analyses. Full details are reported in the Supplementary Materials (Table S6).

	Predicting Internalising (36 mos)				
	Predictor	*β*	*p*	*LLCI 95%*	*ULCI 95%*
Model 1	Infant BI, 8 months	.42	.18	-.16	.89
	Nondirective Parenting, 14 months	.18	.54	-.33	.60
	Group status	.20	.001	.09	.29
	BI*NDP	-.36	.45	-1.04	.54
Model 2	Infant BI, 8 months	.37	.23	-.05	.94
	Sensitive Parenting, 14 months	.14	.55	-.23	.54
	Group status	.20	.001	.10	.29
	BI*SP	-.28	.49	-.98	.30
	Predictor	*Mediator*	*Total Effect (SE)*	*Direct Effect (SE)*	*Indirect effect (95% CI Bootstrap)*
Model 3	Nondirective Parenting, 8 months	Effortful Control, 24 months	-.09 (.09)	-.05 (.09)	-.05 (-.11, -.01)

Table 6.3 Standardised model results of moderation and mediation analyses. Models 1-3 refer to hypotheses 1-3 shown in Figure 6.1; BI - behavioural inhibition; NDP – nondirective parenting; Group status – membership of the Typical Likelihood or Elevated Likelihood group; SP – sensitive parenting; BI*NDP – interaction term, behavioural inhibition x nondirective parenting; BI*SP – interaction term, behavioural inhibition x sensitive parenting; LLCI – lower limit confidence interval; ULCI – upper limit confidence interval; CI – confidence interval. In model 3, group status was entered as a covariate. * $p \leq .05$.

6.3.4 Model 3: effortful control as a mediator of nondirective parenting and internalising symptoms

In model 3, tests of direct effects demonstrated that nondirective parenting at 8 months was positively associated with effortful control at 24 months (β=.18, *SE*=.09, *p*=.04). The model also demonstrated that effortful control at 24 months inversely associated with internalising symptoms at 36 months (β=-.25, *SE*=.09, *p*=.006). There was no significant direct effect present between nondirective parenting and internalising symptoms (β=-.05, *SE*=.09, *p*=.62). Group status was significantly associated with effortful control at 24 months (β=-.22, *SE*=.08, *p*=.007) and internalising scores at 36 months (β=.15, *SE*=.06, *p*=.02). Predictor variables can exert an indirect effect on an outcome variable through a mediating variable in the absence of an association between predictor and outcome variable (given that a total effect is the sum of many different paths of influence, direct and indirect, not all of which may be part of the formal model; Hayes, 2009). As such we proceeded to investigate indirect effects of nondirective parenting on internalising symptoms through effortful control. Results from tests of indirect effects indicated that, consistent with our hypothesis, effortful control at 24 months lies on the path between nondirective parenting at 8 months and internalising symptoms at 36 months when controlling for group status (β=-.05, 95% CI BS [-.11, -.01]). Direct and indirect effects are shown in Figure 6.1 and Table 6.3, respectively.

A variant of model 3 conducted using effortful control at 14 months rather than 24 months (model 3.2, Table S3, SM) was found to be non-significant. A model variant including parenting measured at 14 months rather than 8 months was also conducted and found to be non-significant (model 3.3, Table S3, SM). A post-hoc exploratory moderated mediation analysis tested the extent to which nondirective parenting predicting child internalising through effortful control varied contingent on the level of behavioural inhibition (Figure S1, SM). The effect was significant, suggesting that higher levels of behavioural inhibition would make infants less susceptible to the effects of parenting on effortful control (Table S7, SM).

To assess whether diagnosis of ASD at 36 months influenced the main effects, we also repeated the original analyses adding diagnostic outcome as a binary variable, representing diagnosis of ASD at 36 months. Excluding children with an ASD diagnosis at 36 months in the mediation model led to no indirect effect (β=-.03, 95% CI BS [-.09, .02]). Full details are reported in the Supplementary Materials (see section 6). Control analyses of the influence of participants' inclusion in an RCT resulted in null findings, suggesting the absence of confounding effects in this regard (see section 5 in SM).

6.4 Discussion

Three hypotheses were tested to understand the role of temperament in the relationship between early parenting behaviour and internalising problems within ASD. Evidence supported our third hypothesis

in our enriched-ASD sample: more nondirective parenting behaviour in the first year of life was related to less child internalising at three years via the mediating variable of effortful control in toddlerhood. No direct link was found between nondirective parenting behaviour and child internalising, thus highlighting the mediating role of effortful control in toddlerhood which develops with parental support. However, it is notable that the main effect resulting from tests of our third hypothesis disappeared once children with an ASD diagnosis were removed from the model. While this difference may be explained by a reduction in statistical power, it could suggest that the diagnosed children were driving the effect. No support was found for our two other hypotheses regarding the moderating impact of either more nondirective parenting behaviour or more sensitive parenting behaviour at 14 months on the relationship between behavioural inhibition at 8 months and internalising problems at 36 months.

6.4.1 Behavioural Inhibition (hypotheses 1 and 2)

Early behavioural inhibition predicts internalising problems later in life in typically developing populations (Clauss & Blackford, 2012; Kostyrka-Allchorne et al., 2019; Muris et al., 2011) as well as those at elevated likelihood of developing ASD (Ersoy et al., 2020; Shephard et al., 2018). Although we found a bivariate correlation between behavioural inhibition at 14 months and internalising scores at 36 months (Table S1, SM), our findings give no indication that nondirective nor sensitive parenting would act to mitigate or alter the path from early behavioural inhibition to child internalising problems in an ASD-enriched cohort. This null finding corroborates several studies that suggest no risk-enhancing effects of traditionally negative parenting behaviours, such as parental overprotection, when interacting with infant temperament in typically developing populations (Sentse et al., 2009; Vreeke et al., 2013). An exception to this pattern is Rubin and colleagues' (2002) finding that intrusive parenting behaviour significantly moderated the relationship between toddler inhibition and preschool social reticence; this discrepancy may be explained by different assessment methodologies (i.e., the use of behavioural paradigms to measure inhibition as opposed to parent-report) as well as sample characteristics.[12]

[12]An alternative explanation for these null findings pertains to the role of the eliciting context. In the present study, a free-play interaction task was used to measure parental behaviour. This may have been insufficient to elicit inhibited behaviour in the infant, which is itself linked to controlling and directive parental behaviour (Hastings et al., 2010). Behavioural paradigms designed to elicit child inhibition (e.g., the Stranger Approach task; Buss, 2011; Buss et al., 2004) have been associated with more directive parenting behaviour and toddler anxiety in both community samples (Kiel & Buss, 2013) as well as an autism-enriched cohort related to the present study (Ersoy, 2019). To detect relations between infant inhibition, anxiety-related parental behaviour, and anxiety precursor symptoms in the future, it may therefore be necessary to examine parent-infant interaction in a range of familiar and unfamiliar contexts.

Based on our null findings and the pattern of our bivariate correlations, as well as the previous literature, evidence suggests sensitive parenting behaviour does not seem to act as a protective factor for children who show high behavioural inhibition, and the relative tendency toward low nondirective behaviour observed in parents of infants at elevated likelihood of ASD (Wan et al., 2013) does not interact with behavioural inhibition to explain internalising behaviour at 36 months.

6.4.2 Effortful control (hypothesis 3)

Recent research has implicated a role of low effortful control in the development of internalising-related distress in young children with (Ersoy et al., 2020) and without (White, McDermott, et al., 2011) ASD. Our results extend on this by identifying, for the first time, the role of effortful control in elucidating the link between parenting behaviour and internalising symptoms in an ASD-enriched cohort. Although previous research has found evidence for the contribution of parenting behaviour and behavioural inhibition to later internalising symptoms (Ryan & Ollendick, 2018), the pathway from nondirective parenting to internalising behaviour via effortful control in this population is novel.

Our post-hoc moderated mediation analysis also indicated that nondirective parenting has a greater effect on effortful control (and subsequent internalising symptoms) when infants have less behavioural inhibition. This exploratory analysis suggests a potential alternative risk path, whereby children low in behavioural inhibition are more sensitive to the protective factor of nondirective parenting, but children high in behavioural inhibition are less so. This potential differential susceptibility to parenting behaviour, based on infant temperament, may be important to conceptualise when investigating parent-mediated risk for the development of internalising-related distress in such cohorts in the future. Indeed, an alternative approach to the present study would be to test temperamental moderators of the relationship between early parenting and later child adjustment outcomes. These relationships can be studied within two relevant frameworks: the goodness-of-fit concept (proposing a match between parental behaviour and child temperament gives rise to optimal development, whereas a mismatch leads to suboptimal functioning; Thomas & Chess, 1977), and differential susceptibility theory (proposing that certain children have greater sensitivity to supportive and stressful environments, ‘for better and for worse’; Belsky et al., 2007). Such an approach would facilitate study of the effects of ‘type of child’ on the relationship between parenting and anxiety within ASD, representing a possible direction for future research.

One question raised by our findings, relating to differential susceptibility, is why the mediation effect in Hypothesis 3 was no longer significant once infants who went on to develop an ASD diagnosis were removed from the model. This may simply be explained by reduced statistical power. An alternative explanation could be that these children (whose parents score low on nondirective behaviour on average) may be more susceptible to the effects of parenting on their levels of effortful

control, and may subsequently be more likely to develop internalising-related distress. This raises an important possibility for a parent-mediated intervention targeting effortful control in this group.

6.4.3 Clinical and theoretical implications

Exploring the relationship between parental behaviour and infant temperament factors may be fruitful for understanding parent-mediated risk for psychopathology in ASD-enriched cohorts. Future studies focusing on the potential for parenting behaviour to support the development of infant effortful control may provide further evidence for parent-mediated interventions. Parenting may be a suitable intervention target for several reasons. Firstly, parent-mediated interventions within ASD-enriched cohorts have already been successful in increasing parental nondirectiveness by enriching parenting sensitivity and increasing parental awareness of the importance of their own behaviours in relation to the infant, which may be particularly relevant when an infant is displaying communicative cues that are more subtle than usual (Green et al., 2015, 2017). Secondly, less nondirective behaviour in parents may reflect parental stress or mood problems (Möller et al., 2015), both of which are likely to be heightened in the postnatal period; parents may use a less nondirective approach if they are unsure how to be effective in their parenting behaviour, or if they are otherwise low in emotional availability (for example, if caught up with financial or relational stress). If nondirective parental behaviour facilitates the development of child self-regulatory skills by giving the child more time and opportunity to use these skills without intrusion, then interventions incorporating components such as sensitivity training and increased social support may help increase parental nondirectiveness and subsequent infant effortful control. These questions represent a promising avenue for further study.

The current findings also add to the broader evidence base for the potential role of effortful control as a protective or compound risk factor in child development (e.g., Taylor et al., 2013). Low effortful control in infancy is commonly seen in children who go on to have ASD and ADHD (Johnson et al., 2015) or internalising difficulties (Kostyrka-Allchorne et al., 2019). It has been suggested that high levels of effortful control may compensate for a range of different atypicalities early in life, explaining why infants with high effortful control are less likely to receive any diagnosis later in childhood (Johnson, 2012). Higher levels of effortful control in early childhood also correlate with a range of socio-economic and health outcomes in adulthood, even when controlling for intelligence, social class and shared family background (Moffitt et al., 2011). While our moderated mediation findings suggest that effortful control confers more benefits in the context of lower behavioural inhibition, indicating that effortful control may be more or less protective contingent on other temperamental dimensions, taken together the evidence suggests that effortful control could be a useful target for intervention, given increased effortful control has positive benefits in a range of cases (though see Henderson et al., 2015).

While our findings suggest effortful control represents a potentially 'malleable' factor that may modify developmental trajectories, behavioural inhibition may instead represent a more 'fixed' risk for later psychopathology. The age of emergence of behavioural inhibition is thought to be from 4 months, with physiological antecedents detectable earlier on (Pérez-Edgar & Fox, 2018). Inhibited social behaviour shows longitudinal stability from the first year of life to early and middle childhood, as well as into adolescence (e.g. Brooker et al., 2016; Calkins et al., 1996; Pérez-Edgar et al., 2010). By contrast, it is difficult to measure effortful control before the second year of infancy. Top-down effortful processes required for executive function are not sufficiently developed in the early developmental stages (Kochanska et al., 2000), consistent with the fact that we found a weaker relationship when we substituted effortful control at 14 months into model 3, than when it was originally conducted with effortful control at 24 months (compare Table 6.3 and Table S3, SM). This developmental timing may make the processes associated with effortful control more susceptible to environmental input than inhibitory processes. The potential, relative fixedness of behavioural inhibition compared with the malleability of effortful control suggests that these two temperamental factors could act separately on later psychopathology risk, representing two distinct paths.

As in the wider literature (Pérez-Edgar & Fox, 2018; Rubin et al., 2002), our findings show that higher levels of infant behavioural inhibition relate to higher levels of child internalising. We also show that low levels of nondirective parenting relate to later reduced child internalising, through effortful control, and that this relationship may be stronger in the context of low behavioural inhibition. However, our findings suggest that the predictive value of behavioural inhibition on later internalising is not altered by or dependent on nondirective parental interactions. This counterintuitive finding could be explained by age specificity. In model 3, we show that our mediation analyses are significant when parenting is measured at 8 months – but this significance disappears when parenting is measured at 14 months (model 3.3, Table S3, SM). Our moderation analyses remain unchanged when we adjust for age (Table S2, SM), but this may be because there is no direct relationship between nondirective parenting and later child internalising; without effortful control in the model, differences are undetectable (though see null results in model 2.5, Table S2, SM).

6.4.4 Limitations

Findings from this study should be considered in light of several limitations. While we found support for parental nondirectiveness measured at 8 months associating with decreasing internalising problems via 24-month effortful control, it was not possible to disentangle whether nondirective parental interaction impacts on effortful control or whether this behaviour in the parent emerges as a consequence of early emerging signs of effortful control in the child (e.g., early compliance that allows the parent to avoid giving too much direction). In addition, while parental nondirectiveness was measured from observational data, temperament and internalising measures were based on

parent-report, which (as well as being potentially susceptible to shared method variance effects; Podsakoff et al., 2012) may be affected by parent psychopathology.

Finally, the generalisability of the present study of infant siblings may be limited in two ways: (i) generalisation to the broader population of children with ASD, but without a sibling with the condition, may be limited since having a first-degree relative with ASD may have influenced sampling of families, and long-term monitoring and evaluation of the development of the infant sibling might have influenced their developmental trajectory (Szatmari et al., 2016); (ii) generalisation to typically developing children may be limited since the modest sample size of the TL group in this study prohibited us from examining multi-group models, which would indicate whether the findings were consistent, and therefore likely generalisable, for both EL and TL groups.

6.4.5 General conclusion

Our data show that effortful control, itself influenced by nondirective parenting behaviour, can act as an ameliorating influence on the path to internalising-related distress within ASD-enriched cohorts; nondirective parenting behaviour may impact on effortful control in toddlerhood. Studies using more specific anxiety measures, as well as multi-method methodologies to examine multidirectional relations between parenting and infant temperament (including subcomponents of effortful control, representing different attentional processes) may be promising steps on the path to informing early intervention approaches.

6.5 Supplementary information

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[13]Supplementary materials are also reproduced for convenience in Appendix C.

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6.8 Conflict of interest

The authors declare that they have no conflict of interest.

III. SYSTEMATIC REVIEW

CHAPTER 7 – The effect of perinatal interventions on parent anxiety, infant socio-emotional development and parent-infant relationship outcomes: a systematic review

This chapter presents a systematic review of the research on perinatal interventions as they relate to improvements in parent anxiety, infant socio-emotional functioning and the parent-infant relationship. This chapter reviews study outcomes, intervention components, and the potential for interventions predominantly focused on the adult to improve infant outcomes (and vice versa). This approach was taken in an effort to focus on the mechanisms of treatment outcomes while adhering to theoretical accounts regarding the dyadic nature of young children's regulatory systems. The supplementary materials (SM) for this chapter are available in Appendix D.[14]

Abstract

Infants of parents with perinatal anxiety are at elevated likelihood of experiencing disruption in the parent-infant relationship, as well as atypical or impaired socio-emotional functioning in later development. Interventions delivered in the perinatal period have the potential to protect the early dyadic relationship and support infants' ongoing development and socio-emotional outcomes. This review primarily aimed to examine the efficacy of perinatal interventions on parent anxiety, parent-infant relationship outcomes, and infant socio-emotional development as well as temperament. Secondarily, the review sought to understand how adult-focused interventions affected infant outcomes, and vice versa, and which intervention components were common to successful interventions. Five electronic databases as well as manual search procedures were used to identify randomised controlled trials according to a PICO eligibility criteria framework. Risk of bias assessments were undertaken, and a narrative synthesis was conducted. Twelve studies were analysed and grouped to identify interventions with effects on parent or infant outcomes. Interventions incorporating cognitive behavioural strategies for affective disorders were found to improve parent anxiety outcomes, and interventions focusing on altering distorted maternal internal representations were found to improve dyadic and infant outcomes. There was also evidence that infant-focused interventions led to improved parent outcomes, and vice versa. However, evidence was of mixed methodological quality. Implications for clinical practice and future intervention trials are discussed. The review was pre-registered on PROSPERO (CRD42021254799) and funded by the London Interdisciplinary Social Science Doctoral Training Partnership.

[14]I owe MSc students Dean Jacobs and Cassie Fitzpatrick many thanks for their diligent and thoughtful work on this project, and for helping with proofreading this chapter.

7.1 Introduction

7.1.1 The relationship of perinatal anxiety to infant and parent-infant outcomes

Perinatal anxiety refers to a set of mental health conditions characterised by cognitive distortions, physiological arousal, and behavioural avoidance; these are experienced either in the prenatal period, or in the immediate year after birth (Harrison & Alderdice, 2020). Due to high prevalence rates, perinatal anxiety has become recognised as a prominent public health issue (Dennis et al., 2017; Leach et al., 2017). The condition has been associated with numerous adverse maternal and neonatal outcomes, including fear of childbirth (Demšar et al., 2018), maladaptive maternal coping strategies (George et al., 2013), maternal suicidality (Farias et al., 2013), birth complications (Dowse et al., 2020), preterm birth, and low birth weight (Ding et al., 2015). In addition, perinatal anxiety has been associated with a range of negative consequences for the parent-infant relationship, and for later child development (O'Connor et al., 2002; O'Donnell et al., 2014; Polte et al., 2019; Rees et al., 2019).

Perinatal anxiety is known to perturb the early parent-infant relationship. Higher maternal state anxiety is associated with lower levels of sensitive behaviour during mother-infant interactions at three months (where sensitivity is defined as parental responsivity to infant activities and affective states; Ierardi et al., 2019). This is important, as insensitive parental behaviour plays a causal role in shaping insecure child attachment (Bakermans-Kranenburg et al., 2003). In addition, when compared to controls, perinatal anxiety has been associated with: higher levels of parental behaviour during interaction (e.g., infant-directed speech, positive facial expressions, gaze frequency: Murray et al., 2008; Granat et al., 2017), higher unpredictability (Holmberg et al., 2020), increased intrusive behaviour (Hakanen et al., 2019), and highly coordinated parent-infant behaviour (Beebe et al., 2011; Granat et al., 2017). This overloaded, highly stimulating and overly synchronised behaviour is considered to be less contingent on infant cues (Feldman, 2007). It is also thought to act as a mechanism by which social abilities - such as symbolisation, social reasoning and empathy – become impaired in the child (Feldman, 2015).

There is further evidence from experimental and longitudinal studies that perinatal anxiety associates with impaired infant socio-emotional development. A recent prospective study of mothers and their two year-old children found that perinatal anxiety significantly increased the odds of deficits in children's socio-emotional competencies by a factor of four (Polte et al., 2019), equivalent to a large Cohen's *d* effect size (Chen et al., 2010). This finding is consistent with evidence indicating that perinatal anxiety relates to early signs of avoidant behaviour in children (Aktar et al., 2013; Murray et al., 2008), and atypical social information processing (Creswell et al., 2008, 2011).

While there is preliminary evidence that perinatal interventions for anxiety have a positive effect on parent outcomes, this represents very few studies, and less still is known about the effect of interventions for perinatal anxiety on infants (Loughnan et al., 2018). Interventions have typically

focused on only the adult member of the dyad (Loughnan et al., 2019; Maguire et al., 2018; Sockol, 2018). However, interventions that incorporate a focus on the infant or the dyadic relationship may serve to improve parent-infant relationship dynamics and subsequent child outcomes. This view is coherent with the mutual regulation model, which holds that infant socio-emotional function is fostered through dyadic, coregulatory behaviours (Tronick, 2007). Perinatal mental illness interferes with this process through unresponsive, insensitive parental behaviour that leads to dysregulation of infants' affective states, even when interacting with others (Field et al., 1988; Weinberg & Tronick, 1998). Efforts to modify parental behaviour in perinatal interventions may therefore help promote coregulation, and improve child outcomes (Stein et al., 2014).

7.1.2 Perinatal mental illness interventions and infant outcomes

According to international review databases, there have been no previous systematic reviews or meta-analyses addressing the question of how perinatal interventions relate to parent anxiety, the parent-infant relationship and infant socio-emotional development. This may be due in part to the historical emphasis on interventions for postnatal depression, which has been the focus of the vast majority of studies on perinatal mental illness over the past thirty years (Howard et al., 2014).

There have been numerous reviews on the efficacy of interventions for postnatal depression in relation to infant outcomes (Letourneau et al., 2017; Poobalan et al., 2007; Tsivos et al., 2015). The most recent review found little evidence for therapeutic effects (Rayce et al., 2020). It is also worth noting that, though perinatal anxiety frequently co-occurs with depression (Falah-Hassani et al., 2017), none of these reviews have extracted data on parent anxiety outcomes from the included studies (Letourneau et al., 2017; Poobalan et al., 2007; Tsivos et al., 2015).

In addition, a review of the effects of perinatal interventions on infant and dyadic outcomes has recently been conducted, spanning a broad range of study designs and perinatal disorders (Newton et al., 2020). This found that interventions incorporating video feedback, facilitation of mother-infant interaction, or support with understanding their infant's perspective were effective for infant and parent-infant outcomes. These findings are consistent with a previous review that showed, with 'moderate-certainty,' that video feedback may improve parental sensitivity among young children at risk of poor attachment outcomes (O'Hara et al., 2019). Combined, these reviews suggest that infant-focused perinatal interventions may be beneficial in a range of clinical contexts.

Despite these recent advances, there remains a gap in the intervention literature. Both Newton et al. (2020) and O'Hara et al. (2019) are broad in scope and do not provide a specific focus on perinatal anxiety or its particular developmental sequelae in children. In addition, Newton et al. (2020) includes numerous studies at high risk of bias due to lack of randomised allocation, and lack of masking among outcome assessors. O'Hara et al. (2019) also omits studies of multifactorial psychosocial interventions; given that multifactorial parental interventions are the most widely available treatments

within health systems, reviews evaluating these types of interventions are necessary. Finally, there have been a number of large studies in the recent period that focus on interventions for perinatal anxiety and infant outcomes, which have not been captured by extant reviews (e.g., Burger et al., 2020; Holt et al., 2021). Hence there is a need for a specific review of multifactorial perinatal anxiety interventions with respect to parent and infant outcomes.

7.1.3 The present review

'Perinatal anxiety is a highly morbid and prevalent condition with limited evidence as regards treatment (Dennis et al., 2017; Loughnan et al., 2018; Maguire et al., 2018). It also associates with impaired infant socio-emotional development (Aktar et al., 2013; Aktar & Bögels, 2017) as well as parent-infant relationship perturbations (Feldman et al., 2009; Ierardi et al., 2019; Rees et al., 2019). Given this, it is important that we establish which perinatal interventions, if any, predict better outcomes for both parent anxiety and infant socio-emotional development. To address this, the following systematic review examines the efficacy of perinatal interventions on parent anxiety, infant socio-emotional development or temperament outcomes, and parent-infant relationship outcomes. Following the theoretical framework of Tronick (2007), we also explore the potential for predominantly adult-focused interventions to improve infant or dyadic outcomes, and vice versa. Finally, we take a mechanistic approach, exploring whether there are any common components among the interventions that demonstrate significant improvement in the outcomes of interest.

7.2 Method

7.2.1 Eligibility criteria

To review how perinatal interventions affect parent anxiety, infant socio-emotional development, and parent-infant relationship outcomes, we aimed to identify all peer reviewed papers on this topic. The review protocol was preregistered with the NIHR international prospective register of systematic reviews (PROSPERO; CRD42021254799). Studies were included if they met the following criteria:

(1) participants were pregnant people or parents (of any age or gender) of infants up to 24 months of age at study entry; parents were identified to either (a) meet criteria for a psychiatric disorder according to a diagnostic assessment or (b) indicate risk of a psychiatric disorder (indexed by elevated symptoms on a dimensional measure); psychiatric disorders could include affective disorder, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), or specific phobia (e.g., tokophobia);

(2) a psychosocial and/or pharmacological intervention was delivered either postnatally or a combination of pre- and postnatally; interventions delivered only prenatally, but with an infant follow-up were also considered; group/individual/web/in-person delivery formats of any duration were all acceptable;

(3) a control group was present, and participants were randomly allocated to either the control or the intervention group(s);

(4) parent anxiety was measured both pre- and post-intervention by a continuous or categorical variable. One or more of the following infant outcome measures was also measured pre- and post-intervention (or only post-intervention if interventions were delivered exclusively in the prenatal period): infant socio-emotional development, infant temperament, and parent-infant bonding;

(5) studies conformed to randomised controlled trial standards, by use of randomisation procedures outlined in the CONSORT 2010 guidance (Schulz et al., 2010). No minimum sample size was required.

Studies were excluded if they met the following criteria:

(1) infant participants were exclusively preterm or cared for in neonatal intensive care units;

(2) no control group was present, or there was no random allocation of participants to the control group;

(3) studies did not conform to randomised controlled trial standards (e.g., case controls, case series, and all other non-randomised control trials were all excluded).

To allow greater comparability and generalisation to clinical populations, the review included studies where: (a) samples were recruited on the basis of parent psychopathology; (b) the infant or dyadic outcome measures pertained specifically to infant rather than fetal phenomena, and (c) the parent outcome measure pertained to anxiety symptomatology or disorders, including disorders previously classified under the category of anxiety in diagnostic manuals (e.g., PTSD and OCD; Craske et al., 2017). Studies were therefore excluded if the sample was recruited on the basis of broad risk categories, such as economic disadvantage, transition to parenthood, infertility, or having a child with a behavioural problem or developmental condition. Studies were also excluded if the intervention or outcome was focused on parent psychopathology, but the recruitment was not. Further detail on population scoping is given in the SM (section 1).

In addition, studies were excluded if the parent anxiety outcome was part of a broad mood measure (e.g., the self-reporting questionnaire, SRQ-20; Husain et al., 2016), or if the measure related to the construct of stress rather than anxiety per se. With regard to child age, studies that included children both below *and* above 24 months of age were screened according to mean child age. Due to specialist advice that methodological filtering by English language represents a ‘blunt tool,’ preventing the retrieval of eligible records, this was not part of the search strategy. However, publications written in languages other than those spoken by the review team (English, German) were excluded.

7.2.2 Search strategy

Both manual and electronic database searches were included in the search strategy. Manual searches included both hand searching and contact with key experts.

7.2.2.1 Electronic searches

Between 17th May and June 5th 2021, five electronic databases were searched via two interfaces: MEDLINE (via OvidSP), EMBASE (via OvidSP), APA PsychINFO (via OvidSP), MIDIRS (via OvidSP), and the Cochrane Central Register of Controlled Trials (via CENTRAL). Search terms were developed with guidance from an information specialist at King's College London and were optimised for each database. Electronic searches used MeSH and other subject headings as well as adjacent word searching and truncation. An expansive approach to field searching was taken (e.g. mp *v.* ti.ab) so as not to omit records that included key outcome measures in the main text but not the title or abstract. All search terms are detailed in the SM (Tables S1-S5).

7.2.2.2 Manual searches

After the electronic searches were complete, manual searching was performed. For all included records, this involved reference list searching, whereby any titles that appeared relevant were identified by hand and subsequently retrieved. In addition, citation searching was performed using the citation search function on Google Scholar and the interactive infographic accompanying searches on Connected Papers. Finally, twelve key experts were contacted to identify any recent and eligible records (experts were senior authors of the included studies).

7.2.3 Procedures

Retrieved records were downloaded into bibliographic software (Zotero Desktop Reference Manager, version 5.0.96.2). Duplicates were removed first through automation using the online web application Deduplicator (Rathbone et al., 2015) and then checked by hand by the lead author (CS). Two reviewers (CF, DJ) independently conducted title and abstract screening via the platform Screenatron (Clark et al., 2020; Scott et al., 2021), marking records as 'Included' if they met all the inclusion criteria and 'Excluded' if they did not. The review team also created a 'Maybe' category for records meeting all inclusion criteria except the parent anxiety outcome measure. This was due to a scoping exercise conducted prior to the review that indicated the high frequency with which secondary or tertiary anxiety measures tended to be omitted in the abstract but present in the full article. Accuracy measures were calculated on included records, and disputes between reviewers were identified using the online web application Disputatron (Clark et al., 2020; Scott et al., 2021). Disputed records were screened and reclassified by CS. Subsequently, all records marked included/maybe from the electronic search were screened at full text by CS. Records retrieved through manual searching were

also screened at full text. The lead author's judgements were verified through discussion with the review team.

7.2.4 Data extraction and risk of bias assessments

The Cochrane Collaboration data extraction form for randomised controlled trials (Cochrane Collaboration, 2014) was used across all eligible studies. To ensure our review represented the latest developments in quality assessment, risk of bias (RoB) assessments were conducted using the Cochrane Collaboration's RoB Tool (Sterne et al., 2019). The updated tool marks a departure from earlier versions based on subjective ratings across broad domains of bias (selection bias, performance bias, attrition bias, and reporting bias; Higgins et al., 2011). Instead, algorithmically informed bias assessments are conducted across five more specific domains: bias arising from the randomisation process, bias due to deviations from the intended intervention, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Cochrane Collaboration's macro-enabled Microsoft Excel tool was used to perform structured assessments (RoB 2, version 22 Aug 2019). Fifty percent of the bias assessments were also performed independently by a separate reviewer (DJ) to identify any discrepancies and reach consensus judgements. The results were plotted using the Robvis tool due to good interoperability with the Excel tool (McGuinness & Higgins, 2020).

7.2.5 Analysis

Using an approach adapted from a previous review of perinatal interventions, components of interventions from the included studies were extracted and tabulated to 'develop a matrix mapping the key components of the studies against the study results' (Newton et al., 2020, p. 3). The matrix was split according to whether the intervention predominantly focused on the parent or the infant/dyad. This allowed for an examination of whether there were 'symmetrical' effects (adult-focused interventions that led to improved parent outcomes, and infant/dyad-focused interventions that led to improved infant/dyad outcomes) and 'asymmetrical' effects (infant/dyad-focused interventions that led to improved parent outcomes, and vice versa). In order to facilitate a consideration of the mechanisms of treatment outcomes, we also used the intervention components matrix to identify any components common to interventions that demonstrated significant improvements in the outcomes of interest. There were three reasons we elected not to perform a meta-analysis: both categorical and dichotomous variables were included in the review, the infant outcome measures were highly heterogeneous, and there were practical time constraints.

On occasion, deviations from the intended intervention were identified from inspecting trial registry records, trial protocols and journal articles for each study. For the purposes of being consistent and precise, the decision was taken to restrict the component analysis to the information available in the journal article and trial protocol. These documents are more contemporaneous with one another than the trial registry record, and more comprehensive. To mitigate bias toward interventions familiar to

the lead author, the final intervention component list was discussed and agreed by the full review team.

7.3 Results

7.3.1 Search results

A total of 2070 records were retrieved from electronic searches. Before title and abstract screening, 318 duplicate records were excluded, with 1752 records remaining. Accuracy measures calculated from title and abstract screening indicated high inter-rater reliability between two independent reviewers (DJ and CF screened all 1752 records; $\kappa = .78$; prevalence and bias adjusted kappa [pabak] = .98). Subsequently, 1585 records were excluded due to ineligibility and 167 records were retrieved for full text screening. Of these, the following records were excluded: 95 records reporting no specific parent anxiety outcome at pre/post-intervention, one featuring no relevant infant/dyad outcome, 27 featuring child participants who were too old, and 18 featuring samples that were not recruited on the basis of parent psychopathology. We also excluded: ten conference abstracts, five duplicates not previously identified due to inconsistent metadata, and one record written in a language not spoken by the review team. One record was also excluded due to unreliable reporting indicated by numerous inconsistencies in the manuscript (including those pertaining to the main findings, outcome measures, and intervention description).

A total of 16 records were also retrieved from manual searching. Full texts of these were inspected and the following exclusions were made: four records for which there was no specific parent anxiety measure reported at pre/post-intervention; two records featuring no relevant infant/dyad outcome; four records for which parent psychopathology was not the focus of recruitment; two records featuring child participants who were too old, and one record that had not been peer reviewed (an unpublished thesis).

Consequently, 12 studies were included in the final review, including nine from the electronic search and three from the manual search. Figure 7.1 details the full screening results in a PRISMA flow diagram. In addition, reasons for exclusion and inclusion of all studies screened at full text are detailed in Tables S6-S7 respectively (SM).

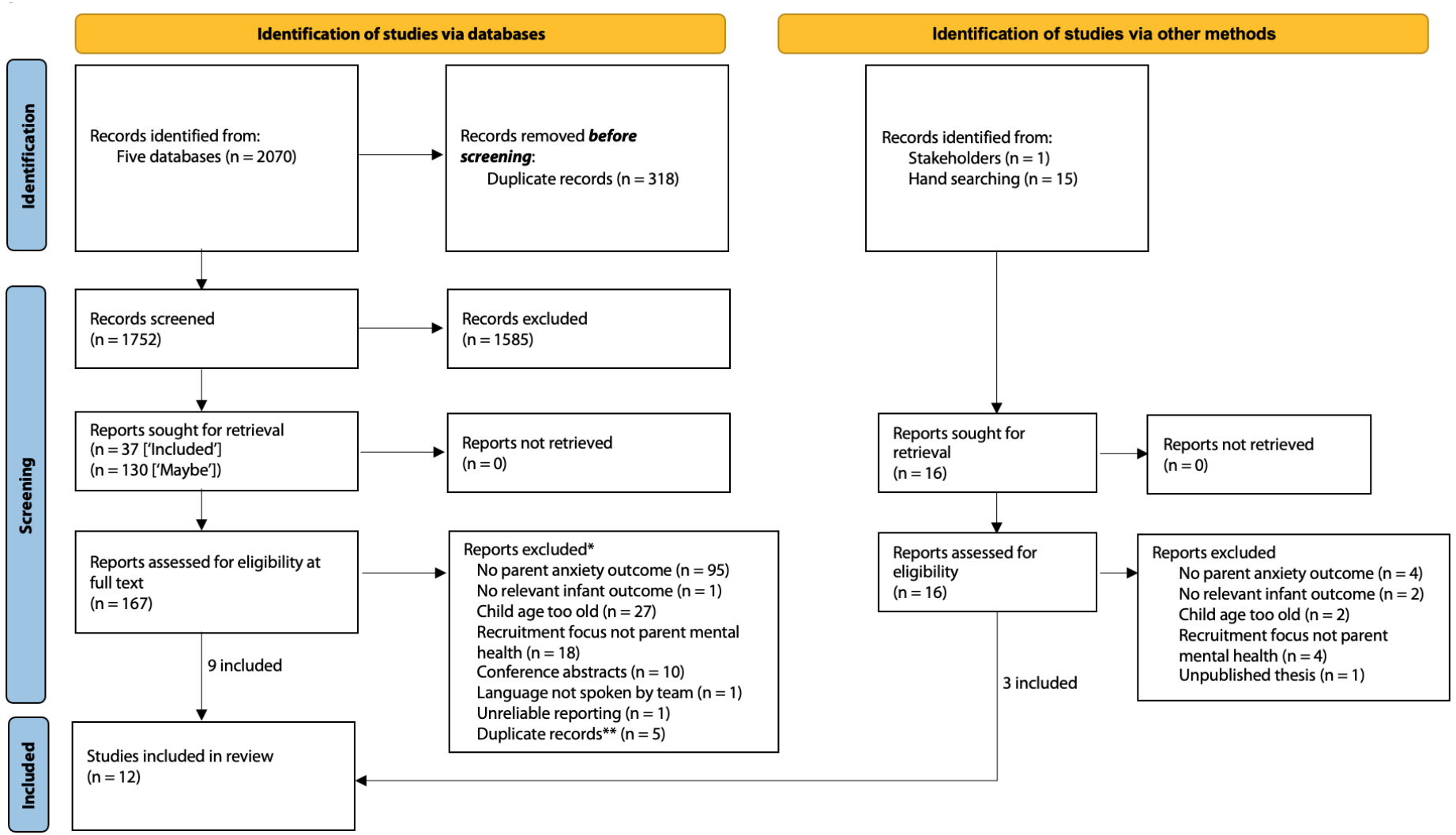

Fig. 7.1 PRISMA flow diagram. Note that hand searching comprises both citation and reference searching. *This list represents one failed inclusion criterion per study – however, multiple studies failed to meet more than one inclusion criteria, as detailed in Table S6. **These records had not been previously identified due to inconsistencies between database metadata. Adapted from Page et al. (2021).

7.3.2 Risk of bias assessments

An overview of the results from the risk of bias assessments is presented in Figure 7.2. The majority of studies were at low risk of bias arising from the randomisation process - perhaps due to standard reporting guidelines, which state randomisation methods must be detailed (Schulz et al., 2010). In addition, most studies were at low risk of bias with respect to missing data. This was mainly due to low rates of attrition, or as a result of sensitivity analyses that were able to demonstrate that results were little changed under a range of plausible assumptions about the relationship between missingness in the outcome and its true value. There was one major exception to this: where lack of detail regarding missing outcome data and information available about the trial context led to a judgement of high risk (Werner et al., 2016; see Table S19).

With regard to bias arising from deviations from the intended intervention, risk levels were mixed. Five studies were judged to be low risk due to consistency between the intended intervention detailed in trial protocols/registry records and the final intervention reported (Ericksen et al., 2018; Goodman et al., 2015; Holt et al., 2021; Lenze et al., 2020; Milgrom et al., 2015). Any inconsistencies that were identified were justified by the authors (e.g., Milgrom et al., 2015). The remaining studies were judged to be of some concern due to inconsistencies between the intended interventions and the final interventions reported, or inadequate detail about the intended interventions (Burger et al., 2020; Challacombe et al., 2017; O'Higgins et al., 2008; O'Mahen et al., 2014; Stein et al., 2018; Trevillion et al., 2020; Werner et al., 2016). Where it was clear that deviations had occurred, these were either balanced between the intervention and control groups (Stein et al., 2018; Werner et al., 2016) or were unlikely to affect the outcome of interest (Burger et al., 2020; Trevillion et al., 2020).

With regard to bias in outcome measurement, risk levels varied again. Four studies were judged to be low risk due to the outcome assessor being masked to participants' group allocation (Challacombe et al., 2017; Goodman et al., 2015; Holt et al., 2021; O'Higgins et al., 2008). Seven studies were judged to be of some concern due to the outcome being measured by participant-report, despite participants being unmasked to group allocation (Burger et al., 2020; Ericksen et al., 2018; Milgrom et al., 2015; O'Mahen et al., 2014; Stein et al., 2018; Trevillion et al., 2020; Werner et al., 2016). While outcome assessment could have been influenced by knowledge of the intervention received, this was not thought to be likely due to the participants' low probability of 'therapy allegiance.[15] For one study, it was not clear from the information provided whether the research team responsible for outcome assessment were masked to group allocation (Lenze et al., 2020). If unmasked, it is possible the research team held some degree of allegiance to the trial intervention that would bias their outcome

[15]Typically, therapy allegiance occurs among those familiar with a specific treatment, such as researchers or therapists. Individuals who have not previously received therapy are unlikely to be partial to one or another type of treatment (Dragioti et al., 2015).

assessment (Dragioti et al., 2015). However, such researcher allegiance was not reported. Consequently, a judgement of 'some concern' was made (see Table S13).

Concern was most substantive with regard to bias in the selection of the reported result. This was because half of the studies did not provide adequate detail on the intended analyses of the trial, either as a result of not registering their trials (Challacombe et al., 2017; O'Higgins et al., 2008; O'Mahen et al., 2014), or as a result of limited detail within available trial registry records (Ericksen et al., 2018) or the trial protocol (Trevillion et al., 2020). Five studies were also judged to be of some concern in this domain. This was either due to intended analyses being partly misaligned with the final analyses reported (Burger et al., 2020; Stein et al., 2018) or indicative of internal consistency despite a lack of adequate detail regarding the intended analyses (Goodman et al., 2015; Lenze et al., 2020). Two were judged to be high risk, due to a timepoint reporting discrepancy that indicated potential selectivity (Holt et al., 2021; Werner et al., 2016).

Consensus judgements for bias assessments are further detailed in the SM (Tables S8-S19). Note that one specific outcome measure and numerical result were used for the risk of bias assessments, for which the rationale is described in the SM (section 2).

7.3.3 Bias arising from wait-list or treatment as usual control conditions

The above bias assessments do not account for bias arising from the design of the control condition. Research has shown that less specific control conditions (e.g., wait-list or treatment as usual groups) amplify the apparent efficacy of the intervention group. Placebo controls outperform wait-list groups, and provide benefit, such that the effect size of a cognitive behavioural therapy (CBT) intervention is halved by comparing it to a placebo rather than a wait-list group (Zhu et al., 2014). There is also evidence that the effect size of all psychotherapies for depression drops by 19% by removing wait-list controlled studies (Cuijpers et al., 2018). This is worth noting, as at least half of the studies in the present review used a treatment as usual or wait-list control condition (Burger et al., 2020; Challacombe et al., 2017; Ericksen et al., 2018; Goodman et al., 2015; Milgrom et al., 2015; Trevillion et al., 2020).

7.3.4 Statistical power limitations

The above bias assessments also do not account for the studies' statistical power. As insufficient power can lead to inflated effect sizes (Button et al., 2013; Ioannidis, 2008), this information is important for interpreting results.

Half of the studies within this review were pilot studies (Challacombe et al., 2017; Ericksen et al., 2018; Goodman et al., 2015; Lenze et al., 2020; Milgrom et al., 2015; Werner et al., 2016). Of these, one study met the intended sample size identified through power calculations (based on the primary outcome measure of maternal mood; Milgrom et al., 2015), while another did not (Ericksen et al.,

2018). The remaining four studies did not include formal power calculations, prohibiting an assessment of statistical power (Challacombe et al., 2017; Goodman et al., 2015; Lenze et al., 2020; Werner et al., 2016). Most of these four studies directly acknowledged the potential for underpowered analyses, particularly in relation to assessment of between group differences (Goodman et al., 2015; Lenze et al., 2020; Werner et al., 2016).

The remaining six studies of this review represent mixed levels of statistical power. Three studies were adequately powered, meeting the intended sample size identified through power calculations (Burger et al., 2020; O'Mahen et al., 2014; Stein et al., 2018). Power calculations by Burger et al. (2020) were based on an outcome measure relevant to this review – that is, a measure of infant socio-emotional development - whereas Stein et al. (2018) and O'Mahen et al. (2014) were not. By contrast, two studies conducted analyses based on smaller than intended sample sizes, resulting in potentially insufficient power (Holt et al., 2021; Trevillion et al., 2020). One study made no mention of power calculations, prohibiting assessment of statistical power (O'Higgins et al., 2008).

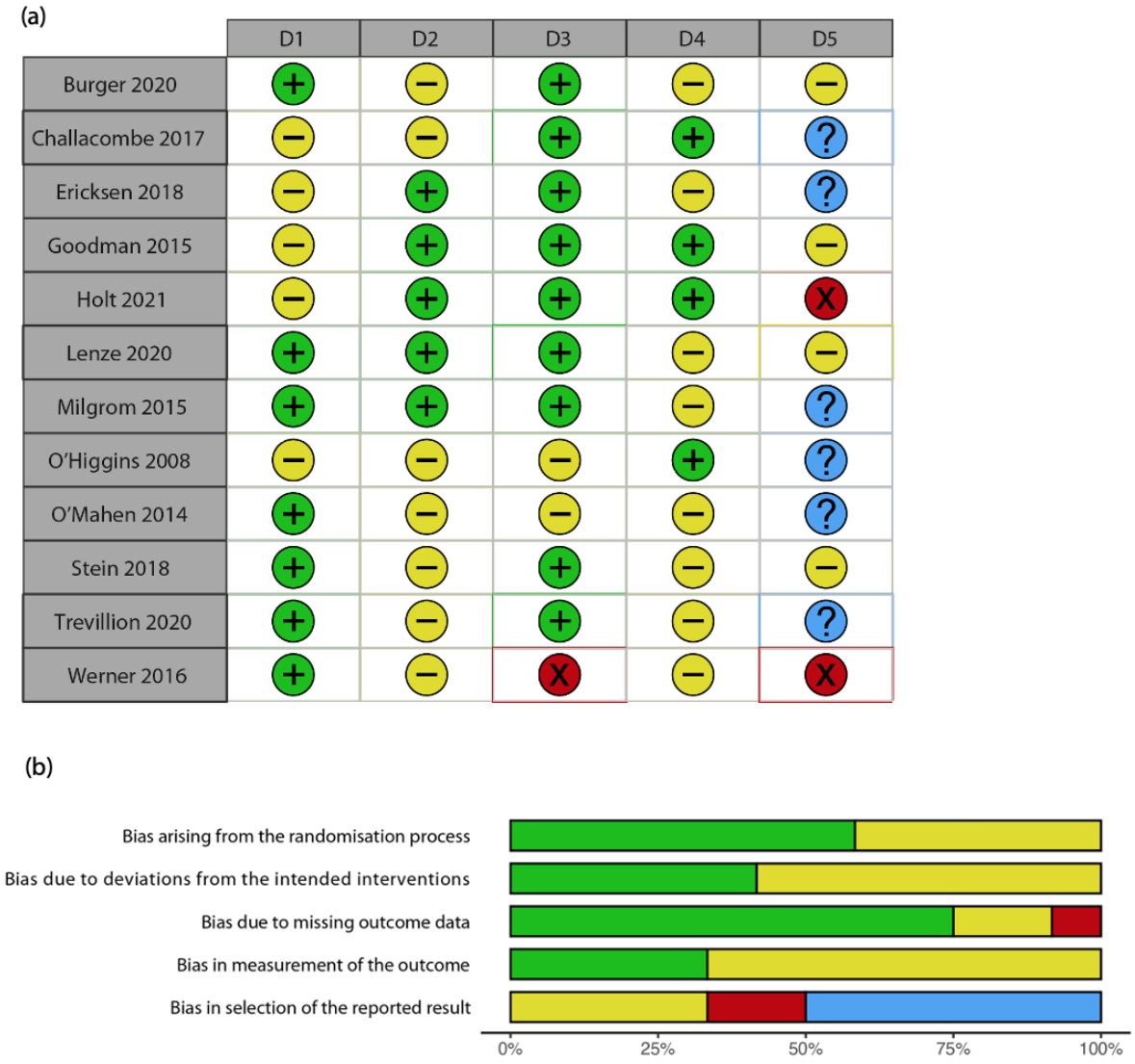

Fig. 7.2 (a) Traffic light plot summarising Cochrane risk of bias assessments; D1 - bias arising from the randomisation process; D2 – bias due to deviations from the intended intervention; D3 – bias due to missing outcome data; D4 – bias in measurement of the outcome; D5 – bias in selection of the reported result; (b) summary plot aggregating the bias assessment results across the twelve studies for the five listed domains. Colours: **red** – high risk of bias; **yellow** – some concerns; **green** – low risk of bias; **blue** – no or inadequate information available for assessing intended analyses.

7.3.5 Study characteristics

Twelve studies involving 1029 participants were included in the review in total (see Tables 7.1 and 7.2).[16] Half of the studies were published within the last three years (Burger et al., 2020; Ericksen et al., 2018; Holt et al., 2021; Lenze et al., 2020; Stein et al., 2018; Trevillion et al., 2020) while half spanned the period between 2008 and 2017 (Challacombe et al., 2017; Goodman et al., 2015; Milgrom et al., 2015; O'Higgins et al., 2008; O'Mahen et al., 2014; Werner et al., 2016). Studies were conducted in the UK (Challacombe et al., 2017; O'Higgins et al., 2008; O'Mahen et al., 2014; Stein et al., 2018; Trevillion et al., 2020), Australia (Ericksen et al., 2018; Holt et al., 2021; Milgrom et al., 2015), the USA (Goodman et al., 2015; Lenze et al., 2020), and the Netherlands (Burger et al., 2020).

All the studies' adult participants were women of working adult age (treatment and control groups combined mean age: 31.33 years). The studies reported mixed parity; in five studies, mothers were mostly or entirely primiparous (Challacombe et al., 2017; Ericksen et al., 2018; Goodman et al., 2015; Holt et al., 2021; Milgrom et al., 2015), while in five studies the sample included a spread of multiparous and primiparous mothers (Burger et al., 2020; O'Mahen et al., 2014; Stein et al., 2018; Trevillion et al., 2020; Werner et al., 2016). One study did not report parity (O'Higgins et al., 2008) while another reported that the majority of the sample had had more than one pregnancy (Lenze et al., 2020; Lenze & Potts, 2017). Infants were a range of ages at study entry. Five studies included infant participants aged between 2.5 and 6.8 months postpartum (Challacombe et al., 2017; Ericksen et al., 2018; Holt et al., 2021; O'Higgins et al., 2008; Stein et al., 2018) while five studies included fetuses between 2.5 and 9.5 months gestation who were later assessed in the postpartum period (Burger et al., 2020; Lenze et al., 2020; Milgrom et al., 2015; Trevillion et al., 2020; Werner et al., 2016). Two studies did not report specific infant ages (Goodman et al., 2015; O'Mahen et al., 2014). A breakdown of age by group and by dyad partner is shown in Table 7.1.

Most study samples consisted of majority white nationals; there were two studies where over eighty percent of participants were from black and minority ethnic backgrounds (Lenze et al., 2020; Werner et al., 2016), and two studies where over a third of participants were from black and minority ethnic backgrounds (Goodman et al., 2015; Trevillion et al., 2020). A breakdown of ethnicity by group is shown in Table 7.1.

Inclusion criteria varied between studies. Four studies included adults with an anxiety-related condition or co-occurring anxiety and depression according to diagnostic assessments (Challacombe et al., 2017; Trevillion et al., 2020), questionnaire cut-offs (Burger et al., 2020), or self-referral behaviour (i.e., professional consultation regarding 'symptoms of depression or anxiety'; Ericksen et al., 2018). The remaining studies included adults scoring above cut-offs on questionnaires for

[16]If excluding non-randomised participants (such as those assigned to 'healthy comparison' groups surplus to randomised control groups), the total number of participants across the twelve studies would be 958.

postnatal depression risk (Goodman et al., 2015; Lenze et al., 2020; O'Higgins et al., 2008; Werner et al., 2016), or who were diagnostically assessed as having major depression (O'Mahen et al., 2014; Stein et al., 2018) or either minor or major depression (Holt et al., 2021; Milgrom et al., 2015). Specific measures are included alongside participant descriptions in Table 7.2.

The twelve included studies examined a variety of outcome measures. The majority measured parent anxiety levels at pre- and post-intervention using questionnaires with well-established psychometric properties, except for three studies using either diagnostic assessments (Goodman et al., 2015; Stein et al., 2018) or artificial dichotomisation of a dimensional scale (Trevillion et al., 2020). At baseline, the majority of adult participants in the review scored in the range of moderate to severe anxiety (as shown in Table 7.1). In addition to this, the studies taken together reported 32 instruments for measuring infant or parent-infant relationship outcome measures, many of which had numerous subscales. Due to the heterogeneity of the infant/dyad outcome measures, baseline scores for the infant partner were not tabulated. However, all outcome measures for both partners are listed in Table 7.2.

Finally, the twelve studies investigated a range of interventions that varied both in terms of content and delivery format. While the interventions were complex, it was possible to identify interventions that predominantly focused on either the adult or the infant/dyad. These groupings are shown in Table 7.3 and discussed in more detail below.

	N	Mean (SD) parent age		Mean (SD) infant age in postpartum mos unless specified		Mean (SD) anxiety score (or % with diagnosis)		Parent anxiety measure	Black and ethnic minority (including 'other') %	
		Intervention	Control	Intervention	Control	Intervention	Control		Intervention	Control
Burger 2020	282	33.4 (4.6)	32.1 (4.5)	3.5 gestation		48.6 (8.7)	48.5 (8.4)	Brief STAI[1]	6.0	2.2
Challacombe 2017	71	32.4 (no SD)	32.7 (no SD)	~6		24.82 (5.19)	24.47 (5.81)	YBOCS[2]	18	12
Ericksen 2018	31	32.31 (6.04)	33.00 (6.38)	4.94 (2.91)	4.87 (1.81)	17.25 (no SD)	14.67 (no SD)	DASS anxiety[3]	Not reported	
Goodman 2015	42	30.57 (4.760)	30.81 (5.316)	Not reported		43.62 (9.47)	36.00 (10.39)	STAI-S[4]	42.9	38.1
Holt 2021	77	32.13 (5.04)	33.33 (3.85)	3.13 (2.67)	3.97 (2.87)	15.4 (9.29)	13.66 (7.35)	BAI[5]	Not reported	
Lenze 2020*	42	26.90 (5.81)	26.38 (5.90)	~3-7.5 gestation		15.6 (6.5)	15.0 (4.2)	Brief STAI-S[6]	81	86
Milgrom 2015	54	32.79 (5.97)	30.78 (5.86)	4.99 gestation	5.24 gestation	22.37 (10.05)	20.59 (10.67)	BAI[5]	Not reported	
O'Higgins 2008	96	Not reported		~2.5		44.7 (11.25)	45.49 (12.84)	STAI-S[4]	Approx. 30	
O'Mahen 2014	83	Not reported (except: >18)		Not reported (except: <12 mos)		13.90 (3.82)	14.12 (4.78)	GAD-7[7]	7.2	7.2
Stein 2018	144	31.7 (5.7)	32.2 (5.3)	6.8 (2.0)	6.8 (1.9)	48.6%	32%	SCID-IV-R[8]	15.3	19.4
Trevillion 2020	53	30-39 (~69%)	30-39 (~67%)	2.5 gestation	2.78 gestation	52%	59.26%	≥ 8 on GAD-7[9]	30.77	37.04
Werner 2016	54	30.87 (6.51)	29.60 (5.67)	9-9.5 gestation		19.35 (13.79)	13.67 (10.11)	HAM-A[10]	80.7	92.59

Table 7.1 Participant characteristics including age of both parent and infant, as well as parent anxiety level, and ethnicity; collected at baseline across all studies. 'Control' refers to randomised comparison groups only. Infant/fetal ages reported in weeks have been converted to months for interpretability (on the basis of 1 month = 4 weeks). * = informed by Lenze & Potts (2017). Anxiety measures as follows: 1 = the 6-item State–Trait Anxiety Inventory (Brief STAI; Marteau & Bekker, 1992); 2 = Yale-Brown Obsessive-Compulsive Scale (YBOCS; Goodman et al., 1989); 3 = Depression Anxiety Stress Scales - anxiety

scale (DASS; Lovibond & Lovibond, 1995); 4 = Strait Trait Anxiety Inventory – state scale (STAI-S; Spielberger, 1970); 5 = Beck Anxiety Inventory (BAI; Beck & Steer, 1991); 6 = the 6-item State-Trait Anxiety Inventory – state scale (Brief STAI-S; Berg et al., 1998; no interpretation of scores available); 7 = the Generalised Anxiety Disorder screening tool (GAD-7; Spitzer et al., 2006); 8 = posttraumatic stress disorder or generalised anxiety disorder assessed via the Structured Clinical Interview for DSM-IV-R for Axis I disorders (SCID-IV-R; First et al., 1998); 9 = participants scoring ≥ 8 on the GAD-7; 10 = Hamilton Anxiety Rating Scale (HAM-A, Hamilton 1959). Colour shading indicates anxiety severity level: **orange** – severe; **yellow** – moderate/'moderately severe'**;** **green** – mild/mild to moderate levels. Sources for interpretation of dimensional anxiety scores included relevant studies (e.g., Werner 2016 for HAM-A), original work (e.g., Spitzer et al., 2006; GAD-7) or the broader anxiety literature (e.g., Julian, 2011; BAI, STAI).

7.3.6 Study outcomes

Table 7.2 presents an overview of studies' participants, interventions, comparison groups, outcome measures, as well as effect sizes. Although practical time constraints and heterogeneity of outcome measures precluded formal meta-analysis, Hedges *g* was calculated and reported where possible to aid interpretability. This was based on means, standard deviations, and group sizes available from the main trial article. Hedges' approach has the benefit of avoiding a slight overestimation bias compared to Cohen's *d* (Borenstein et al., 2009). Where studies derived their effect size from analyses of dichotomous data, odds ratios have been presented as in the original article. A guide to interpreting odds ratios in terms of effect sizes is given in the SM (Table S20). The below narrative synthesis relays study outcomes with a focus on magnitude of effect sizes, and statistical significance.

7.3.6.1 Interventions demonstrating between group improvements in parent anxiety outcomes

Three studies reported post-intervention changes in parent anxiety outcome that indicated medium to large effect sizes (Challacombe et al., 2017; Milgrom et al., 2015; O'Mahen et al., 2014; outcome measures detailed in Tables 7.1 and 7.2, omitted here for brevity). Challacombe et al. (2017), following a two-week intervention at approximately six months postpartum, reported a large, significant between group effect size at 12 months postpartum, representing a reduction in OCD symptoms within the intervention group. Milgrom et al. (2015), following an eight-week intervention delivered in the prenatal period, also reported a large, significant effect at post-intervention, representing a reduction in anxiety levels in the intervention group. However, this did not remain significant at nine months postpartum (Milgrom et al., 2015). O'Mahen et al. (2014) also reported a medium, significant between group effect post-intervention, representing a reduction in anxiety for the intervention group.

Two studies found smaller or inexact treatment effect sizes in relation to parent anxiety outcomes (Werner et al., 2016; Ericksen et al., 2018). Werner et al. (2016), examining an intervention that was conducted in the first six weeks postpartum, found evidence that the intervention led to improved anxiety outcomes; significant reductions in anxiety symptoms were reported immediately post-intervention (six weeks) and at a follow-up assessment (16 weeks), albeit with a non-significant reduction in the interim (10 weeks). These represented small effect sizes. Finally, Ericksen et al. (2018) investigated the effects of a therapeutic playgroup conducted in the infant's first year of life; significant between group differences were identified post-intervention, representing a reduction in anxiety symptoms for the intervention group; however, follow-up assessment indicated this was not stable over time (Ericksen et al., 2018). Effect sizes were not calculable for these results.

In addition, two studies indicated small to medium sized, directional improvements in parent anxiety, though these were not found to reach significance when comparing groups. This included the guided self-help intervention evaluated by Trevillion et al. (2020), and the dyadic psychotherapy intervention

investigated by Goodman et al. (2015). One study, evaluating a combined CBT and therapeutic playgroup intervention, found a small, directional improvement in anxiety for the index group post-intervention, but this was not stable at the six-month follow-up, and did not reach significance (Holt et al., 2021).

For the remaining studies, it was not possible to calculate effect sizes for between group differences, nor were any significant between group differences identified. This included the combined CBT and video feedback therapy intervention investigated by Stein et al. (2018), the dyadic psychotherapy intervention studied by Lenze et al. (2020), and the infant massage intervention investigated by O'Higgins et al. (2008). The results of Burger et al. (2020) indicated adverse treatment side-effects for parent anxiety, discussed below.

7.3.6.2 Interventions demonstrating between group improvements in infant/parent-infant relationship outcomes

Multiple studies identified small to medium sized improvements in parent-infant relationship outcomes. Firstly, Holt et al. (2021) used the Postpartum Bonding Questionnaire (PBQ; Brockington et al., 2006), a parent-report measure capturing impairment in parent-infant bonding. Holt et al. (2021) also used the observer-rated measure, the Parent Child Early Relational Assessment (ERA; Clark, 2015), specifically its first factor ('Parental Positive Affective Involvement and Verbalisation'). The trial authors define this as a measure of 'maternal tone of voice, positive affect, mood, enjoyment in the interaction, amount and quality of visual contact and verbalisation with the child, social initiative with the child, structuring of the environment, mirroring, and consistency/predictability' (Holt et al., 2021, p. 6). Following a two-part intervention run over ~13 weeks during the first year postpartum, Holt et al. (2021) reported small to medium effect sizes at six-month follow-up that represented significant reductions in impaired bonding and significant improvements in positive parental involvement for the intervention group. Larger improvements in positive parental involvement were identified immediately post-intervention in the intervention group compared to the control group, but between group differences were not significant until six months.

In addition to this, both Trevillion et al. (2020) and O'Mahen et al. (2014) observed a medium sized, directional improvement on the PBQ (Brockington et al., 2006), while Burger et al. (2020) observed a similar pattern, though with a smaller effect size. Goodman et al. (2015) found small to medium treatment effects on several dyadic behaviours assessed using the Coding Interactive Behavior manual (dyadic reciprocity, infant involvement, maternal sensitivity; Feldman, 1998) and the Parenting Stress Index (PSI; Abidin, 1995), while Stein et al. (2018) found small treatment effects indicative of increased attachment security, measured by the Attachment *Q* Sort (AQS; van IJzendoorn et al., 2004). None of these effects were statistically significant.

Several studies also identified improvements in infant socio-emotional functioning. Stein et al. (2018) found small treatment effects indicative of reduced child externalising, measured by the Child Behavioural Checklist (CBCL; Rescorla, 2005), though these were not significant. Milgrom et al. (2015) used two parent-report measures: the Social-Emotional Ages and Stages Questionnaires (ASQ:SE; Squires et al., 2002), and the Revised Infant Behaviour Questionnaire Short Form (IBQ-R; Gartstein & Rothbart, 2003). Following an eight-week intervention conducted during the prenatal period, Milgrom and colleagues (2015) reported large treatment effects at nine months postpartum that represented significant differences in measures of infant self-regulatory and communicative behaviours. Those in the intervention group scored higher on numerous scales probing these developmental capacities (see Table 7.2). However, these measures were only assessed at nine months postpartum, precluding any analyses of change over time.

Werner et al. (2016) also examined between group differences in infant fussing and crying behaviour, using the Baby's Day Diary (Barr et al., 1988), a parent-report measure. Fuss and cry behaviour is closely related to the temperament construct of soothability, i.e., the extent to which reductions in infant fuss and cry behaviour occur in the context of caregiver soothing techniques (Gartstein & Rothbart, 2003). Following an intervention delivered over six weeks postpartum, infants in the intervention group exhibited significantly fewer episodes of fuss/cry behaviour based on a four-day average collected post-intervention. Effect sizes were not calculable.

With respect to infant or dyadic outcomes, effect sizes indicating between group differences were not calculable for Lenze et al. (2020), Higgins et al. (2008), or Challacombe et al. (2017), and none reported statistically significant improvements. The results of Ericksen et al. (2018) indicated adverse treatment side-effects for parent-infant relationship outcomes, as discussed below. All infant and dyadic outcome measures for each study are shown in Table 7.2.

7.3.6.3 Interventions demonstrating deteriorations in outcome measures

Two studies identified medium sized treatment effects indexing deterioration in relevant outcome measures (Burger et al., 2020; Ericksen et al., 2018).

Burger et al. (2020), using the Brief State-Trait Anxiety Inventory (Brief STAI; Marteau & Bekker, 1992), noted a significant, medium sized treatment effect on anxiety symptoms during the intervention at 24 weeks gestation, such that anxiety scores were higher in the intervention group (g = 0.4). This effect disappeared thereafter. The trial authors suggested this result was related to the exposure component of the intervention, which involved approaching fear-provoking stimuli as a means of overcoming avoidance behaviour and its unintended consequences (Burger et al., 2020). The authors also performed a subgroup analysis on mothers meeting diagnostic criteria for anxiety disorders; this showed a significant result for birth outcomes, such that infants' gestational ages were lower in the intervention group compared with the control condition if they had anxious parents. The

trial authors speculated that the increased anxiety effect at 24 weeks gestation may have been correlated with increased physiological arousal, in turn adversely affecting intrauterine development of the fetus (Burger et al., 2020). This outcome is not strictly within scope of the present review – however, the potential link to parent anxiety renders it of interest. It is also worth highlighting that, post-intervention, ratings of anxiety remained slightly elevated in the intervention group compared to the control. Child internalising and externalising scores also remained slightly elevated in the intervention group compared to the control at 18 months postpartum. These results represented small, non-significant effects (Burger et al., 2020).

Ericksen et al. (2018) also identified adverse treatment side-effects. The authors, using the Parenting Stress Index Short Form (PSI-SF; Abidin, 1995), found that average scores on the 'difficult child' subscale remained higher in the intervention group compared to the control condition. The difficult child subscale includes 12 items probing both elements of infant temperament (e.g., 'My child gets upset easily over the smallest thing') and the impact of this on the parent (e.g., 'My child makes more demands on me than most children'; PSI-SF; Abidin, 1995). This medium sized effect (g = 0.3) remained significant after adjustment for baseline imbalances between groups. There were also small, directional deteriorations on the 'parent-infant dysfunctional behaviour' subscale, and in parent-infant interaction, the latter assessed via the Paediatric Infant Parent Exam (Fiese et al., 2001). Neither of these reached significance, and these analyses were underpowered.

Study author & year **Country**	**Participants** **(N = total sample)**	**Intervention**	**Control**	**Parent anxiety outcome(s)**	**Infant/parent-infant outcome(s)**	**Post-intervention effect size** **(Hedges *g* calculated where possible)**	
		N = total participants assigned to group		**measures and assessment timepoints**		**parent anxiety**	**infant/dyad**
Burger 2020 Netherlands	Pregnant women screening positive for symptoms of depression (≥12 score on EDPS) and/or anxiety (≥42 score on STAI); once born, infants participated in the study up to 18 months postpartum (N = 282)	Prenatally initiated CBT: 10-14 [x] individual sessions (unspecified length) delivered from 20 weeks gestation to 3 months postpartum (6-10 sessions during pregnancy) (N = 140)	Care as usual (N = 142)	Brief STAI assessed at baseline, 24 and 36 weeks gestation and at 6 weeks and 3, 6, 12 and 18 months postpartum	CBCL – total problems, internalising, externalising scales; assessed at 18 months postpartum PBQ – between 6 and 18 months postpartum	Post-intervention ratings, postpartum, for **Brief STAI:** 3 mos: *g* = .21 6 mos: *g* = .10 12 mos: *g* = .03 18 mos: *g* = .07	Post-intervention ratings, 18 months postpartum for **CBCL:** **Total problems**: *g* = .17 **Internalising**: *g* = .22 **Externalising**: *g* = .08 **PBQ:** *g* = -.10
Challacombe 2017 UK	Mothers diagnosed via SCID with OCD and an infant <6 months of age (N = 71)	Time intensive CBT (iCBT): typically 4 [x] 3 hour individual sessions, delivered in two weeks, with up to 3 [x] 1 hour follow-up sessions offered monthly (between 6-9 months postpartum)	Randomised treatment as usual (N = 17) Non-randomised healthy controls (N = 37)	YBOCS and DASS assessed at baseline, and 6 and 12 months postpartum	(1) Ainsworth sensitivity scale; (2) Ainsworth cooperation-interference scale; (3) Maternal warmth; (4) Maternal	12-month post-intervention ratings for **YBOCS:** *g* = -.91[†] Pre/post DASS scores not reported in main paper	Not reported

		(N = 17)			vocalisations during nappy change (%); (5) Over-conscientiousness (%), and (6) Dyadic synchrony scale; all assessed at 6 and 12 months postpartum via videotaped interaction Attachment – assessed via Ainsworth SSP at 12 months postpartum		
Ericksen 2018 Australia	Mothers with an infant < 12 months who had recently consulted with a health professional regarding their mental health (e.g., 'symptoms of depression or anxiety') (N = 31)	Community HUGS (CHUGS): 10 x 60-90 minute therapeutic playgroup sessions targeting mother-infant relationship over 10 weeks; 4-8 dyads in each group including interaction coaching, play, music, movement, and psychoeducation on CBT and parenting strategies (N = 16)	Wait-list control, receiving care as usual (N = 15)	DASS assessed at baseline, post-intervention (after session 10) and 6-month follow-up	PIPE scores PSI-SF - parent-child dysfunctional interaction scale, difficult child scale All assessed at baseline and post-intervention (after session 10)	Not reported	Post-intervention ratings (after 10 sessions): **PIPE:** *g* = .07 **PSI difficult child:** *g* = .29 **PSI parent-child dysfunctional interaction:** *g* = .21
Goodman 2015 USA	Primiparous mothers with newborns, scoring >9 and	Perinatal dyadic psychotherapy: 8 x 60 minute individual sessions over three months;	Usual care (N = 21)	Any anxiety diagnosis assessed by SCID at post-	PSI-SF – total score CIB – maternal sensitivity, infant	Post-intervention ratings:* **STAI-state:**	Post-intervention ratings:* **Total PSI:** *g* = -.55

	<20 on the EPDS on two screens one week apart (N = 42)	incorporates both standard and parent-infant psychotherapy (N = 21)		intervention and 3-month follow-up STAI-state – assessed at baseline, post-intervention and 3-month follow-up	involvement and dyadic reciprocity assessed via videotaped interaction All assessed at post-intervention and 3-month follow-up	*g* = -.42	**CIB** **Maternal sensitivity:** *g* = .46 **Infant involvement:** *g* = .19 **Dyadic reciprocity:** *g* = .18
Holt 2021 Australia	Mothers with an infant < 12 months meeting SCID diagnosis of current major or minor depressive disorder (N = 77)	CBT + HUGS: 12 x 90 minute group CBT sessions (including 3 attended by partners) spread over 9 weeks, followed by 4 x 90 minute therapeutic playgroup sessions including interaction coaching, 'good enough' parenting psychoeducation, play, and challenging infant-centric cognitive distortions (N = 38)	CBT + control playgroup: CBT programme as per intervention group + 4 x 90 minute nondirective group sessions with dyads and facilitator (N = 39)	BAI assessed at baseline, post-CBT intervention, post HUGS intervention, and 6-months follow-up	ERA Factor I (FI) and items 19 and 22 assessed via videotaped interaction at baseline, post HUGS intervention, and 6-months follow-up PBQ, STSI/STST, ASQ:SE, PSI-4 assessed at baseline, post CBT intervention, post HUGS intervention, and 6 months follow-up	Post-intervention ratings on the **BAI**: *g* = -.10 6-months follow-up: *g* = .31	Post-intervention measures:* **PBQ:** *g* = -.26 **ERA FI:** *g* = .11 6-months follow-up: **PBQ:** *g* = -.49† **ERA FI:** *g* = .05† ERA F1 effects calculated using adjusted means.
Lenze 2020 USA	Pregnant women between 12-30 weeks	IPT-Dyad: 9 x psychotherapy sessions (unspecified length) focused on the mother-infant	Enhanced treatment as usual: regular contact; 15 nappies given per assessment;	Brief STAI-S assessed at baseline, 37-39 weeks	ITSEA – externalising, internalising, dysregulation and	Not reported for parent or infant/dyad outcomes	

	gestation scoring ≥10 on the EDS; once born, infants participated in the study up to 12 months postpartum (N = 42)	relationship, delivered during the prenatal period and followed up with up to 10 postpartum 'maintenance' sessions; including interaction coaching, exploration of maternal mental representations of the infant, and psychoeducation on attachment, developmental stages, and parenting (N = 21)	engagement with health services encouraged (N = 21)	gestation, and 3, 6, 9 and 12 months postpartum	'competence' scales. Assessed at 9 and 12 months postpartum IBQ-VS – affect, control, surgency scales, and PSI – total score. Assessed at 6 and 12 months postpartum CIB – parent sensitivity, intrusiveness, and limit setting; child involvement; dyadic reciprocity, dyadic negative states. Assessed at 3, 6, 9 and 12 months postpartum		
Milgrom 2015 Australia	Pregnant women < 30 weeks gestation with a DSM-IV diagnosis of minor or major depressive, once born, infants participated in the study up to	Beating the Blues Before Birth: 8 x 60 minute individual sessions of pregnancy-specific cognitive behavioural therapy, with one session including partners, over eight weeks (N = 27)	Usual care (N = 27)	BAI assessed at baseline, 9 weeks post-randomisation (post-intervention), and at 9 months postpartum	ASQ:SE and IBQ-R assessed at 9 months postpartum	Post-intervention ratings of the **BAI:** 9-weeks post-randomisation: *g* = -.90† 9 months postpartum: *g* = -.64	Post-intervention ratings at 9 months postpartum:* **ASQ:SE self-regulation**: *g* = .83† **ASQ: SE communication:** *g* = .82† **IBQ-R falling reactivity/recovery:** *g* = 1.08†

	9 months postpartum (N = 54)						**IBQ-R negative affectivity:** *g* = -.85† **IBQ-R high intensity pleasure:** *g* = .83†
O'Higgins 2008 UK	Mothers of newborns scoring > 12 on the EPDS (N = 96)	Infant massage class: 6 x 60 minute group sessions, including training on various massage strokes and responsivity to infant cues (N = 31)	Randomised support group: practical help on accessing helplines and welfare support (N = 31) Non-randomised non-depressed group (N = 34)	SSAI assessed at baseline, 19 weeks postpartum (post-intervention) and 12 months postpartum	ICQ and Global Ratings for mother-infant interaction (maternal sensitivity; infant performance in interaction; overall interaction) – all assessed at baseline, 19 weeks postpartum (post-intervention) and 12 months postpartum	Not reported for parent or infant/dyad outcomes	
O'Mahen 2014 UK	Mothers who meet ICD-10 criteria for major depressive disorder and who have a baby aged 0-12 months old (N = 83)	NetmumsHWD: 12 x individual online sessions, each designed to be completed in 1 week, supplemented with weekly 20-30 minute phone call support and access to web resources (e.g. peer chat room and networking); five sessions focused on behavioural activation with the remainder addressing	Treatment as usual (with access to NetmumsHWD web resources) (N = 42)	GAD-7 assessed at baseline and 17 weeks post-randomisation (post-intervention)	PBQ assessed at baseline and 17 weeks post-randomisation (post-intervention)	Post-intervention ratings: **GAD-7:** *g* = -.51†	Post-intervention ratings: **PBQ:** *g* = -.41

		interpersonal issues, or parenting skills and infant behaviour (N = 41)					
Stein 2018 UK	Mothers meeting diagnostic criteria for major depressive disorder and had been depressed for at least the previous 3 months or the first 3 months postpartum, along with their infants aged 4.5 – 9 months old (N = 144)	CBT + VFT; 11 x 90 minute individual sessions of combined CBT + VFT (6 weekly and 5 fortnightly), followed by 2 post-therapy boosters; VFT involves feedback on videotaped excerpts of dyadic interaction, plus coaching in parental responsivity, emotional scaffolding, sensitivity, and treating child as a psychological agent (N = 72)	CBT + PMR; 11 x 90 minute individual sessions of combined CBT + PMR (6 weekly and 5 fortnightly), followed by 2 post-therapy boosters; PMR involves tensing and relaxing major muscle groups combined with attention to sensations (N = 72)	GAD and PTSD assessed via SCID at baseline, and 12 and 24 months partum	CBCL externalising scale; AQS attachment security; child emotion regulation (Lab-TAB), ECBQ effortful control, emotion discrimination (visual discrimination task) −all assessed and reported at two years postpartum Maternal following of child attention, responsivity, sensitivity, and warmth assessed and reported at baseline, 1 year and 2 years postpartum Maternal mind-mindedness assessed and reported at baseline and 1 year postpartum	None reported for GAD and PTSD	Post-intervention ratings at 2 years postpartum for primary measures:* **CBCL externalising**: *g* = -.20 **AQS attachment security**: *g* = .09

Trevillion 2020 UK	Pregnant women at no further than 26 weeks gestation who met criteria for diagnostic depression or mixed anxiety and depressive disorder on the SCID (N = 53)	Usual care + guided self-help: 8 x 30 minute ~weekly telephonic or face to face individual sessions, as well as a prior face-to-face initial session, and an additional telephone call at 6-8 weeks postpartum; involves working through a booklet including psychoeducation on prenatal depression, interpersonal issues, planning for parenthood and health and lifestyle (N = 26)	Usual care (N = 27)	GAD-7 assessed at baseline, 14 weeks post-randomisation, and 3 months postpartum	PBQ assessed and reported at 3 months postpartum	Adjusted odds ratio for **GAD-7**. 14-weeks post randomisation (post-intervention but not postpartum): -.48 3 months postpartum: -.37	Statistics unavailable for calculating Hedges *g* but 'effect size' reported for post-intervention ratings at 3 months postpartum: **PBQ:** -.42
Werner 2016 USA	Pregnant women in their second or third trimester who scored ≥ 28 on the predictive index of postnatal depression (N = 54)	PREPP: 4 x individual sessions of unspecified length (3 in-person visits, 1 telephone call) spanning the period between full term and 6 weeks postpartum; involving infant behavioural techniques (e.g., swaddling, increased carrying, daytime stimulation), as well as parent-focused sessions on mindfulness, parental identity, and psychoeducation about the postpartum period (N = 27)	Enhanced treatment as usual; two in-person meetings with a clinical psychologist (who discussed symptoms, offered referrals and provided printed support resources) and 1 telephone call from a research assistant (N = 27)	HAM-A assessed at 34-38 weeks gestation (baseline), as well as 6, 10 and 16 weeks postpartum	Average infant fuss/cry behaviour assessed via parental diary; 4-day average taken from 6-14 weeks postpartum	Post-intervention, postpartum ratings for **HAM-A:** 6 weeks: $g = -.29^{\dagger}$ 10 weeks: $g = -.12$ 16 weeks: $g = -.23^{\dagger}$	None reported for infant outcomes

Table 7.2 Summary of Findings table including details of participants, interventions, comparisons and outcomes, as well as effect sizes. Hedges *g* has been calculated where means, standard deviations, and group sizes were reported at the timepoint for the measure of interest. Results based on dichotomous data have been presented as reported. A negative effect size corresponds to the control arm having a larger mean. For dimensional parent anxiety measures, as well as the CBCL, PBQ, PIPE, PSI, and IBQ-R negative affectivity, higher scores indicate worse outcomes. For all other measures, higher scores indicate better outcomes. Only between group effects of outcomes applicable to the review are shown here. Where studies presented results from both observed and intention-to-treat (ITT) analyses, only results of the ITT analyses have been presented. * = further fine-grain non-significant effect sizes from this study have been omitted from summary table due to volume of results. † = statistically significant difference of at least $p < .05$. ASQ:SE = Ages and Stages Questionnaires, Social Emotional (Squires et al., 2002); AQS = Attachment Q-Sort (van IJzendoorn et al., 2004); BAI = Beck Anxiety Inventory (Beck & Steer, 1991); Brief STAI = six-item State–Trait Anxiety Inventory (Marteau & Bekker, 1992); Brief STAI-S = State Scale of the Brief STAI (Berg et al., 1998); CBCL = Child Behavioural Checklist (Rescorla, 2005); CBT = Cognitive Behavioural Therapy; EDS/EPDS = Edinburgh Postnatal (Depression) Scale (Cox et al., 1987); CIB = Coding Interactive Behavior manual (Feldman, 1998); DASS = Depression Anxiety Stress Scales (Lovibond & Lovibond, 1995); ECBQ = Early Childhood Behavior Questionnaire (Putnam et al., 2006); ERA = Parent Child Early Relational Assessment (Clark, 2015); GAD-7 = Generalised Anxiety Disorder Screener (Spitzer et al., 2006); HAM-A = Hamilton Anxiety Rating Scale (Hamilton, 1959); IBQ-R = Revised Infant Behavior Questionnaire Short Form (Gartstein & Rothbart, 2003); IBQ-VS = Infant Behavior Questionnaire – Revised Very Short Form (Putnam et al., 2014); ICD-10 = International Classification of Diseases – version 10 (World Health Organization, 1990); ITSEA = Infant-Toddler Social and Emotional Assessment (Carter et al., 1999); ITQ/ICQ = Bates Infant Temperament/Characteristics Questionnaire (Bates et al., 1979); Lab-TAB = Laboratory Temperament Assessment Battery (Goldsmith & Rothbart, 1991); PBQ = Postpartum Bonding Questionnaire (Brockington et al., 2006); PIPE = Paediatric Infant Parent Exam (Fiese et al., 2001); PREPP - Practical Resources for Effective Postpartum Parenting (Werner et al., 2016); PMR = Progressive Muscle Relaxation (Carlson & Hoyle, 1993); PSI-4 = Parenting Stress Index (Abidin, 2012); PSI-SF = Parenting Stress Index Short Form (Abidin, 1995); SSAI = Spielberger State Anxiety Inventory (Spielberger et al.,1970); SSP = Strange Situation Procedure (Ainsworth et al., 1978); STAI = State–Trait Anxiety Inventory (Spielberger et al., 1970); STSI = Short Temperament Scale for Infants (Sanson et al., 1987); STST = Short Temperament Scale for Toddlers (Sewell et al., 1998); VFT = Video Feedback Therapy (Juffer et al., 2008); YBOCS = Yale-Brown Obsessive-Compulsive Scale (Goodman et al., 1989).

7.3.7 Intervention components analysis

To probe the study findings further and examine the mechanisms of improved treatment outcome, an analysis of intervention components was conducted from which two broad groupings emerged. One grouping, 'interventions predominantly focused on the adult' included interventions with more adult-focused than infant/dyad-focused components. The second grouping, 'interventions predominantly focused on the infant or parent-infant relationship,' included interventions with more infant and dyad-focused than adult-focused components.

During this analysis, ten infant or dyad-focused components were identified. These included: interaction coaching including support with how to read, understand and/or respond to infant cues; attachment-based exploration of the parent-infant relationship; information on infant temperament and/or developmental stages; practical support in coping with infant behaviours such as colic, fussing, feeding and sleeping; play therapy or sensory activities; treating the infant as a psychological agent; infant massage; 'good enough' parenting principles; support with transition to parenthood, and psychotherapeutic approaches examining the parent's patterns of relating to others, including exploration of maternal representations of the child, and examination of how the parent's own childhood informs the dyadic relationship.

Nine adult-focused intervention components were also identified. These were: cognitive behavioural strategies for mood difficulties, anxiety and PTSD; behavioural activation; mindfulness training; relaxation training; assistance with developing effective coping strategies for interpersonal problems and managing relationships; support with establishing a healthy lifestyle, and resource-based aid (e.g., access to free baby-care products). The intervention components matrix also included components related to the format of delivery (e.g., prenatal *v.* postnatal, individual *v.* group sessions).

All the intervention components and significant results were identified from studies and mapped onto the matrix. From this we were able to identify symmetrical effects and asymmetrical effects, as described in the Methods. The matrix also allowed us to consider whether there were common components among interventions that demonstrated significant improvements in outcomes of interest. The matrix is presented in Table 7.3.

7.3.7.1 How adult-focused interventions affected adults

Five studies investigated mostly adult-focused interventions (Burger et al., 2020; Challacombe et al., 2017; Milgrom et al., 2015; O'Mahen et al., 2014; Trevillion et al., 2020). Of these, three led to significantly improved parent anxiety scores, with medium to large effect sizes (Challacombe et al., 2017; Milgrom et al., 2015; O'Mahen et al., 2014). Trevillion et al. (2020) also demonstrated non-significant, small directional improvement in parent anxiety. As discussed earlier, Burger et al. (2020)

did not demonstrate such improvement, finding instead significant *adverse* treatment effects on parent anxiety.

7.3.7.2 How adult-focused interventions affected infants or the parent-infant relationship

While the intervention investigated by Milgrom et al. (2015) was mostly focused on the adult, as described above, this trial also found higher ratings of social and emotional competencies, as well as lower negative affect and greater high intensity pleasure, in infants in the intervention group compared to the control condition; these represented large effect sizes. O'Mahen et al. (2014) and Trevillion et al. (2020), two adult-focused, guided self-help interventions, also demonstrated directional non-significant improvements in parent-infant bonding. No improvements in infant or dyadic outcomes were demonstrated by the other adult-focused interventions (Burger et al., 2020; Challacombe et al., 2017).

7.3.7.3 How infant-focused interventions affected infants or the parent-infant relationship

Seven studies investigated mostly infant or dyad-focused interventions (Ericksen et al., 2018; Goodman et al., 2015; Holt et al., 2021; Lenze et al., 2020; O'Higgins et al., 2008; Stein et al., 2018; Werner et al., 2016). Of the seven studies within this grouping, two led to significant improvements in infant or dyad-related outcomes, with small effect sizes (Holt et al., 2021; Werner et al., 2016). Holt et al. (2021) found statistically significant improvements in positive parental involvement and parent-infant bonding in the intervention group compared to the control condition. Werner et al. (2016) found significantly lower rates of infant fuss/cry behaviour in the intervention group compared to the control condition. Non-significant directional improvements in infant socio-emotional competencies or the dyadic relationship were also found by two other studies (Goodman et al., 2015; Stein et al., 2018). No improvements in infant or dyadic outcomes were demonstrated by the other infant-focused interventions evaluated (Ericksen et al., 2018; Lenze et al., 2020; O'Higgins et al., 2008). As discussed earlier, Ericksen et al. (2018) found *adverse* treatment effects on the parent-infant relationship, but these were non-significant and likely the result of underpowered analyses.

7.3.7.4 How infant-focused interventions affected adults

While the interventions investigated by Werner et al. (2016) and Ericksen et al. (2018) were mostly focused on the infant, as described above, these trials also found evidence that post-intervention ratings of parent anxiety scores were significantly lower in the intervention group compared to the control condition; these represented small effect sizes within potentially underpowered studies. Similarly, Goodman et al. (2015), an infant-focused intervention, demonstrated non-significant directional improvement in parent anxiety. When comparing groups, parent anxiety scores also appeared to temporarily improve post-intervention in Holt et al. (2021). No such improvements in

anxiety were identified in the remaining infant-focused interventions (Lenze et al., 2020; O'Higgins et al., 2008; Stein et al., 2018).

7.3.7.5 Components common to successful interventions

The intervention components matrix allowed conclusions to be drawn regarding the extent to which interventions focusing on one partner would lead to improved outcomes in the other. Additionally, though the overall number of studies in the review was small, the components matrix allowed patterns to be observed among 'successful' interventions (i.e., those demonstrating significant improvements). As shown by Table 7.3, interventions that demonstrated significant (medium sized) improvements in parent anxiety shared a focus on cognitive behavioural strategies for mood or anxiety (Challacombe et al., 2017; Milgrom et al., 2015; O'Mahen et al., 2014). In addition, interventions demonstrating significant (small) improvements in infant and parent-infant relationship outcomes shared a focus on the exploration of distorted maternal representations (Holt et al., 2021; Werner et al., 2016). A component-by-component breakdown of adult-focused and infant/dyad-focused interventions is included in the SM (sections 3-4).

		Burger 2020	**Challacombe 2017***	**Milgrom 2015 † ***	**O'Mahen 2014***	**Trevillion 2020**	**Ericksen 2018***	**Goodman 2015**	**Holt 2021†**	**Lenze 2020**	**O'Higgins 2008**	**Stein 2018**	**Werner 2016 † ***
		Interventions focused predominantly on the adult					Interventions focused predominantly on the infant or parent-infant relationship						
1	Interaction coaching including support with how to read, understand and/or respond to infant cues						X	X	X	X	X	X	
2	Attachment-based exploration of parent-infant relationship						X			X		X	
3	Information on infant temperament and/or developmental stages						X	X		X			
4	Practical support in coping with infant behaviours such as colic, fussing, feeding and sleeping				X	X							X
5	Play therapy or sensory activities						X		X				
6	Treating infant as psychological agent											X	
7	Infant massage						X		X		X		
8	'Good enough' parenting principles				X				X				
9	Support with transition to parenthood, exploring changing roles and relationships, and balancing being a parent with being a person			X	X	X		X					
10	Psychotherapeutic approaches examining the parent's patterns of relating to others, e.g., how their own childhood informs dyadic relationship, or exploration of maternal representations of parent and child							X	X	X			X

11	Cognitive behavioural strategies for anxiety, e.g., exposure and responsive prevention exercises and cognitive-restructuring; psychoeducation on perinatal anxiety may also be included	X	X		X		X						
12	Cognitive behavioural strategies for mood difficulties, e.g., cognitive-restructuring and problem-solving; psychoeducation on perinatal depression may also be included	X		X		X							
13	Cognitive behavioural strategies for PTSD including exposure, imagery and rescripting work	X											
14	Behavioural activation	X			X								
15	Mindfulness training												X
16	Relaxation training			X					X				
17	Assistance with developing effective coping strategies for interpersonal problems, managing relationships and strengthening social networks			X	X	X				X			
18	Support with establishing a healthy lifestyle (e.g., sleep, self-care)			X	X	X			X				
19	Resource-based aid, e.g., access to free baby care products									X			
20	Predominantly postnatal delivery		X		X		X	X	X	~equal split	X	X	X
21	Predominantly prenatal delivery	X		X		X							
22	Group delivery						X		X		X		

23	Individual or dyadic delivery	X	X	X	X	X		X		X		X	X
24	Guided self-help model (print or e-resources with telephonic support)				X	X							
25	Intensive model (hours compressed to brief period)		X										
		Burger 2020	**Challacombe 2017***	**Milgrom 2015 † ***	**O'Mahen 2014***	**Trevillion 2020**	**Ericksen 2018***	**Goodman 2015**	**Holt 2021†**	**Lenze 2020**	**O'Higgins 2008**	**Stein 2018**	**Werner 2016 † ***

Table 7.3 Summary of components of interventions with the potential to improve parent anxiety, infant development or parent-infant relationship outcomes, split by study intervention focus; 1-10 - components relating to the infant or parent-infant relationship; 11-19 - components relating to the adult; 20-25 - components relating to the medium or format of delivery. A note on Stein et al. (2018) and Holt et al. (2021): as both these studies' intervention and active control groups were treated via a CBT programme prior to the main intervention of interest, only the main interventions are analysed and tabulated here (video feedback therapy and 'HUGS' therapeutic playgroup, respectively). * significant between group parent anxiety outcomes ($p < .05$); † significant between group infant/parent-infant outcomes ($p < .05$).

7.4 Discussion

The present review examined the efficacy of a range of perinatal interventions with regard to their effect on parent anxiety outcomes, parent-infant relationship outcomes, and socio-emotional development or temperament outcomes. Twelve studies were systematically retrieved and included, with no restrictions on whether parent anxiety outcomes were operationalised categorically or dimensionally. The analysis comprised of narrative reporting on the original studies, as well as identifying common components among successful interventions, i.e., those that led to significant improvements in outcomes of interest. The potential for predominantly adult-focused interventions to improve infant or dyad-related outcomes (and vice versa) was also explored. This analysis was conducted in an effort to focus on mechanisms of treatment outcomes that may be informative for trialling and translating future interventions. Importantly, statistical power was limited for the majority of studies included in this review; the evidence amassed must therefore be treated as preliminary and interpreted with caution.

7.4.1 Parent outcomes: symmetrical effects

Firstly, this review evaluated whether parent-focused perinatal interventions led to improvements in parent anxiety, and what commonalities were present among successful interventions. Of five interventions that were mostly adult-focused, three were found to significantly improve parent anxiety symptoms (Challacombe et al., 2017; Milgrom et al., 2015; O'Mahen et al., 2014). These three interventions all incorporated components from cognitive behavioural therapy (e.g., cognitive-restructuring) and generated medium to large effects; all interventions were delivered postnatally, except one (Milgrom et al., 2015). The prenatal, guided self-help intervention investigated by Trevillion et al. (2020) also demonstrated directional improvement in parent anxiety. Though these results were not significant, they were nonetheless consistent with the overall pattern of favourable results for CBT. By contrast, the prenatal CBT intervention investigated by Burger et al. (2020) found evidence that diverged from this. Prenatal CBT was related to a medium sized, significant increase in parent anxiety during pregnancy, as well as a (non-significant) elevation in anxiety post-intervention. The increase in anxiety during pregnancy was associated with adverse birth outcomes among infants of anxious parents in the intervention group, theorised to be a consequence of CBT exposure exercises and the increased physiological stress likely triggered by them.

Given links between prenatal physiological hyperarousal and adverse birth outcomes, researchers have previously questioned whether exposure-based cognitive behavioural therapies are safe during pregnancy (Arch et al., 2012). Despite this, reviews of clinical treatment for perinatal anxiety, which include numerous patients receiving care in the prenatal period, have found significant, medium to large effects of CBT programmes (Loughnan et al., 2018), as well as small between group effects and large within group effects of pooled controlled and uncontrolled CBT trials (Maguire et al., 2018).

This would appear to conflict with the findings from the amply powered study of prenatal provision investigated by Burger et al. (2020). However, it is important to note that the above reviews represent mostly small pilot studies, as well as a mixture of postnatal and prenatal patients (Loughnan et al., 2018; Maguire et al., 2018). In addition, reviews of psychotherapeutic interventions should be interpreted cautiously given the systemic issues with publication bias and allegiance bias in the field (Hengartner, 2018). Overall, the results from this review and the wider literature suggest that CBT for perinatal anxiety appears to be an effective treatment option for reducing parent anxiety, though modifications may possibly be needed for the prenatal period.

7.4.2 Parent outcomes: asymmetrical effects

Secondly, we looked at whether infant or dyad-focused perinatal interventions led to improved outcomes for the parent's anxiety and – if so - what successful interventions had in common. Of seven interventions focused on the infant or dyad, two were found to significantly improve parent anxiety outcomes (Ericksen et al., 2018; Werner et al., 2016). These two interventions shared no components (apart from a predominantly postnatal delivery format). In addition, Werner et al. (2016) was judged to be at high risk of bias, limiting interpretation of its effects.

Ericksen et al. (2018) evaluated a predominantly infant-focused intervention. Interestingly, this did not lead to significant improvements in infant outcomes, but led to reduced anxiety scores among parents. It is possible that equipping parents with a greater understanding of dyadic interaction and infants' regulatory needs increases belief in parenting capacities, in turn reducing anxiety levels. This is suggested by research showing that negative thoughts about parenting efficacy are associated with greater perinatal anxiety and depression (O'Mahen et al., 2012; Sockol et al., 2014). However, the improvements found by Ericksen et al. (2018) were not stable over time, and were based on underpowered analyses. In addition, though other dyad-focused interventions led to directional, non-significant improvements in parent anxiety outcomes when comparing intervention and control groups (e.g., Goodman et al., 2015; see also Holt et al., 2021), it was not possible to identify this in trials of other infant-focused interventions (Lenze et al., 2020; O'Higgins et al., 2008; Stein et al., 2018). Theoretical explanations may therefore be injudicious.

7.4.3 Infant and dyad outcomes: symmetrical effects

Next, we evaluated whether infant or dyad-focused perinatal interventions led to improved outcomes for the infant/dyad, and what successful interventions had in common. Of the seven interventions focused on the infant/dyad, two interventions were found to significantly improve infant or parent-infant outcomes (Holt et al., 2021; Werner et al., 2016). These generated small to medium effects, and shared a focus on distorted maternal internal representations of the child or parent. Non-significant directional improvements in infant socio-emotional competency and the dyadic relationship were further demonstrated by interventions looking at related approaches, including sensitising mothers to

their infants' 'uniqueness', and treating the infant as a psychological agent (Goodman et al., 2015; Stein et al., 2018). Improvements in dyadic or infant outcomes were not demonstrated in two small, underpowered pilot studies (Ericksen et al., 2018; Lenze et al., 2020), nor a study of an infant massage intervention (O'Higgins et al., 2008).

In the wider literature, evidence suggests that the dyadic relationship may be perturbed by distorted maternal representations. Maternal internal representations refer to memories from the parent's own childhood experiences that come to bear on parenting behaviour and identity, or perceptions of infants that are influenced by the parent's own characteristics and expectations (Vreeswijk et al., 2012). Distorted maternal representations may be a potential mechanism of interest in understanding how parent psychopathology leads to negative dyadic outcomes, with recent research suggesting a pathway from early parental trauma, through distorted maternal representations, to negative attachment outcomes (Ahlfs-Dunn et al., 2021). In addition, research has suggested that distorted maternal representations exert a negative influence on later infant socio-emotional functioning via the mediating role of disrupted caregiving (Guyon-Harris et al., 2021). It is also possible that conceptualising the infant as a unique agent, ontologically separate from the parent, may help prevent socio-emotional difficulties arising from overly involved dyadic relations (Feldman, 2021). Taken together, evidence from the present review and wider literature indicate that this approach may help improve the parent-infant relationship. However, a degree of scepticism for this line of argument is warranted, given two studies from this review (Holt et al., 2021; Werner et al., 2016) were judged to be of high risk of bias.

7.4.4 Infant and dyad outcomes: asymmetrical effects

Finally, we looked at whether *adult* focused perinatal interventions led to improved outcomes for the infant or dyad, and what any potentially successful interventions had in common. Of five adult-focused interventions, one intervention was found to significantly improve infant socio-emotional development outcomes (Milgrom et al., 2015), and three adult-focused, CBT-based interventions demonstrated directional improvements in parent-infant bonding (Burger et al., 2020; O'Mahen et al., 2014; Trevillion et al., 2020), though these did not reach significance. No such improvements were demonstrated by the remaining intervention (Challacombe et al., 2017). These results are somewhat at odds with evidence suggesting that perinatal interventions focusing only on parental mood are insufficient for establishing improvements in child/dyadic outcomes (Stein et al., 2014). However, most of these studies were not powered to detect infant or dyadic outcomes (Milgrom et al., 2015; O'Mahen et al., 2014; Trevillion et al., 2020), which may partly explain this inconsistency.

7.4.5 General conclusions

Overall, this review examined the efficacy of perinatal interventions with respect to parent anxiety outcomes, parent-infant relationship outcomes, and infant socio-emotional outcomes. Having set the

findings of this review in the context of the wider literature, we now offer three main conclusions. Firstly, interventions incorporating cognitive behavioural strategies (such as cognitive-restructuring) have the potential to demonstrate improvements in parent anxiety outcomes during the perinatal period, with the exception, perhaps, of exposure-based prenatal CBT (thought to associate with adverse birth outcomes in anxious parents; Burger et al., 2020). This finding extends our understanding of the efficacy of CBT for anxiety by suggesting its application in the perinatal period as in the general population (Cuijpers et al., 2016).

Secondly, interventions addressing distorted maternal representations, and potentially emphasising the infant's uniqueness/individual agency, may facilitate improvements in the parent-infant relationship or infant socio-emotional functioning. Though some studies indicative of this were potentially at high risk of bias (e.g., Holt et al., 2021; Werner et al., 2016), such evidence is aligned with a recent review of interventions for broad perinatal mental illness, which highlights the importance of perceiving the infant from his or her own worldview (Newton et al., 2020).

Finally, the present review provides preliminary evidence that adult-focused interventions might demonstrate improvements in infant or dyadic outcomes, and vice versa. This finding could be interpreted as a sign that improving adult wellbeing might exert a positive influence on infants via the process of coregulation (Cohn & Tronick, 1989; Tronick, 1998). However, this conclusion is based on studies limited by low statistical power, raising questions over its validity (Ericksen et al., 2018; Milgrom et al., 2015; Werner et al., 2016). In addition, transactional models of intervention have highlighted the importance of integrating both parents and children into treatment programmes, on the basis that socio-emotional difficulties in one partner tend to exacerbate difficulties in the other (Sameroff & Fiese, 1990). Such perspectives highlight the complexity inherent in designing interventions that are inextricably linked with family systems.

7.4.6 Implications for practice and future trials

The present review has several implications for clinical practice. Evidence from included studies indicates that interventions for perinatal anxiety may benefit from being informed by CBT strategies, such as cognitive-restructuring; however, it may be prudent to exercise caution with regard to performing exposure therapy work during the prenatal period. Efforts to mitigate impairments in infant socio-emotional development or the parent-infant relationship in the context of perinatal anxiety may also benefit from addressing distorted maternal internal representations, and highlighting the infant as a unique, individual agent. These practices could be incorporated in therapeutic approaches that focus on minimising distress within the parent-infant relationship, such as parent-infant psychotherapy or parent-infant video feedback therapy. When supporting families with perinatal anxiety, it may also be worth monitoring ways in which interventions focusing on one member of the parent-infant dyad have indirect benefits for the other. This information may help

scaffold discussions about the coregulatory nature of the parent-infant relationship, or act as a source of motivation for the anxious parent on their journey of recovery.

7.4.7 Implications for future intervention trials

The results of this review have implications for the design of future trials evaluating interventions for perinatal anxiety and infant outcomes. Firstly, trials may benefit from a focus on anxiety distinct from depression. Trials included in the present review often recruited from populations at risk of depression and anxiety, or depression only. This is representative of the traditional dominance of research attention on perinatal depression compared with other perinatal mental illnesses (Howard et al., 2014). While anxiety and depression often co-occur and share transdiagnostic features (Falah-Hassani et al., 2017; Grisanzio et al., 2018), the impact of the two conditions exerts substantively different effects on the parent-infant relationship in the first year of life (Feldman, 2007; Feldman et al., 2009). Anxious parents also have different biobehavioural patterns of relating to their infants compared with non-anxious or depressed parents (Amole et al., 2017; Granat et al., 2017; Smith, Jones, Charman, et al., 2021). As such, future trials examining interventions specialised for perinatal anxiety may prove to have more substantial benefits for the infants of anxious parents. An example of this approach is already underway (Wilkinson et al., 2016).

Secondly, trials focusing on the mechanisms by which perinatal anxiety leads to atypical or impaired socio-emotional function in infants are needed. From multifactorial, complex interventions, it is not clear which of these components maps to specific outcomes. Dismantling studies, which experimentally manipulate specific components of interventions, may elucidate which aspect of a perinatal intervention includes the active mechanism of change (Gaudiano, 2008; Papa & Follette, 2015).

Finally, this review has highlighted a need for more adequately powered analyses, which may aid more mechanistic analyses of moderation and mediation. This is in contrast to the pilot trials included in this review, which were not powered to detect small to medium effects (though in some instances power calculations were not stated at all; Challacombe et al., 2017; Werner et al., 2016). Where trials are conducted in the future, these should be accompanied by pre-specified and detailed analyses plans, allowing for an informed risk of bias assessment.

7.4.8 Strengths and limitations

This review is characterised by several strengths. The search strategy was comprehensive, including five electronic search databases from a range of disciplines, and multiple manual search procedures. Given perinatal anxiety is an under-researched area compared to other perinatal disorders, the broadness of search terms allowed us to retrieve records that included but did not foreground parent anxiety outcomes. Study screening, data extraction, and risk of bias assessments were conducted according to best practice in systematic reviewing; this included independent coding from two

reviewers during title and abstract screening, team verification of included studies, and a discrepancy check on risk of bias assessments.

The review was also subject to several limitations. Firstly, time constraints prevented the searching of grey literature. In addition, studies published in languages not spoken by the review team were excluded. Both of these factors may have introduced a degree of publication bias and precluded the inclusion of studies with more diverse samples. Our analytical strategy was also limited to a pragmatic, narrative synthesis, which introduces greater subjectivity than quantitative approaches such as meta-analyses. Our approach of grouping studies into 'infant/dyad-focused' or 'adult-focused' interventions was also reductive, and did not allow for conclusions to be drawn about interventions that targeted both parent *and* infant equally. Lastly, bias assessments were conducted by researchers at the pre-doctoral level. Recent controversies surrounding inaccurate bias assessments have highlighted the need for assessors with expertise in forensic numerical data analysis to be involved in quality assessment procedures for reviews of therapeutics (Brown, 2021; Davey, 2021; Meyerowitz-Katz, 2021).

IV. GENERAL DISCUSSION

CHAPTER 8 – General Discussion

This final chapter summarises the three empirical studies conducted for this thesis, as well as the systematic review. The methodological limitations and strengths of the work are then discussed, followed by an interpretation of the thesis findings in the context of the broader literature. Final recommendations for future research are presented, and the implications of the work for clinical practice are considered.

8.1 Synopsis

In the general introduction chapter, perspectives on the aetiology and intergenerational transmission of anxiety were outlined. Acknowledging the wider influence of biopsychosocial factors, it was concluded that anxiety develops in part through associations between parenting behaviour and child characteristics, as well as through the early fostering of emotion dysregulation in young children. Theoretical accounts have suggested that, in infancy, the child's regulatory system is principally shaped through dyadic interaction (Tronick, 1998). This system appears to operate differently in the context of over-stimulating parental behaviours associated with perinatal anxiety. Additionally, studies have indicated that higher physiological synchrony between parents and infants might act as an antecedent to impairments in emotion regulation in elevated-risk contexts. Given this, and given that arousal dysregulation is a core feature of anxiety, two empirical studies were conducted examining the physiological activity of high and low-anxiety parents and their infants. In the first of these, the aim was to examine whether parents and infants in the high anxiety group displayed elevated levels of physiological synchrony versus the low anxiety group. In the second study, the aim was to examine whether spontaneously generated, stimulating parenting behaviour yielded differential arousal responsivity among infants of parents in the high versus low anxiety groups.

Next, attention turned to the longitudinal relations between parenting behaviour, infant temperament and subsequent child self-regulatory problems over time. For this, a sample enriched for the development of autism was examined, on the basis that autism and anxiety often co-occur in children, and that rates of anxiety are common among parents of autistic children. The aim of this study was to examine how parenting behaviours commonly seen in anxious parents associated with infant temperamental traits in relation to later internalising behaviours in children.

Finally, to address the consequences of perinatal anxiety for the parent-infant dyad, and to inform future intervention research and clinical practice, it was important to consider the potential for perinatal treatments to intervene at the level of both the parent and the infant. A theoretically informed systematic review was therefore conducted, aiming to identify interventions that were effective for perinatal anxiety, infant socio-emotional development, and the parent-infant relationship. The review

also aimed to identify common components among successful interventions, and to understand how interventions targeting one member of the dyad could relate to improvements in outcomes for the other.

All the chapters of this thesis examined parent-infant interdependencies in the context of anxiety. Chapters 4 and 5 explored this physiologically at the state level ('the here and now'), and Chapters 6 and 7 examined this behaviourally at the trait level (over the course of months and years). Chapters 4, 5 and 7 were grounded within the mutual regulation model (Cohn & Tronick, 1989; Tronick, 2007; Tronick, 1998), with Chapter 6 rooted in the transactional model of socio-emotional development (Sameroff, 2010; Sameroff & Fiese, 1990, 2000). Both theories inhere a dynamic nonlinear systems perspective, conceptualising parent-child dyads as interactive systems that are embedded in and interact with their surrounding environments, and which change and stabilise over numerous time scales, from seconds to years (Thelen & Smith, 1998). In this way, the different chapters all sought to demonstrate the relational quality of anxiety as it comes to be expressed and regulated.

8.2 Summary of findings

The first empirical study (chapter 4) found support for its predictions. The principal hypothesis that physiological synchrony would be greater in dyads with more anxious parents was confirmed. Although preliminary analyses indicated that the two groups did not differ by mean heart rate or heart rate variability, overall, dyads in the more anxious group showed higher physiological synchrony compared to the less anxious group. It was also found that all parents would upregulate their own low arousal levels if their infant was in a state of high arousal, regardless of anxiety level; however, when both parent and infant were in a state of high arousal, only the parents in the low anxiety group would subsequently downregulate their arousal levels.

Chapter 4 went on to examine spontaneously generated instances of infant arousal and affect. It was found that low anxiety parents showed elevated physiological arousal following only the most extreme instances of peak infant arousal ('selective reactivity'), whereas high anxiety parents showed elevated arousal relative to small-scale changes in infant arousal. Subsequently, it was shown that more selective reactivity in the parent associated with faster infant recovery following naturally occurring peaks of negative affect. Taken together, the pattern of results indicated that more anxious parents (who were *more* physiologically synchronised with their infants, who were *less* likely to downregulate high dyadic arousal levels, and who displayed *less* selective reactivity in response to infant arousal peaks) had infants who tended to show slower recovery times from negative episodes.

The second empirical study (chapter 5) built upon these results. The study found that infants show elevated physiological arousal following instances of peak parental arousal, but only in the high parental anxiety group, as predicted. It was also expected that greater parental arousal would associate with more stimulating behaviours among parents with higher levels of anxiety. Some evidence for this

was found with respect to parental vocal behaviour. Specifically, in the high anxiety group, parents' high arousal levels were more likely to associate with high intensity vocalisations, and parents were more likely to vocalise in high intensity, long-lasting clusters (or 'bursts') compared to the low anxiety group. When examining how these more stimulating parenting behaviours related to infant hyperarousal, it was found that high intensity parental vocalisations were succeeded by sustained increases in arousal among both infants and parents in the high, but not the low, anxiety group.

By contrast, the longitudinal study (chapter 6) produced mixed results. It was initially predicted that either nondirective or sensitive parenting would moderate the relation between infant behavioural inhibition and later child internalising problems. Although a bivariate correlation was found between behavioural inhibition at 14 months and internalising behaviour at 36 months, there was no evidence to suggest a moderating role of parental behaviour. However, support was found for a separate hypothesis, with evidence showing that the level of toddler effortful control mediated the relationship between early nondirective parenting and later child internalising behaviour. Hence a pathway from nondirective parenting to low internalising behaviour via increased effortful control was identified in this population. An exploratory, post-hoc analysis also found evidence of moderated mediation, indicating that the effect of nondirective parenting on effortful control and subsequent internalising was stronger if infants were less inhibited.

Following these studies, a systematic review (chapter 7) explored the efficacy of perinatal interventions in relation to parent anxiety, infant socio-emotional development, and parent-infant relationship outcomes. Following a systematic search strategy and retrieval procedure, twelve studies investigating interventions were included for review. Of these, five demonstrated improvements in parent anxiety outcomes. In addition, three studies demonstrated improvements in infant or parent-infant relationship outcomes. Interventions addressing distorted parental internal representations and using cognitive behavioural strategies were among the most consistently effective. The review also explored the question of whether interventions predominantly directed at the adult could lead to improvements in infant-related outcomes, and vice versa. This was partly suggested by the results of three trials, though these were limited by statistical power. For the review more broadly, risk of bias assessments suggested results be interpreted cautiously.

8.3 Methodological strengths and limitations

Before detailing the limitations of this thesis, the main methodological strengths are outlined below. The first two studies are considered together due to their similar protocols (chapters 4 and 5). For these naturalistic studies of parent and infant physiology and regulatory processes, the use of wearable technologies afforded strong ecological validity. Specifically, these methods overcame the limits of standard approaches, where – under laboratory conditions – a discrete external stimulus is presented and then removed after a brief interval. In these instances, stimuli appear and disappear outside of

participants' control. The laboratory approach contradicts the reality of everyday life, where humans actively select what features of the environment to attend to on a second by second basis; a process of continuous recalibration (Cole et al., 2019; Wass, Smith, Clackson, et al., 2021). In addition, lab-based interaction is potentially constrained by the tacit pressure to be on 'best behaviour' while video-taped. In the two studies presented in this thesis, the use of wearable technologies and high-frequency data analytical techniques allowed for an examination of the ongoing, dynamic process of self-regulation, and its moment-to-moment changes in relation to a dyadic partner, while at home.

A further strength of these two naturalistic studies lies in the relative socio-economic and ethnic diversity of the samples. While not a comprehensive indicator of socio-economic status, the spread of household income in these studies was varied, marking a departure from the traditional skew towards wealthy developmental research samples (Nielsen et al., 2017). The ethnicity distribution was also well-matched with the region in which the research was conducted, which is uncommon in developmental research; a historic and ongoing issue (Syed et al., 2018). These circumstances arose from the recruitment procedure, which focused on involving groups typically excluded from research practices. Strategies included working with third party organisations with detailed knowledge of the local community, promoting a refer-a-friend programme among the participant pool, and demystifying the research process by sharing visuals of wearable technologies worn by previous participants. Though these studies were by no means fully representative, and recruitment methods were not novel, they went some way towards challenging the field's habitual reliance on convenience sampling.

The core strength of the longitudinal study differs from those described above, and relates instead to the use of a prospective design based on infant siblings of autistic children. As noted in chapter 6, this design has the benefit of allowing investigations into novel behavioural - as well as neurophysiological and genetic - markers that indicate early expression of neurodevelopmental and other co-occurring conditions (e.g., anxiety and ADHD; Shephard et al., 2019). Early markers such as these may help to design early support programmes for very young autistic and anxious children, and their families. In addition, the collection of data over numerous ages allows for the study of developmental trajectories (Zwaigenbaum et al., 2007). This helps to move away from conceptualising neurodevelopmental or psychiatric conditions in terms of static deficits (e.g., impaired cognitive control), and instead facilitates a consideration of developmentally plausible, dynamic and interactive models of causation. In this way, the study design allowed us to reflect on how socio-emotional difficulties might develop through 'cascade-like' patterns of systemic change over time (Johnson et al., 2002; Karmiloff-Smith, 1998, 2009).

In the review chapter, it was noted that an element of non-systematicity may be introduced if inter-reviewer reliability goes unchecked. If only one reviewer performs coding during the screening stage, subjective interpretation or miscomprehension of eligibility criteria may restrict the final number of

included studies. Similarly, if only one reviewer conducts the risk of bias assessments, their individual tendency towards leniency or strictness during assessment may lead to substantive differences in study risk status. This would strongly influence the findings of the review. Thus, the decision to use multiple independent reviewers for screening, and also for a subset of the bias assessments, helped to minimise individual differences in interpretation. Finally, the use of broad search terms across numerous databases, as well as manual search procedures, also likely helped to avoid a narrow scope. While search terms could have been even broader (for instance, including universal as well as clinical samples), the search strategy nonetheless represents a rigorous attempt to provide a comprehensive review. Aside from these strengths, and those discussed above, there are a series of methodological limitations to set out before going on to interpret the thesis findings. Though specific study limitations are discussed at the end of each individual chapter, there are some further, more general topics that require attention.

8.3.1 Sample size

The sample sizes of the two studies involving physiological data met intended recruitment targets. In addition, the sample in the longitudinal study was likely adequately powered to detect small to moderate effect sizes, though no calculations specific to the analyses were made (see Appendix E). Nonetheless, the relatively modest sample sizes may have led to issues such as Type II error. Meta-scientists have also suggested that much developmental and psychological research is underpowered, leading to inflated effect sizes and problems with reproducibility (Bishop, 2019; Davis-Kean & Ellis, 2019). Larger scale and highly powered international studies, such as the EU-AIMS Longitudinal European Autism Project (e.g., Loth et al., 2017; Tillmann et al., 2019), have sought to address these issues by aggregating data from multiple research groups across different countries.

8.3.2 Self-selection bias

Another pertinent issue to be considered among all the studies of the present thesis is self-selection bias. A source of sampling bias, self-selection bias relates to the various factors acting on individuals when they choose to take part in a given research project. One example of this, in the vast majority of developmental research, is the preponderance of maternal as opposed to paternal participants. This may be a consequence of numerous combined factors, e.g. paternity leave length, or traditional beliefs regarding caregiving practices (for review, see: Costigan & Cox, 2001). This is a particular issue in studies examining perinatal anxiety, given gender differences in parental behaviour are thought to associate with different child anxiety outcomes (though these differences may possibly reflect primary versus secondary caregiving roles, rather than gender; Majdandžić et al., 2018; Möller et al., 2015).

There are also other sources of self-selection bias that may have impacted the likelihood of participants taking part in the research of this thesis. In the studies presented in chapters 4 and 5, which involved a concerted recruitment effort to include families with low household incomes,

individuals may partly have been motivated to participate by the offer of financial remuneration in the form of shopping vouchers. Equally, however, individuals may have been less inclined or able to participate due to employment commitments; for example, shifts confirmed at short notice could lead to clashes with research visits, or increased fatigue arising from hours spent both working and caring could render research visits untenable. This may have led to a lower representation of families from low-income households than intended.

8.3.3 Dichotomisation and analytical techniques

One of the core critiques of this thesis - aside from the use of community samples, discussed below - is the use of artificial dichotomisation of a continuous measure (the GAD-7 screening tool for anxiety; Spitzer et al., 2006). This practice is understood to be majorly problematic due to the loss of information and power it produces (Altman & Royston, 2006; Dawson & Weiss, 2012; Royston et al., 2006). While acknowledging this, the decision to dichotomise the data was based on data analysis plans. Where it was possible to analyse variables continuously, this practice was adopted. However, for time series analyses, which make up the majority of the analyses, the temporal element added a third dimension to the data. For primary analyses in chapters 4 and 5, permutation-based clustering techniques were used, which are well adapted to cope with multiple comparison problems inherent in analysing data with a time dimension. However, these only work using dichotomised data (Maris & Oostenveld, 2007). To show that the effects found in these analyses held across a range of scores, quartile and quintile split analyses were also conducted to illustrate a more linear pattern of associations (as shown in appendices A and B).

A critique of artificial dichotomisation also invites a reconsideration of the debate on categorical versus dimensional approaches within psychopathology, which goes beyond the broader literature on dichotomisation. The GAD-7 screening tool, for instance, is a continuous measure that is frequently dichotomised as part of standard clinical practice, involving cut-offs (Spitzer et al., 2006). Statisticians working in the field of clinical research have also suggested that dichotomisation – ‘carving nature at the joints’ - ought neither be dismissed nor elevated, but viewed as one tool by which psychopathology researchers may make results more interpretable and accessible without gratuitous costs to statistical power (Pickles & Angold, 2003).

That said, a final critique of the analyses used in this thesis relate to their complexity and unfamiliarity; in particular, the use of the vector plot in chapter 4. This was necessary for avoiding statistical issues with more straightforward approaches (such as multi-level modelling, which leads to inflated bias when examining lagged effects; Allison, 2015; Hamaker & Muthén, 2020). However, it remains limited by the relative time and effort required for its interpretation.

8.3.4 Fatigue effects and confounding variables

In the longitudinal study, it was mentioned that infants participated in a battery of developmental and play-assessments while their parents filled in numerous questionnaires. It is also worth noting that these research visits ran over the course of a whole day, combining both behavioural and neurophysiological experimental tasks at 24 and 36 months of age. Although breaks were offered to participants, and visits were sometimes split over several days if needed, fatigue may nevertheless have influenced parent and infant behaviour, as well as parent responses on questionnaires.

In the studies examining physiology via the use of wearable technologies, it is also valid to suggest that confounding variables possibly exerted an effect. One measure that the equipment was not developed to detect was the infant's proximity to his or her parent. This factor may have, for instance, influenced the quantity and timing of intense vocalisations produced by the parent. Given the home environment is less controlled compared to the laboratory, there are also numerous other factors that could have potentially influenced the results, such as background noise or the number of other individuals in the locale (Wass, Smith, Daubney, et al., 2019). Arguably, the challenges of control are inherent in endeavours to understand self-regulatory processes in ecologically valid ways; however, the limitation still applies.

8.3.5 Ecological validity

Despite efforts to present ecologically valid research in this thesis, this was only partly successful. The longitudinal study was generally conducted in a laboratory setting, with researchers present in large part during visits. Though no experimental manipulation was used in this study, and the free-play interaction used to measure parental behaviour was designed to be as naturalistic as possible, the data collection nevertheless took place in a controlled and unfamiliar setting that may have influenced both infant and parental behaviour.

8.3.6 External validity

As mentioned in the limitations sections of each individual empirical chapter, caution must be exercised in generalising the thesis findings to clinical populations. This is particularly true of the empirical studies making use of the GAD-7 screening tool (Spitzer et al., 2006), which are most likely to have broad public rather than clinical relevance. That said, a genetic relationship has been identified between anxiety disorder diagnosis and the GAD-7 (Purves et al., 2020), suggesting study findings could be tentatively considered with respect to levels of mild to moderate anxiety among clinical populations (though not in relation to disorder-specific effects).

The findings arising from the longitudinal study also cannot be fully generalised to anxious parents and their children. Though parental anxiety is common among parents of autistic children, it is not

universal, and given the available data it was not possible to perform subgroup analyses related to parental psychopathology.

Additionally, the participants involved in all the studies of this thesis were from the UK. Though the first two studies involved families from diverse backgrounds, it is important to recognise that participants from Western, democratic societies like the UK are imperfect analogues for wider humanity (Henrich et al., 2010). In the systematic review, samples from more nations were included. However, these were only high-income nations from the Organisation for Economic Co-operation and Development (OECD). It is therefore not possible to generalise the findings of this thesis to low and middle-income countries, where the majority of the world's population live. It is worth noting, however, that the findings in this thesis are intended to inform domestic clinical research and practice, and may therefore be generalisable in this sense.

Finally, despite the likely high prevalence of mental health conditions among trans and non-binary parents during the perinatal period (Greenfield & Darwin, 2021), and despite the high rates of child anxiety among trans and non-binary youth (Chew et al., 2020), the studies in this thesis did not include data on trans or non-binary parents. This perpetuates the ongoing invisibility of this population in perinatal and developmental research (Darwin & Greenfield, 2019), and is a further example of limited external validity.

8.4 Interpretation of main findings

Having detailed these general limitations of the thesis, consideration is now given to the main findings and how these relate to the current literature. First, an interpretation is provided of the findings presented in chapters 4 and 5, after which the findings from chapters 6 and 7 are covered.

8.4.1 Chapters 4 and 5: the role of physiological synchrony and parental behaviour in infant dysregulation

Findings reported in chapter 4 of this thesis suggest that joint physiological processes are heightened among anxious parents and infants, potentially signifying a mechanism for the transmission of anxious arousal between parent and child. Previous studies investigating physiological synchrony in anxiety-risk dyads have produced results that both converge with and diverge from this finding. For instance, RSA synchrony has been investigated in a sample of anxious mothers and their infants in the 'reunion' episode of the still face paradigm. This study, measuring synchrony by averaging participant responses over repeated measures, found that small effects for physiological synchrony did not reach significance (Ostlund et al., 2017). In a study using time series analyses similar to those used in this thesis, there was also no evidence that interbeat interval synchrony occurred between fathers and adolescents at risk of anxiety (Roman-Juan et al., 2020). By contrast, a more recent study found evidence that dyads with PTSD characteristics exhibit higher parent-child RSA synchrony, while

resilient characteristics are associated with lower synchrony levels (also using time series analyses; Motsan et al., 2021).

There are several possible explanations for the differences among this small body of evidence. Firstly, null findings could be explained by methodological factors. For instance, averaging indices of participant arousal over a short time interval (e.g., one minute: Ostlund et al., 2017) is unlikely to be sufficient for capturing dynamic changes in arousal over time (Thorson et al., 2018). Secondly, it is possible that physiological synchrony is more likely to be detected in parents with children who are younger (Motsan et al., 2021) rather than older (Roman-Juan et al., 2020), on the basis that adolescents are more independent actors in dyadic interaction (Harrist & Waugh, 2002), and spend increasing amounts of time socialising with peers rather than family (Branje et al., 2012). Thirdly, it is possible that physiological synchrony is only present among anxiety-risk dyads when children interact with primary rather than secondary caregivers, having spent more time with that interaction partner - either in general or during early 'sensitive' periods of life (Feldman, 2015). It is also arguable that parent gender differences play a role in synchronicity, given what is known about behavioural differences between anxious parents of different genders (e.g., overprotective mothers, 'challenging' fathers; Majdandžić et al., 2018; Möller et al., 2015, 2016). However, it is not yet clear whether behavioural differences observed among anxious parents reflect variation in gender versus caregiving role (Möller et al., 2015).

Previous studies have not typically investigated how physiological synchrony in anxiety-risk dyads relates to child self-regulation. In chapter 4, while a relationship between physiological synchrony and infant recovery from negative affect was not directly examined, an indicative pattern emerged from multiple analyses. Results showed that anxious parents tended to be more physiologically synchronised with their infants, and less selectively reactive; low selective reactivity was also associated with slower infant recovery from negative affect. Further studies explicitly analysing the association between physiological synchrony and infant recovery are needed for confirmation, but as initial evidence, these results are consistent with findings suggesting that higher levels of physiological synchrony among elevated-risk samples are associated with poorer self-regulatory outcomes in the child (DePasquale, 2020; Suveg et al., 2016).

The findings from chapter 4 also support, and build upon, models that link parent-infant behaviour with the transdiagnostic development of resilience. Resilience is strongly associated with adaptive emotion regulation (Curtis & Cicchetti, 2007; Kay, 2016; Masten, 2018) and is defined by the ability to cope following adversity or threat to stability (Southwick et al., 2014). According to this theory, resilience is promoted through responsive parental behaviour that is fundamentally flexible and contingent on infant cues (Feldman, 2021). This is in contrast to intrusive parenting behaviour, known as a marker of anxiety (Beebe et al., 2011; Granat et al., 2017). One way intrusive parenting behaviour may impede the development of resilience in children is by restricting adaptable shifts

between moments of mismatch and reparation inherent in any interaction (Cohn & Tronick, 1989; Granat et al., 2017; Tronick, 1998). The finding from this thesis that anxious parents over-respond to small-scale physiological changes in their infant maps onto this, acting as an autonomic signal of over-sensitive, intrusive parenting behaviour. Similarly, the finding that anxious parents tend to sustain rather than dynamically downregulate high arousal levels within the dyad may represent a physiological instantiation of unresponsive parental behaviour.

Overall, the results from chapter 4 suggest that physiological synchrony is elevated among anxiety-risk dyads, and may be linked with dysregulatory processes in infants. In addition, the study implicates parental dysregulatory processes. This was suggested by the finding that more anxious parents tended not to downregulate high arousal levels in the dyad, as less anxious parents did. This absent regulatory process may be illustrative of anxious individuals' low self-awareness of internal bodily states (Khalsa et al., 2018) or poorer emotion regulation capacities (Hofmann et al., 2012; Mennin et al., 2007). While the study requires replication, the findings are preliminary evidence of how anxious parents' patterns of physiological change relate to atypical self-regulatory processes in both parents and infants.

Findings reported in chapter 5 extend the results discussed above by incorporating information on parental vocal behaviour. Specifically, high intensity parental vocalisations were suggested to represent a mechanism by which initial increases in arousal become amplified over time within dyadic interaction. This was suggested by the findings that, in the high anxiety group: (i) increased parental arousal levels associated with high intensity parental vocalisations, and (ii) high intensity parental vocalisations led to sustained increases in both parent and infant arousal. These results are suggestive of a cycle, from high arousal states, to high intensity vocalisations, back to a sustained state of high arousal again. Patterns like this are echoic of behavioural evidence from neurodevelopmental studies. For instance, autism research has shown that children's low interactive engagement leads to parents' reduced efforts to engage with their children, contributing to a cycle of non-engagement (Wan et al., 2019). Similarly, ADHD research has shown that hostile parenting behaviour, operationalised as a tendency to get into arguments and be angry with one's child, has been identified as both a cause and consequence of children's symptomatic behaviour (Harold et al., 2013). These examples have been linked together in a 'metastatic' theory of emotion dysregulation, which describes how actors interact with the social environment in such a way that increases or decreases in arousal become reinforced (Wass, 2021a). This is in contrast to allostasis, a dynamic, re-balancing regulatory process (Atzil et al., 2018; Atzil & Barrett, 2017).

To conclude this section, it remains to highlight the fit between the results of this thesis and the wider literature on contagion. Linked closely with the construct of synchrony, contagion has been described as the 'exchange or transfer of some aspect of emotion from one person to another' (Butler, 2011, p. 375; see also Bolger et al., 1989; Hatfield et al., 1993; Herrando & Constantinides, 2021). The level of

contagion observed between partners depends on the social environment; whether partners are proximal or touching (Chatel-Goldman et al., 2014; Waters et al., 2017), whether a partner uses maladaptive regulatory strategies (Waters et al., 2020), or whether a partner has an affective disorder (e.g., depression; Joiner Jr. & Katz, 1999). However, despite the putative role of the parent in regulating infant arousal states, studies have not directly examined arousal contagion in parent-child dyads where the parent's arousal system is likely to be dysregulated (as in the case of anxiety). Nor have studies of parental anxiety examined intra-dyadic chain-reactions, whereby an event causing hyperarousal in the adult leads to increased arousal in the child, subsequently amplifying the arousal levels of the adult, and so on; akin to the concept of the 'vicious cycle' within CBT (Butler et al., 2010; see also, network theory: Robinaugh et al., 2020). The present thesis expands our understanding in this area by suggesting that increases in infant arousal associate with increases in the arousal level of anxious parents, in turn triggering intense vocal behaviour, which further triggers an increase in infant arousal. These results move beyond ideas of arousal contagion to develop our understanding in two ways. Firstly, they highlight high intensity vocal behaviour as a process leading to amplification of dyadic partners' joint affective states. Secondly, they indicate a mechanistic role for parental vocal behaviour in the dyadic transmission of anxious arousal. This has potentially important translational implications, particularly for thinking about how vicious cycles of anxious arousal that occur between partners can be broken down.

8.4.2 Chapters 6 and 7: transactional models of socio-emotional development and intervention

Having contextualised the findings from chapters 4 and 5 on joint physiological processes within the dyad, it now remains to make sense of the results from chapters 6 and 7, derived from evaluating parent and infant relations at the behavioural level. The finding that more directive parenting in infancy associates with reduced toddler effortful control and subsequently higher levels of child internalising symptoms (36 months), within an autism-enriched cohort, raises the question of whether this parental behaviour acts as a proxy for caregiver psychological distress. Given the high prevalence of anxiety and other psychological disorders among parents of autistic children (Schnabel et al., 2020), and given what is known about the relationship of parental anxiety to directive, intrusive interactional behaviour (Hakanen et al., 2019; Ierardi et al., 2019; Kaitz & Maytal, 2005), it is plausible that parental behaviour is indicative of mood in this context. This view appears to be complemented by findings from a recent study examining the relation between caregiver psychological distress, infant self-regulatory temperament, and subsequent internalising symptoms in an autism-enriched cohort (Chetcuti et al., 2021). In line with previous findings from the depression literature (Allen et al., 2019; Roman et al., 2016), it was found that high caregiver psychological distress led to lower infant self-regulation and subsequently greater levels of child internalising symptoms. In a close parallel to the mediation model presented in this thesis, a study of typically developing children also showed that increased parental anxiety in infancy predicted lower effortful

control at 24 months, which, in turn, predicted higher levels of child socio-emotional difficulties at 36 months (Behrendt et al., 2020). Combined, these findings suggest that parents' anxious mood and behaviour have a role in shaping aspects of child temperament, and subsequent socio-emotional function, from an early stage of development.

An additional question raised by the findings outlined above is how transactional relations between parent and child characteristics contribute to early emotion dysregulation. A transactional model of child development explains 'behavioural outcomes as the mutual effects of context on child, and child on context' (Sameroff & Fiese, 1990, p. 136). This has traditionally been studied at the trait-level (e.g., 'does intrusive parental behaviour tend to be increased on average at T2, following an average increase in child anxiety at T1, and vice versa?') as opposed to the state-level (e.g., 'at times when a child is more aroused, does the parent interact more intrusively, and vice versa?'). Though it has long been established that parents and children exert some influence over each other in the early dyadic relationship (Abidin, 1992; Belsky, 1984; Pettit & Loulis, 1997), less is known about the time-scale of these processes. For instance, when in development they emerge, when children are most likely to be susceptible to them, and what the structure of these relations looks like on a day-to-day, moment-by-moment basis.

Though the study presented in chapter 6 found evidence of parent-to-child associations, the sample size was not sufficiently large to fit models capable of detecting further child-to-parent associations. In addition, while a post-hoc, moderated mediation analysis indicated that children might be differentially susceptible to the effects of parental behaviour, this was not a hypothesis-driven, confirmatory analysis. However, transactional associations have been investigated in recent research with young children. In a large sample of typically developing children, multi-group longitudinal path analyses were used to identify transactional associations between parental anxiety and child self-regulation as early as the first three years of life (Behrendt et al., 2020). These findings are in line with previous research with samples including typically developing children (Pesonen et al., 2008) and atypically developing children (Neece et al., 2012), which found a transactional relationship over time between increased parental stress and low child self-regulatory behaviours. Cross-lagged models have also been used in an autism-enriched study examining similar associations, but these analyses were underpowered, potentially explaining the finding of only parent-to-child, and not child-to-parent associations (Chetcuti et al., 2021). Taken as a set, these findings have important implications for early intervention programmes aiming to mitigate the development of emotion dysregulation in children of anxious parents. Under a transactional model of socio-emotional development, interventions cannot be successful if changes are made in only one member of the parent-child dyad.

The findings of the systematic review presented in this thesis, though they must be interpreted cautiously, may help inform transactional models of intervention for early developing emotion dysregulation (Sameroff & Fiese, 1990). Specifically, the review suggested one way that perinatal

interventions – which typically focus on the parent's presenting mental health need - could incorporate a focus on the infant. Two perinatal interventions addressing distorted parental representations of their infant demonstrated improvements in infant socio-emotional function, or parent-infant interaction (Holt et al., 2021; Werner et al., 2016). Though these interventions were multifactorial and involved other intervention components, the pattern of results across trials suggested that infant regulatory processes are partly shaped by the parent's perception of their child as distinct from themself. This is in line with a recent review indicating that, for a broad range of perinatal mental illnesses, infant outcomes are strengthened by interventions helping the parent to see the infant differently; to perceive the infant's 'world, needs, and unique perspective' (Newton et al., 2020). Being able to differentiate the infant from the adult self may promote infant outcomes in a process akin to overcoming 'enmeshed relations.' In family systems theory, enmeshed relations refer to relationships that become dysfunctional when they impede the separate functioning of individuals involved (Green & Werner, 1996). While the early parent-infant relationship is necessarily inter-dependent, a degree of autonomy or 'looseness' in interaction may nonetheless be instrumental for infants' emerging self-regulatory development (Beebe & Lachmann, 2020; Feldman, 2021; Granat et al., 2017). This is likely to be especially applicable in the context of perinatal anxiety, where intrusive parental behaviour - strongly associated with interference in infant autonomy - is common (Feldman, 2007; Hauser Kunz & Grych, 2013; Kaitz & Maytal, 2005).

To develop perinatal anxiety interventions in the future, there may be benefit in considering the example of research on child anxiety treatment. Perinatal anxiety interventions often focus on mitigating the parent's primary diagnostic symptoms, with infant involvement increasingly recognised as a factor that may help promote infant outcomes (Marchesi et al., 2016; Newton et al., 2020). Inversely, child anxiety interventions are principally focused on mitigating the child's primary diagnostic symptoms, with parental involvement thought to play some role in child outcomes (Wei & Kendall, 2014). However, research into both child and perinatal interventions has not conclusively identified how secondary partners might be most effectively integrated within treatment to optimise outcomes. The systematic review presented in this thesis shows that a range of infant-oriented components have been included in perinatal interventions; however, due to the nascence of this research area, such trials do not represent efforts to identify the effect of individual components. It is therefore not possible to robustly infer the superiority of one infant-oriented component over another. In the child intervention literature, which is better established, there is greater awareness of the need for dismantling studies, and investigation into how, rather than simply if, parents can be involved within interventions to produce optimal outcomes (Creswell, Cruddace, et al., 2020; Creswell, Waite, et al., 2020). Child anxiety researchers have also gone further to consider factors that may moderate the effects of dyadic partner involvement, such as child age (James et al., 2020), as well as parent negativity and child oxytocin levels (implicated in parent-child interactional processes; Lebowitz et

al., 2021). As the research on perinatal anxiety treatment develops, it may benefit from adopting a similarly targeted and mechanistic approach. Specific examples of this are suggested below.

8.5 Future directions

To further our understanding of the mechanisms of developing emotion dysregulation, there are two programmes of work for future research that follow logically from this thesis: addressing the methodological shortcomings of the studies conducted, and building upon the overall findings.

Efforts to overcome the limitations of this thesis should begin with replication. This would involve conducting high-powered studies with a greater diversity of participants, including those from sex, gender and ethnic minorities, as well as from clinical populations with moderate to severe levels of anxiety. In studies examining mechanisms of emotion dysregulation at the state rather than trait level, analytical techniques allowing for the inference of causal chains of events would also be advisable; neuroimaging research offers applicable examples (Friston et al., 2003).

For future studies with clinical populations, researchers would need to consider several additional variables. For instance, it would be useful to examine discontinuous measures of parent anxiety, such as diagnostic classifications, alongside continuous measures. This would allow for conclusions to be drawn regarding disorder-specific associations. If psychophysiology measures were being collected, close attention would also need to be paid to adult medication, in case this exerted a confounding influence.

Several novel studies could also be conducted in light of the thesis limitations. Firstly, with adequate power, a fully cross-lagged model including data from multiple timepoints could be used to analyse transactional pathways to parent and children's socio-emotional difficulties, allowing for greater insight into the directionality of effects. Secondly, potentially confounding variables could be taken into account in naturalistic, home-based research by incorporating proximity sensors within wearable technologies; these could be used to probe for the influence of parent-infant closeness during interaction, a factor thought to play a role in both child and family functioning (Feldman, 2007; Feldman et al., 2003). Finally, to facilitate the assessment of early parent-infant synchrony in low resource settings across the globe, cost-effective and clinically-usable tools could be adapted for use, such as automated, video-coding systems that have been recently developed using machine learning principles (Addyman et al., 2019).

To build on the findings of this thesis, researchers could use models with multiple waves of data collection. For example, to extend the notion that the early parent-infant dyadic system has a coregulating role over affect, longitudinal studies could be conducted to examine if and when children transition from coregulatory to self-regulatory systems over time. Put another way, studies could examine whether affective states become progressively less contingent on others throughout development. It would also be interesting to examine how these developmental pathways differ

depending on the level of parental anxiety, given the tendency for anxious parents to be overinvolved partners. Longitudinal path analyses could also be used to examine whether physiological synchrony acts as a mechanism of the intergenerational transmission of anxiety (DePasquale, 2020), by mediating the relationship between infant exposure to perinatal anxiety and child anxiety outcome.

A crucial goal for the development of perinatal anxiety interventions is identifying how best to involve infants in treatment so as to promote their socio-emotional development outcomes. Future perinatal interventions may benefit from targeted intervention trials seeking to isolate the 'critical ingredient' of treatment for infant outcomes, as well as large trials powered to detect the role of moderating factors on treatment outcomes. These would be strengthened by further foundational research identifying the factors most likely to perturb anxious parents' interactions with their infants during the first year of life. Examples suggested by the novel findings of this thesis, and the wider literature, include arousal-triggering parental vocal behaviour, 'vicious cycles' of intra-dyadic arousal, highly synchronous parent-infant interaction, and parental over-responsivity to minor stress events in the infant. It would be useful to directly examine whether these processes associate with poorer socio-emotional outcomes in young children over time.

On a more general note, it might be helpful for theorists to conduct a formal integration of the two core models of emotion dysregulation development described in this thesis: the mutual regulation (or 'coregulation') model (Cohn & Tronick, 1989; Tronick, 2007; Tronick, 1998), and the transactional model (Sameroff, 2010; Sameroff & Fiese, 1990, 2000). The coregulatory perspective suggests that infant affect regulation occurs through dyadic processes, and is strengthened through responsive, contingent parenting that scaffolds the child's later self-regulatory capacities. By contrast, the transactional model holds that children's emotional development is determined not only by aspects of their social environment (e.g., parental emotion dysregulation; anxious parental behaviour), but also by the child's influence over the social environment (e.g., effect of infant hyperarousal on parental behaviour). While the two models are related, these perspectives have potentially different implications for the development of interventions for emotion dysregulation in young children.

8.6 Implications for clinical practice

As discussed throughout this thesis, little attention has been paid to treatments aiming to counter the consequences of perinatal anxiety for infants. Though CBT for perinatal anxiety is recommended for routine provision by national clinical guidelines, there are also surprisingly few trials on the efficacy of such treatment for parents themselves (Loughnan et al., 2018). This may be a consequence of apprehensive attitudes towards the exposure component of CBT for anxiety - which involves confronting a known stressor - given associations between prenatal physiological stress reactivity and adverse birth outcomes (Arch et al., 2012). Findings from the present systematic review appear to support this concern; an amply powered trial showed that infants' gestational ages were lower in the

prenatal CBT group compared to the control condition if they had anxious parents (Burger et al., 2020). While there is evidence that CBT is effective for reducing anxiety symptoms across both the prenatal and postnatal period (Challacombe et al., 2017; Milgrom et al., 2015; O'Mahen et al., 2014; see also reviews: Loughnan et al., 2018; Maguire et al., 2018), caution may nonetheless be needed with respect to prenatal provision. Potential risks to the developing fetus could be reduced by minimising exposure components of prenatal CBT for anxiety, or increased monitoring of fetal development during prenatal CBT treatment.

Aside from these precautionary principles, there are also several other implications of the thesis findings that may be used to inform clinical practice. For instance, evidence from all three empirical studies is suggestive of systemic approaches to both child and parent functioning. Systemic practices focus on distress arising from the context of relationships, and cover treatments such as parent training, parent-delivered behavioural programmes, and parent-infant psychotherapy (Carr, 2019). In infancy, parent training has been achieved through video feedback therapy (Juffer et al., 2008). This approach uses reviews of video recordings to help individuals learn about their own behaviour as well as that of their interaction partner, with the aim of developing insight and behavioural change (Aldred et al., 2018). Parenting behaviours highlighted in this thesis (e.g., nondirectiveness, high intensity vocal behaviour) could be reviewed using video feedback methods in the future, with clinician and parent collaboratively observing the effect of this on parent-infant interaction. Such treatment might nurture parental self-blame for having caused atypical infant behaviour (as has been noted within early intervention research for autism; Manzini et al., 2021), so maintaining a non-judgemental and strengths-based approach is likely to be important.

Alternatively, clinical practice may be informed by the novel physiological findings of this thesis. The finding that anxious parents tend not to downregulate high arousal levels in the parent-infant dyad, combined with the finding that anxious parents over-respond to small physiological changes in their infants, provides initial evidence that greater parental body awareness may be a useful target for intervention. Body awareness may include conscious perception of one's own bodily sensations related to internal organ function, or related to the social environment (interoception and exteroception respectively; Vaitl, 1996; Valenzuela-Moguillansky et al., 2017). Empirical evidence has linked interoceptive awareness and emotion regulation, demonstrating a connection between a lack of internal body awareness and affective disorders, including anxiety (Craig, 2014; Khalsa et al., 2018; Paulus, 2007). Several therapeutic approaches related to interoception have also been suggested for improving emotion regulation in anxious adults, including heart rate variability biofeedback therapy (Goessl et al., 2017), mindfulness-based stress reduction (Nyklíček et al., 2013), and mindful awareness in body-oriented therapy (Price, Thompson, Crowell, & Pike, 2019; Price, Thompson, Crowell, Pike, et al., 2019; Price & Hooven, 2018). In the perinatal period, these approaches could support anxious parents with gaining more awareness of and control over their own arousal levels,

helping to bring down high arousal levels across the dyad. Parents could also be supported to perceive how infant hyperarousal triggers increased arousal in the parent, and how this in turn affects the infant. By becoming familiar with this dynamic, parents may become better able to downregulate their own arousal during difficult episodes, protecting against mutually reinforcing stress states.

Arousal-triggering parental vocal behaviour may also prove a useful target for intervention. By adopting a parent-mediated, cognitive behavioural model, treatment could focus on formulating both parent and infant distress as a product of a vicious cycle, in which high physiological arousal in the anxious parent triggers intense parental vocal behaviour, which subsequently triggers increases in infant arousal; thus, in turn, increasing parent arousal. Intervening by identifying and averting high intensity vocal behaviour in the parent may help to break the cycle, helping to reduce stress in both partners, and foster calmer dyadic relations. This approach may have particular pragmatic utility because, as previously highlighted, CBT is already the most commonly used model for perinatal anxiety in the UK.

Finally, it is worth mentioning several caveats. Firstly, the clinical implications described here are couched in the biomedical model, characterised by a focus on impairment or deficits related to perinatal anxiety and subsequent child development. This model makes it hard to assume ability, or potentially advantageous traits in those who are more likely to be anxious (Manzini et al., 2021). Defining anxiety by its disadvantageous components might also impede the development of interventions whose efficacy is dependent upon more advantageous traits (e.g., reflexivity, deliberation; Kurth, 2018). In addition, while it is important to develop theoretically informed, targeted interventions for perinatal anxiety, it is essential to note that this condition commonly co-occurs with other mental health difficulties, medical needs and socio-economic stressors. Ultimately, intervention programmes incorporating knowledge of families' more complex needs are likely to be necessary, and may be developed through greater dialogue with and involvement of service users during research practice.

8.7 Concluding remarks

The contributions of this thesis arise from a multidisciplinary approach, including a systematic review of clinical populations, as well as longitudinal and naturalistic-electrophysiological research among community samples. At the state level, the identification of interrelatedness in physiological activity specific to anxious parents and their infants provides a first step towards understanding joint mechanisms of emotion dysregulation in early childhood. In addition, at the trait level, evidence from an autism-enriched sample suggests transactional relations between parental behaviour and infant temperament are linked with early socio-emotional difficulties in young children. Consequently, the concept of emotion dysregulation arising from parent-infant relations may benefit from further examination using multi-level approaches. Future research may move the field forward by

incorporating cross-lagged, longitudinal designs and naturalistic approaches within well powered community and clinical samples, providing further insight into the mechanisms of emotion dysregulation and anxiety development in children. Further evidence on how affective states are regulated in a relational sense will provide both theoretical and clinical benefit. Theoretically, knowledge of socio-emotional development and developmental psychopathology will be enhanced. Clinically, interventions in the perinatal period may become more targeted towards improving child, as well as parent, outcomes.

V. APPENDICES

Appendix A - Supplementary Materials for: Anxious parents show higher physiological synchrony with their infants

The following supplementary materials accompany the publication presented in chapter 4, which investigates the physiological processes in parents with higher or lower levels of anxiety, and their infants (Smith, Jones, Charman, et al., 2021). Subheadings and figure captions have been adapted to conform to the general thesis format.[17]

1 Supplementary Methods

1.1 Experimental participant details

This sample size was selected prior to the commencement of the study based on power calculations presented, and approved by peer review, in the funding application that supported this work (ESRC ES/N017560/1). Exclusion criteria included: complex medical conditions, skin allergies, heart conditions, parents below 18 years of age, and parents receiving care from a mental health organisation or professional.

1.2 Additional information for parent screening

The relationship between increased exposure to stressful life events and risk of generalised anxiety disorder is well established (Blazer et al., 1987; Francis et al., 2012; Muhsen et al., 2008). A life events scale was therefore administered, calculating the quantity of stressors (e.g., serious illness or injury, bereavement, abuse, unemployment, relocation, or contact with the criminal justice system) experienced by the participant or immediate family in the previous 12 months. In line with expectations, participants in the high anxiety group indicated significantly higher quantities of stressful life events, $t(76) = -3.30$, $p = .001$.

1.3 Autonomic data parsing

ECG data were parsed to identify RR intervals using custom-built Matlab scripts, employing an adaption of a standard thresholding procedure (Wass et al., 2015), and verified post hoc via visual inspection. Heart rate variability (HRV) was calculated using the PhysioNet Cardiovascular Signal Toolbox (Vest et al., 2018). A 60-second window with an increment of 60 seconds was implemented, and the default settings were used with the exception that the min/max interbeat interval was set at 300/750 milliseconds for the infant data, and 300/1300 milliseconds for the adult data. The Root Mean Square of Successive Differences (RMSSD) measure was taken to index HRV, but other frequency domain measures were additionally inspected and, as expected (Vest et al., 2018), showed

[17]For further information on the inclusion criteria for this study, see Appendix B.

highly similar results. To parse the actigraphy data, we first manually inspected the data, then corrected artefacts specific to the recording device used, and then applied a Butterworth low-pass filter with a cut-off of 0.1Hz to remove high-frequency noise.

1.4 Justification for use of composite autonomic arousal measure

Previous research has identified strong patterns of tonic and phasic covariation between different autonomic measures collected from infants (Wass, Clackson, & de Barbaro, 2016; Wass, de Barbaro, & Clackson, 2015). Here, we include plots showing that the present analyses replicated and extended these results. The plots only show the sections of the data when participants were at home, comparing sections in which the infants were awake and asleep. Figure S1a shows cross-correlation plots examining the relationship between heart rate and movement. In both waking and sleeping sections, the zero-lag correlation is 0.5. Figure S1c shows how these zero-lagged correlations vary on a per-participant basis. Figure S1b shows an illustrative sample from a single participant. Sleeping sections show very low movement levels and lower heart rate. Of note, heart rate and movement do still inter-relate during the sleeping sections of the data (Figure S1c), albeit that the variability in heart rate and movement is lower. Panels d-f of Figure S1 show similar relationships between heart rate and HRV, illustrating the strong and consistent negative relationships that were observed between these variables, as predicted. Based on these data, and following the approach we have taken in previous research (de Barbaro, Clackson, & Wass, 2016), we elected to calculate a composite measure of arousal for the analyses presented in the main text. This was done by calculating the natural logarithm of the actigraphy data, inversing the HRV data, epoching all three measures into 1Hz epochs, calculating a *z*-score separately for each participant and each measure, and then averaging the three measures into a single *z*-score.

Extensive previous research has identified fractionation, and differentiation, within our autonomic nervous systems (Lacey, 1967; Levenson, 2014; Quas et al., 2014; Jänig & Habler, 2000; Kreibig, 2010) – suggesting, for example, that the sympathetic and parasympathetic subdivisions may, to an extent, operate in a non-additive manner (Samuels & Szabadi, 2008). Although indubitably true, these findings should not be seen as rendering incorrect our treatment of autonomic arousal as a one-dimensional construct here. Like many other arguments concerned with general versus specific factors, the question is rather one of the relative proportions of variance that can be accounted for by a single common factor in comparison with the variance accounted for by the sum of specific factors (Graham & Jackson, 1970; see Wass, 2018).

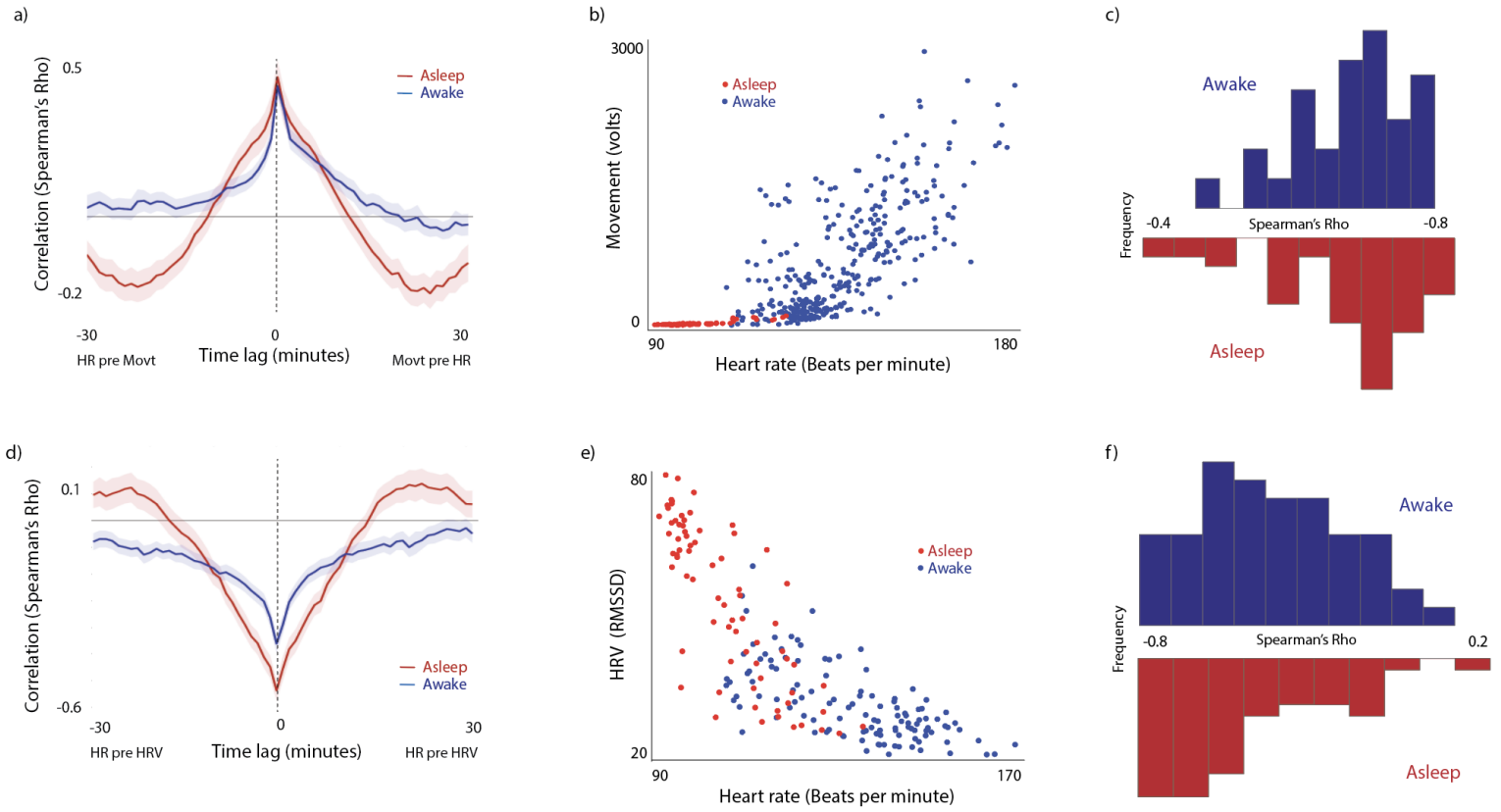

Fig. S1 Illustrating the relationship between the individual physiological measures included in the composite measure. (a) Cross-correlation of the relationship between heart rate and movement. (b) Scatterplot from a sample participant. Each datapoint represents an individual 60-second epoch of data. (c) Histograms showing the average zero-lagged correlation between 60-second epochs, calculated on a per-participant basis and then averaged. (d)-(f) Equivalent plots for heart rate and heart rate variability.

1.5 Home/Awake coding

Coding when participants were at home was performed using the global positioning system (GPS) monitors built into the recording devices. The position of the participant's home was calculated based on the postcode data that they supplied, and any GPS samples within a circa 50m area of that location were treated as 'home' (corresponding to the accuracy of the GPS devices that we were using). To identify samples in which infants were sleeping, parents were asked to fill in a logbook identifying the times of infants' naps during the day. This information was manually verified by visually examining the actigraphy and ECG data collected, on a participant-by-participant basis. Actigraphy, in particular, shows marked differences between sleeping and waking samples (see SM, Figure S1 and So et al., 2005), which allowed us to verify the parental reports with a high degree of accuracy.

1.6 Calculation of permutation-based temporal clustering analyses

To estimate the significance of the time-series relationships in the results, a permutation-based temporal clustering approach was used. This involved two different analytical techniques. One analysis (Method 1) looked at whether 'peak' reactions were observed relative to a known 'Time=0' moment (such as relative to a particular event). This was used for the analyses in Hypothesis 3.

The other analysis (Method 2) examined temporally contiguous patterns of change in instances where the centre-point of the expected response window was unknown, or unimportant (Maris & Oostenveld, 2007). This was used for the analysis in Hypothesis 1 and 4.

Method 1: This analysis examines whether significant clusterings of elevated values around time=0 are observed. To estimate this, the following procedure was used. If y is Time=0, then, for the first time interval (t=1), the observed data from y-1 to y+1 was excerpted (i.e., from 1 bin before to 1 bin after time=0). The proportional size of the excerpted data relative to the entire dataset was used to calculate a centile threshold (e.g., the central 10% of the data). The entire dataset was then rank ordered, and the highest 10% of the data was calculated. The proportion of highest data that was contained within the central segment of the data was also calculated. The same calculation was then repeated for increasing values of t ranging from 1 to the total time window of the sample. Thus, for each value of t, if the observed data had been 'perfectly' ordered, with the highest value at time=0 and gradually decreasing values at increasing time lags, then the proportion of highest data contained within the central segment of data would always be 1. In this way, we quantified whether higher values were more commonly observed around the time=0 point in the data.

A thousand random datasets were then generated with the same dimensions as the original input data. To ensure that the same level of autocorrelation was present in the simulated data as in the original datasets, multivariate autoregressive (AR) models were fitted to each sample included in the original dataset using the Matlab function ARfit.m (Neumaier & Schneider, 2001). The matching AR

parameters were used to generate each of the random datasets using the Matlab function ARsim.m (Neumaier & Schneider, 2001).

For each random dataset, the same series of calculations as described above was performed. In this way we estimated how, for each of the random datasets, the proportion of highest data contained within the central segment of the data varied across increasing time windows from the time=0 point. The results obtained from the random datasets were used to generate a histogram, and the likelihood of observed results being obtained by chance was calculated by comparing the observed values with the randomly generated values using a standard bootstrapping procedure. Thus, a p value of <.01 indicates that the observed concentration of high values around the time 0 moment was observed in 10 or fewer of the 1000 simulated datasets generated for that time window.

Method 2: This analysis examines whether temporally contiguous patterns of change are observed in situations where the centre point of the expected response window is unknown or unimportant (Maris & Oostenveld, 2007). In each case, the test statistic was calculated independently for each time window (e.g., in the case of Figures 4.3a-b, an independent samples *t*-test). Series of significant effects across contiguous time windows were identified using an alpha level of .05. A thousand random datasets were then generated using the same procedures as described for Method 1, above. The same sequence of analyses was repeated, and the longest series of significant effects across contiguous time windows was identified. The results obtained from the random datasets were used to generate a histogram, and the likelihood of observed results having been obtained by chance was calculated by comparing the observed values with the randomly generated values using a standard bootstrapping procedure. Thus, a p value of <.01 indicates that an equivalent pattern of temporally contiguous group differences was observed in 10 or fewer of the 1000 simulated datasets created.

2 Supplementary Results

2.1 Hypothesis 1: Synchrony between infant and parent arousal – differences contingent on parental anxiety – further analyses

In addition to the analyses presented in the main text, we also examined how the association between parent and infant arousal varies as a function of increasing the time-lag between the two variables (Fig 4.3b). In the low anxiety group, significantly negative associations were observed between parental arousal at time t and infant arousal at time t+6 to 10 minutes, suggesting that lower levels of parent arousal were associated with subsequently elevated levels of infant arousal (p < .001 after correcting for multiple comparisons using permutation-based cluster analysis; see SM section 1.2). This relationship was absent in the high anxiety group sample. No significant group differences were observed in the opposite direction, when considering how infant arousal forward-predicted subsequent levels of parental arousal. These results indicate that, in the low anxiety group, lower levels of

parental arousal were associated with subsequently higher levels of infant arousal. This relationship was absent in the anxious parent group.

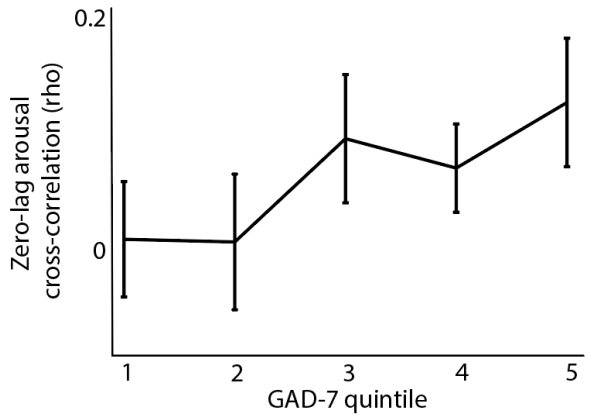

Fig. S2 Relationship of GAD-7 score to arousal cross-correlation; the same relationship shown in Figure 4.3a, but subdivided using a quintile split by GAD-7 score. The raw GAD-7 scores contained in each quintile group were: 1st quintile – 0; 2nd quintile – 1; 3rd – 2; 4th – 3 to 5; 5th – 6-17.

Appendix B - Supplementary Materials for: Vocalisation and physiological hyperarousal in parent-infant dyads where the parent has elevated anxiety

The following supplementary materials accompany the main material presented in chapter 5, which investigates differences in parental vocal behaviour, and corresponding changes in dyadic arousal, among parent-infant dyads in high and low anxiety groups.

1 Participant demographic details

This sample size was selected prior to the commencement of the study based on power calculations presented, and approved by peer review, in the funding application that supported this work (ESRC ES/N017560/1). Inclusion criteria included: parental age of at least eighteen years or above; infant age of at least 6 months and no older than 15 months; willingness and ability of participant to provide informed consent (with parent providing consent on behalf of their infant); in good health/not referred to a mental health service at present. Exclusion criteria included: complex medical conditions, skin allergies, heart conditions, parents below 18 years of age, and parents receiving care from a mental health organisation or professional.

2 Exclusion/outlier criteria

A consistent outlier-detection strategy was applied equally for all analyses, by excluding outliers that were >2 inter-quartile range (IQR) from the mean, to avoid violating the assumptions of the statistical tests being conducted.

3 Autonomic data parsing

3.1 Autonomic ECG data parsing

ECG was recorded at 250Hz. Analysis of the interbeat intervals (IBIs) was performed using custom-built Matlab scripts. These scripts were designed through an extensive piloting process to be optimal for the ECG device used for this study. First, data were parsed using a simple amplitude threshold (see, e.g., Aurobinda et al., 2016 for a similar approach), with R peaks identified as moments where the raw ECG signal exceeded the threshold value. Initially, the threshold value was set high; the same process was then repeated at incrementally decreasing thresholds.

At each threshold value, the R peaks identified were automatically subjected to the following checks. Firstly, minimum temporal threshold check: does the R peak occur at a time interval of greater than 300 milliseconds since the previous R peak (corresponding to a heart rate of 200 BPM). Secondly, maximum temporal threshold check: does the R peak occur at a time interval of less than 850 milliseconds since the previous R peak (corresponding to a heart rate of 70 BPM). And thirdly, maximum rate of change check: when we calculate the R to R interval between this peak and the subsequent peak, and compare it with the R to R interval between this peak and the previous peak, is

this difference less than 300 milliseconds? In setting these threshold values, careful attention was paid to visual inspection to determine the maximum and minimum 'genuine' heart rates observed in our infant data. In setting the maximum rate of change criterion, careful attention was paid to identify the maximum rate of vagally mediated heart rate changes in infants.

Figure S1 shows a sample screenshot from the Matlab processing algorithm that was used. Two separate types of artefacts are shown. The first, highlighted by the call-out figures *a* and *d*, are instances where the ECG signal for a particular beat was lower than the threshold, and a genuine beat was missed. It can be seen that, in both instances, the R peaks either side of this missing beat have been automatically identified, and excluded. These artefacts were identified based on the maximum temporal threshold criterion in example *a* and *d*, and additionally based on the maximum rate of change criterion in example *d*. The second, highlighted by the call-out figures *b* and *c*, are instances where the ECG signal exceeded the amplitude threshold, and an incorrect R peak was identified. In both instances, the incorrect beat has been identified based on the minimum temporal threshold criterion, and the R peaks either side of this incorrect beat have been identified and excluded. Of note, the sample below has been selected to demonstrate how the programme identified the most common artefacts in the data. Overall, the occurrence of both types of artefacts in our data is relatively rare, as is shown in Figure S2, below.

The three checks/criteria described here were applied separately to data after it had been parsed. Following this, at each threshold value, the proportion of candidate R peaks that was rejected was compared with the proportion of candidate R peaks that passed all three criteria. The threshold value with the lowest proportion of rejected candidate R peaks was chosen as the threshold used for that participant.

In addition, and as a further check, a trained coder who was naïve to study hypotheses double-coded a randomly selected subsample of 1000 beats for 20% of the participants, coding them as genuine or artefactual. Cohen's kappa was calculated to measure inter-rater reliability between the manual coding and the automatic coding, based on the best-fitting threshold level. This was found to be 0.97, which is high (McHugh, 2012).

The same process was also performed with a second derivative of the raw ECG signal after it had been smoothed using the Matlab algorithm fastsmooth.m (see Figure S2). However, when applied to our data this process produced a higher rate of R peaks identified as artefactual compared with the parsing described above, and so it was not used.

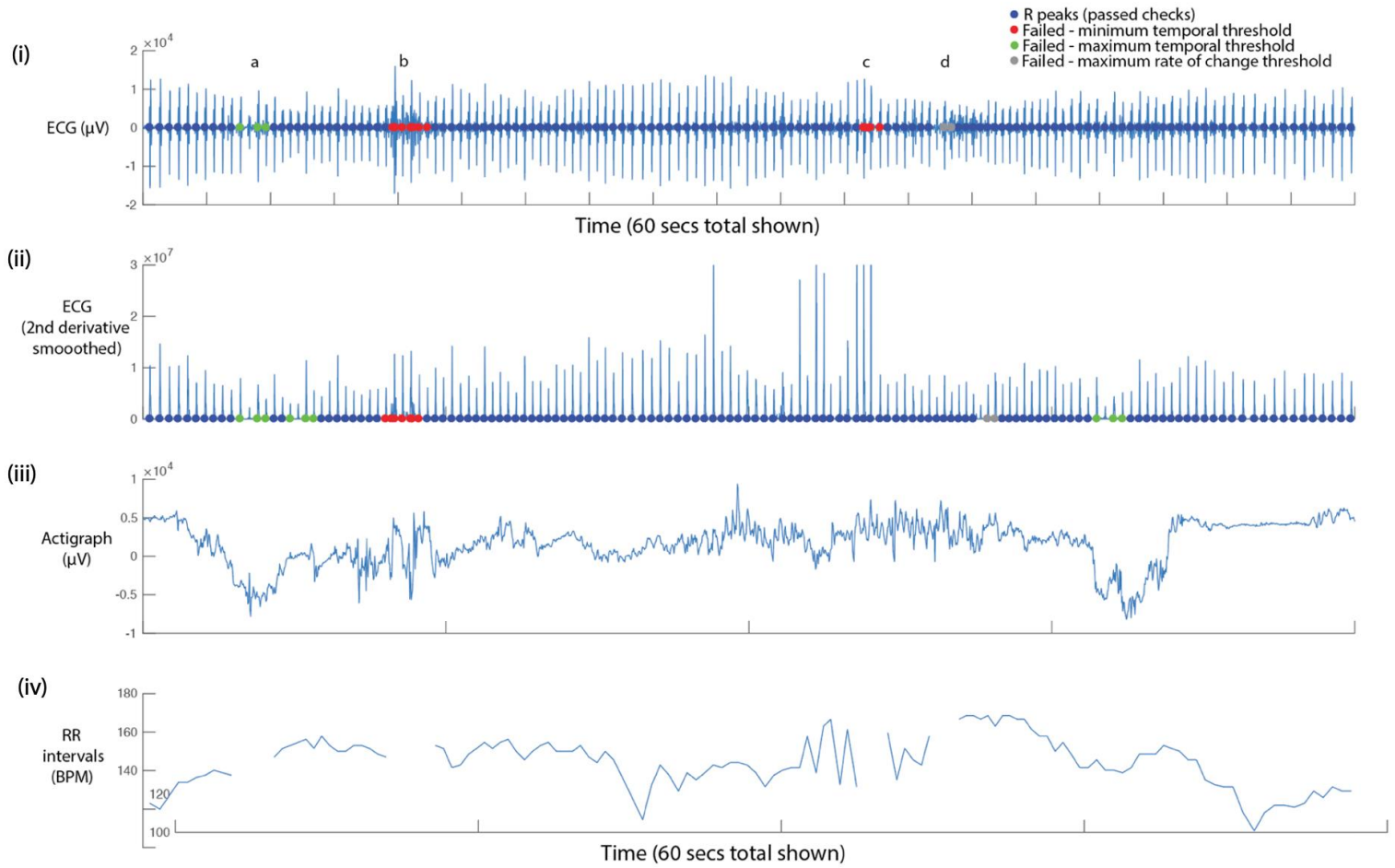

Fig. S1 Sample screenshot from ECG parsing algorithm. Sixty seconds' data is shown. From top to bottom: (i) raw ECG signal. Coloured dots show the results of the three checks described in the text above (see also the Figure legend); (ii) smoothed second derivative of ECG signal. This measure was not used as our pilot analyses found it to be less effective than applying the processing to the raw signal; (iii) raw (unprocessed) actigraph data. This information was only used for visual inspection, and was not used in parsing; (iv) RR intervals (in BPM), with rejected data segments excluded.

Figure S2 below shows a histogram of the proportion of candidate R peaks rejected for each participant, based on the best-fitting threshold value. The median (SE) is 1.07 (0.36) percent data rejected. This relatively low figure was achieved through very close attention during the piloting phase to the selection and placement of the ECG electrodes, to the design of the device, and the gain settings on the recording device.

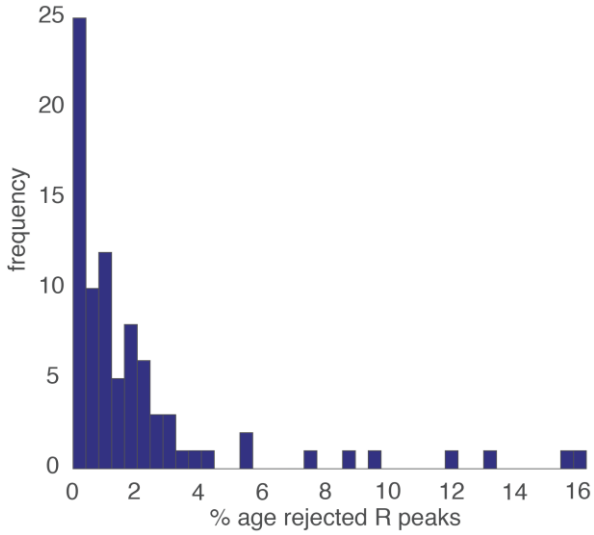

Fig. S2 Histogram showing the proportion of rejected R peaks (as identified using the three criteria described above).

3.2 Parsing of other autonomic variables

3.2.1 Heart rate variability (HRV)

HRV was calculated using the PhysioNet Cardiovascular Signal Toolbox (Vest et al., 2018). In these scripts, which performed a completely separate analysis of the ECG data, a 60-second window with an increment of 60 seconds was implemented, and the default settings were used with the exception that the min/max interbeat interval was set at 300/750 milliseconds for the infant data and 300/1300 milliseconds for the adult data. The Root Mean Square of Successive Differences (RMSSD) measure was taken to index heart rate variability, but other frequency domain measures were additionally inspected and showed highly similar results, as expected (Vest et al., 2018).

3.2.2 Actigraphy

Actigraphy was recorded at 30Hz. To parse the actigraphy data we first manually inspected the data. Subsequently, we corrected artefacts specific to the recording device used, then applied a Butterworth low-pass filter with a cut-off of 0.1Hz to remove high-frequency noise, and then averaged from three dimensions into one. Actigraphy data were available for all participants tested.

3.3 Arousal composite

Previous research has shown significant patterns of tonic and phasic covariation between different autonomic measures collected from infants (Wass et al., 2016; Wass et al., 2015). Here, we include plots showing that the present dataset replicated and extended these results. The plots only show the sections of the data when participants were at home, comparing sections in which the infants were awake and asleep. Figure S3a shows cross-correlation plots examining the relationship between heart rate and movement. In both waking and sleeping sections the zero-lag correlation is 0.5. Figure S3c shows how these zero-lagged correlations vary on a per-participant basis. S3b shows an illustrative sample from a single participant. Sleeping sections show very low movement levels and lower heart rate. Of note, heart rate and movement do still inter-relate during the sleeping sections of the data (Figure S3c), albeit that the variability in heart rate and movement is lower. Figure S3d-f show similar relationships between heart rate and heart rate variability, illustrating the strong and consistent negative relationships that were observed between these variables, as predicted.

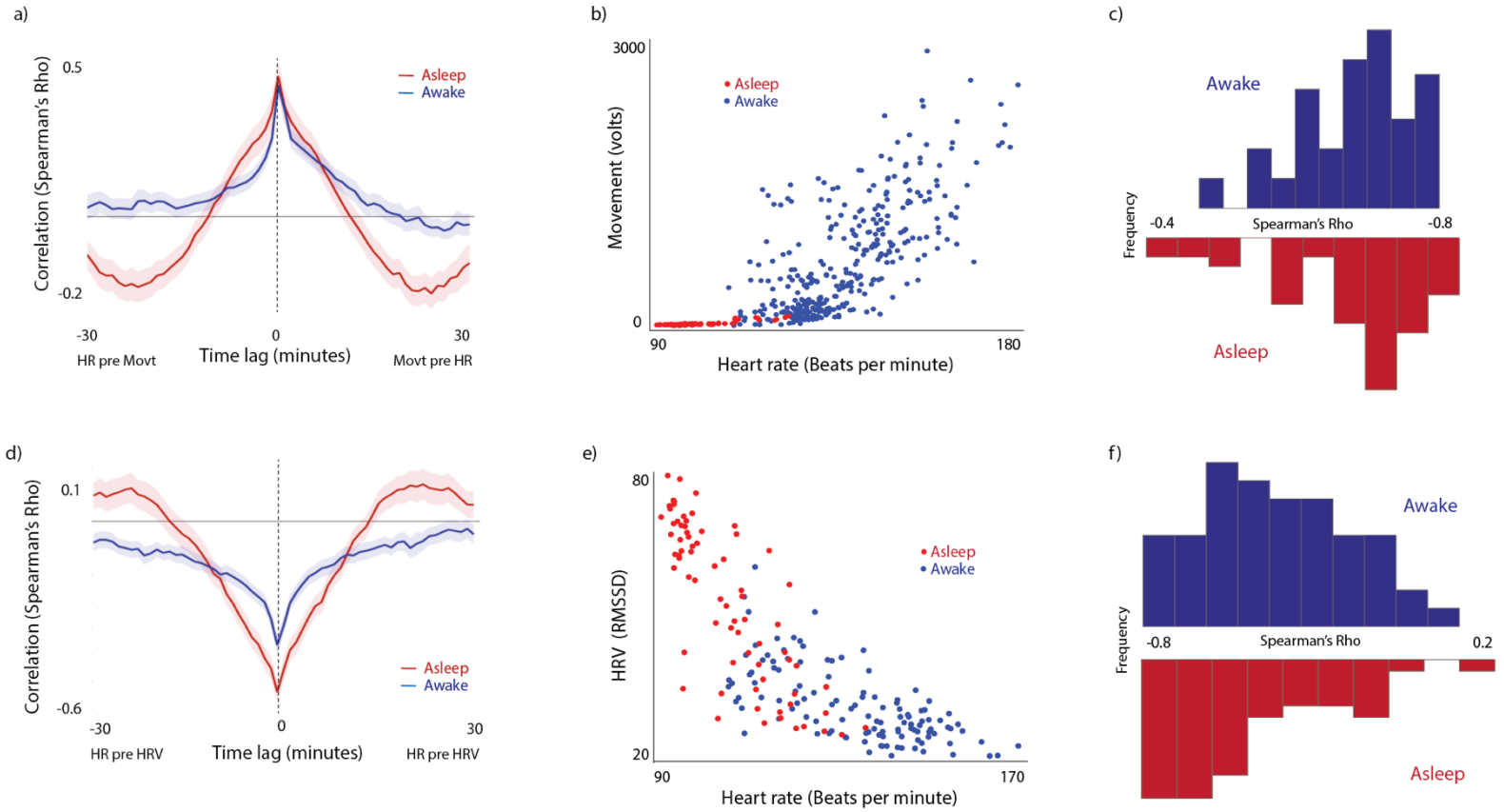

Fig. S3 Illustrating the relationship between the individual physiological measures included in the composite measure. (a) Cross-correlation of the relationship between heart rate and movement. (b) Scatterplot from a sample participant. Each datapoint represents an individual 60-second epoch of data. (c) Histograms showing the average zero-lagged correlation between 60-second epochs, calculated on a per-participant basis and then averaged. (d)-(f) Equivalent plots for heart rate and heart rate variability.

Extensive previous research has identified fractionation, and differentiation, within our autonomic nervous systems (Jänig & Habler, 2000; Kreibig, 2010; Lacey, 1967; Levenson, 2014; Quas et al., 2014) – suggesting, for example that the sympathetic and parasympathetic subdivisions operate, to an extent, in a non-additive manner (Samuels & Szabadi, 2008). Although indubitably true, these findings should not be seen as rendering incorrect our treatment here of autonomic arousal as a one-dimensional construct. Like many other arguments concerned with general versus specific factors, the question is rather one of the relative proportions of variance that can be accounted for by a single common factor in comparison with the variance accounted for by the sum of specific factors (Graham & Jackson, 1970; see also Calderon et al., 2016).

As a result of these considerations, the three autonomic measures were collapsed into a single composite measure. To do this, the actigraphy data was first subjected to a log transform (Thomas & Burr, 2008), to correct the raw results, which showed a strong positive skew (Wass et al., 2016; Wass et al., 2015). Second, all three variables were converted to *z*-scores. Third, the HRV data were inversed because of the overall negative relationships noted between HRV and the other two measures (see Figure S4). Fourth, the three *z*-scores were averaged.

On the occasions where heart rate data were excluded due to artefacts, data from actigraphy alone was used for the composite variable. Note that these occasions were relatively rare (accounting for a median ~1% of all data; see Figure S3), and that the zero-lag cross-correlation between movement and heart rate across all available data was high (~.5; see Figure S4).

3.4 Removal of autocorrelation from arousal data

Autonomic arousal time series are known to show autocorrelation (Wass et al., 2016). In order to preclude the possibility that differences in the autocorrelation may have influenced results, the autocorrelation was removed from the data prior to performing all calculations, using the following procedure. First, best-fit bivariate polynomials were calculated for the two time series independently, in order to remove linear and quadratic trends. The residuals obtained were subjected to the Dickey-Fuller test to check that they showed stationarity, which they did. Next, in order to remove the autocorrelation component from each time series independently, univariate autoregressive models were fitted to each time series, and the residuals were calculated (see, e.g., Feldman et al., 1999; Feldman et al., 2011; Jaffe et al., 2001; Suveg et al., 2016 for similar approaches). The residual values were used for all subsequent analyses.

4 Home/awake coding

Coding when participants were at home was performed using the global positioning system (GPS) monitors built into the recording devices. The position of the participant's home was calculated based on the postcode data that they supplied, and any GPS samples within a circa 50m area of that location were treated as 'home' (corresponding to the accuracy of the GPS devices that we were using). To

identify samples in which infants were sleeping, parents were asked to fill in a logbook identifying the times of infants' naps during the day. This information was manually verified by visually examining the actigraphy and ECG data collected, on a participant-by-participant basis. Actigraphy, in particular, shows marked differences between sleeping and waking samples (see SM, Figure S3 and So et al., 2005), which allowed us to verify the parental reports with a high degree of accuracy.

5 Calculation of permutation-based temporal clustering analyses

To estimate the significance of the time-series relationships in the results, a permutation-based temporal clustering approach was used. This involved two different analytical techniques. One analysis (Method 1) looked at whether 'peak' reactions were observed relative to a known 'Time=0' moment (such as relative to a particular event). This method was used to test Hypotheses 1-3. The other analysis (Method 2) examined temporally contiguous patterns of change in instances where the centre-point of the expected response window was unknown, or unimportant (Maris & Oostenveld, 2007). This method was used to test Hypothesis 4.

Method 1: This analysis examines whether the significant clusterings of elevated values around time=0 are observed. To estimate this, the following procedure was used. If *y* is Time=0, then for the first time-interval (t=1) the observed data from *y*-1 to *y*+1 was excerpted (i.e., from 1 bin before to 1 bin after time=0). The proportional size of the excerpted data relative to the entire dataset was used to calculate a centile threshold (e.g., examining the central 10% of the data). The entire dataset was then rank ordered, and the highest 10% of the data was calculated. The proportion of highest data that was contained within the central segment of the data was calculated. The same calculation was then repeated for increasing values of t ranging from 1 to the total time window of the sample. Thus, for each value of t, if the observed data had been 'perfectly' ordered, with the highest value at time=0 and gradually decreasing values at increasing time lags, then the proportion of highest data contained within the central segment of data would always be 1.

In this way, we quantified whether higher values were more commonly observed around the time=0 point in the data. A thousand random datasets were then generated with the same dimensions as the original input data. To ensure that the same level of autocorrelation was present in the simulated data as in the original datasets, multivariate autoregressive models were fitted to each sample included in the original dataset using the Matlab function ARfit.m (Neumaier & Schneider, 2001), and the matching AR parameters were used to generate each of the random datasets using the Matlab function ARsim.m (Neumaier & Schneider, 2001).

For each random dataset, the same series of calculations as described above was performed. In this way we estimated how, for each of the random datasets, the proportion of highest data contained within the central segment of the data varied across increasing time windows from the time=0 point. The results obtained from the random datasets were used to generate a histogram, and the likelihood

of observed results have been obtained by chance was calculated by comparing the observed values with the randomly generated values using a standard bootstrapping procedure. Thus, a *p* value of <.01 indicates that an equivalent pattern of temporally contiguous group differences was observed in 10 or fewer of the 1000 simulated datasets created.

Method 2: This analysis examines whether temporally contiguous patterns of change are observed in situations where the centre point of the expected response window is unknown. In each case, the test statistic is calculated independently for each time window. Series of significant effects across contiguous time windows are identified using an alpha level of 0.05. A thousand random datasets are then generated using the same procedures as described for Method 1, above. The same sequence of analyses is repeated, and the longest series of significant effects across contiguous time windows are identified. The results obtained from the random datasets are used to generate a histogram, and the likelihood of observed results being obtained by chance is calculated by comparing the observed values with the randomly generated values using a standard bootstrapping procedure. Thus, a *p* value of < 0.01 indicates that an equivalent pattern of temporally contiguous group differences was observed in 10 or fewer of the 1000 simulated datasets created.

6 Hypothesis 2: further analyses

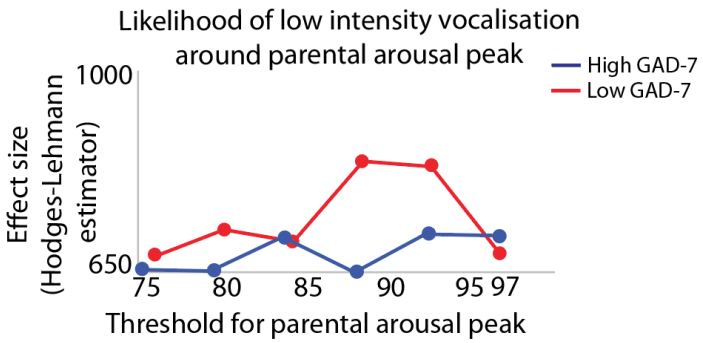

Fig. S4 Identical to Figure 5.3a in the main text, but examining the likelihood of low intensity vocalisations around parental arousal peaks.

7 Hypothesis 4: arousal increases following parental vocalisations - differences contingent on parental anxiety – further analyses

In addition to the analyses presented in the main text, we also examined how the relationship between hyperarousal and vocalisations varied contingent on the level of parental anxiety. We conducted the same analyses in Hypothesis 4, but subdivided by a quartile split of the GAD-7 scores. For the sake of brevity, we have not included the control analyses (drawn as grey lines on Figure 5.4). Instead, we have only plotted the observed data. Thus, Figure S5a shows the black lines from Figures 5.4a (low GAD-7 group) and Figures 5.4b (high GAD-7 group) – but subdivided into four groups by GAD-7

score instead of two. For analyses we used an identical procedure to the permutation-based temporal clustering analyses used in the main text (see SM section 5). But instead of performing *t*-tests to examine group differences in each time window before correcting for multiple comparisons, we instead repeatedly performed a 1-way ANOVA in each time window before correcting for multiple comparisons.

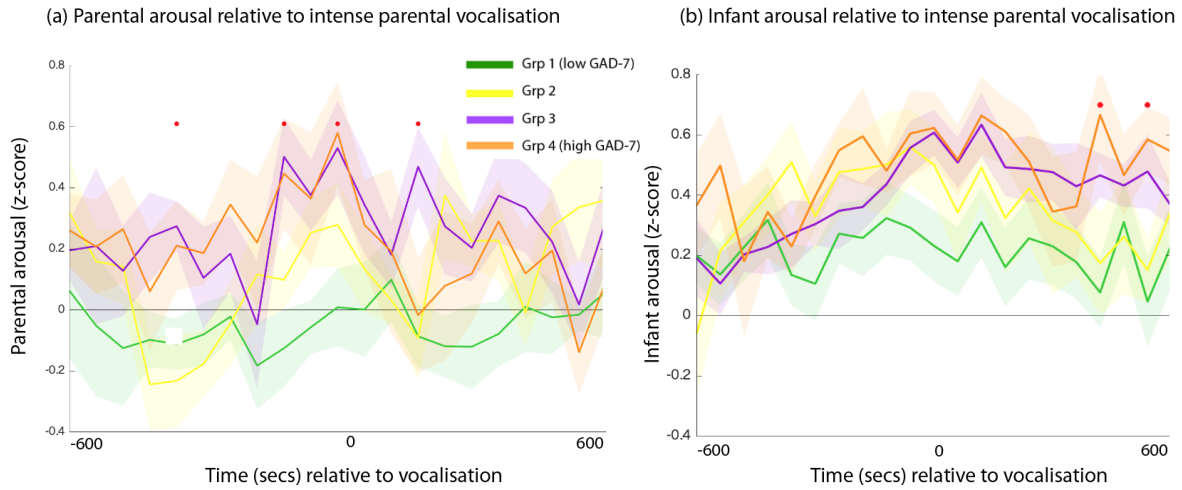

Fig. S5 Increases in (a) parental and (b) infant arousal at moments of high maternal vocal intensity, with maternal anxiety scores split by quartiles. The higher the anxiety level, the greater the hyperarousal. Red dots indicate significant group differences at the time bins indicated (all *ps* <.001).

Appendix C - Supplementary Materials for: Infant effortful control mediates relations between nondirective parenting and internalising-related child behaviours in an autism-enriched infant cohort

The following supplementary materials accompany the publication presented in chapter 6, which investigates the associations between parenting behaviour, infant temperament, and subsequent child internalising behaviours in an autism-enriched cohort (Smith, Jones, Wass, et al., 2021). Subheadings and figure captions have been adapted to conform to the general thesis format.

1 Sample characteristics

1.1 Diagnostic status of participants' older siblings

For all 89 children with an older sibling with a community clinical diagnosis of ASD (hereafter probands), parents completed the Development and Well-Being Assessment (DAWBA: Goodman et al., 2000) and/or the Social Communication Questionnaire (SCQ: Rutter et al., 2003). Sixty-seven probands met criteria on both the DAWBA and SCQ. Eight children scored below threshold on the SCQ and two were missing the SCQ, but no exclusions were made due to meeting threshold on the DAWBA and expert opinion. For 12 probands, confirmation of local clinical diagnosis was only available via the SCQ. Screening for possible ASD in the older siblings of the typical likelihood (TL) infants was undertaken using the SCQ, with no child scoring above the instrument cut-off for ASD (>15). For one TL child the SCQ was missing. Medical history review confirmed a lack of ASD within first-degree relatives.

2 Bivariate correlations

		1	2	3	4	5	6	7	8	9	10
1	Infant BI (8 m)	--	--	--	--	--	--	--	--	--	--
2	Infant BI (14 m)	.56**	--	--	--	--	--	--	--	--	--
3	Child internalising (3 years)	.13	.25**	--	--	--	--	--	--	--	--
4	Infant RC (14 m)	-.10	-.18**	-.33**	--	--	--	--	--	--	--
5	Infant EC (24 m)	-.09	-.19**	-.37**	.54**	--	--	--	--	--	--
6	Nondirective parenting (8 m)	.06	-.06	-.15	.19*	.24**	--	--	--	--	--
7	Nondirective parenting (14 m)	.06	.11	-.08	-.06	.08	.28**	--	--	--	--
8	Sensitive parenting (8 m)	.07	.05	-.09	.06	.18*	.61**	.29**	--	--	--
9	Sensitive parenting (14 m)	.12	-.01	-.02	-.01	.003	.21*	.60**	.40**	--	--
10	Group status	.17**	.21**	.25**	-.22**	-.21**	-.19*	-.14	-.11	-.01	--

Table S1 Bivariate correlations for all model variables. Items 1-5 are parent-report measures; items 6-11 are parent-child interaction observations; group status indicates likelihood of developing ASD based on the presence of a diagnosis amongst a first-degree relative (two groups: typical likelihood or elevated likelihood). BI – behavioural inhibition; RC – regulatory capacity; EC – effortful control. * = $p < .05$, ** = $p < .01$.

3 Moderation model variants

Our first hypothesis predicted that nondirective parenting at 14 months would moderate the relationship between infant behavioural inhibition at 8 months and internalising at 36 months; our second hypothesis predicted that sensitive parenting at 14 months would moderate the relationship between infant behavioural inhibition at 8 months and internalising at 36 months. Results from tests of these hypotheses were all found to be non-significant. To test for consistency, post-hoc analyses were also conducted to investigate whether the moderating relationship remained non-significant if the same variables measured at different timepoints were entered into the model. For reader interest, we also probed the role of effortful control as a moderator of the relationship between nondirective parenting and later internalising. Results of the tests of moderation were all non-significant, even when multiple timepoints were tested in different configurations (see Table S2).

	Predicting Internalising (36 mos)				
	Predictor	β	*p*	LLCI 95%	ULCI 95%
Model 1.2	Infant BI, 14 months	.17	.60	-.70	.92
	Nondirective Parenting, 8 months	-.29	.39	-1.2	.48
	BI*NDP	.18	.71	-.87	1.7
Model 1.3	Infant BI, 8 months	.45	.14	-.40	1.1
	Nondirective Parenting, 8 months	.05	.85	-.73	.65
	BI*NDP	-.31	.43	-1.2	.96
Model 1.4	Infant BI, 14 months	.48	.14	-.42	1.3
	Nondirective Parenting, 14 months	.16	.66	-.73	1.1
	BI*NDP	-.39	.48	-1.7	1.1
Model 2.2	Infant BI, 14 months	.36	.33	-.64	1.2
	Sensitive Parenting, 8 months	-.01	.99	-.85	.79
	BI*SP	-.14	.78	-1.2	1.2
Model 2.3	Infant BI, 8 months	.51	.12	-.34	1.2
	Sensitive Parenting, 8 months	.11	.60	-.48	.64
	BI*SP	-.38	.31	-1.2	.63
Model 2.4	Infant BI, 14 months	.28	.33	-.46	1.1
	Sensitive Parenting, 14 months	.05	.87	-.77	.87
	BI*SP	-.08	.86	-1.2	1.1
Model 2.5	Nondirective parenting, 8 months	-.37	.71	-1.96	1.34
	Effortful control, 24 months	-.37	.19	-.83	.10
	NDP*Effortful control	.34	.75	-1.41	2.03
Model 2.6	Sensitive parenting, 8 months	-.24	.74	-2.9	2.06
	Effortful control, 24 months	-.40	.15	-.3.4	.51
	SP*Effortful control	.23	.77	-.46	.62

Table S2 Standardised model results of exploratory moderation analyses (model variants 1-2). Models 1.2-1.4 and 2.2-2.6 are variants of hypotheses 1 and 2 respectively, replicated with all available timepoints (see Figure 6.1 in main text); BI - behavioural inhibition; NDP – nondirective parenting; SP – sensitive parenting; BI*NDP – interaction term, behavioural inhibition x nondirective parenting; BI*SP – interaction term, behavioural inhibition x sensitive parenting; SP*Effortful

Control – interaction term, sensitive parenting x effortful control; LLCI – lower limit confidence interval; ULCI – upper limit confidence interval; * $p \leq .05$.

4 Mediation model variants

Our third hypothesis predicted that nondirective parenting would lead to later infant effortful control and subsequent reductions in internalising problems. In our main mediation model, we measured nondirective parenting at 8 months, effortful control at 24 months and internalising behaviour at 36 months; this was on the basis of temporal precedence, which is thought to be theoretically relevant to longitudinal designs (George & Jones, 2000). To test for consistency, post-hoc analyses were also conducted to investigate whether the mediating relationship remained significant if the same variables measured at different timepoints were entered into the model. Nondirective parenting at 8 months, effortful control at 14 months and internalising behaviour at 36 months were tested (model 3.2), as were nondirective parenting at 14 months, effortful control at 24 months and internalising behaviour at 36 months (3.3). Model 3.2 was not significant (β=-.08, 95% CI BS [-.16, .02]), neither was Model 3.3 (β=-.03, 95% CI BS [-.10, .01]). For reader interest, we also probed the role of sensitive parenting as a predictor variable, as well as behavioural inhibition/shyness as a mediator variable. See Table S3 below.

Model	**Predictor**	**Mediator**	**Outcome**	**Total Effect (SE)**	**Direct Effect (SE)**	**Indirect Effect (95% CI Bootstrap)**
3.2	NDP, 8m	Infant regulatory capacity, 14m	Internalising, 36m	-.15 (.08)†	-.07 (.08)	-.08 (-.16, .02)
3.3	NDP, 14m	Effortful control, 24m	Internalising, 36m	-.004 (.09)	.03 (.08)	-.03 (-.10, .01)
3.4	NDP, 8m	Shyness, 24m	Internalising, 36m	-.21 (.14)	-.21 (.13)	-.003 (-.12, .11)
3.5	SP, 14m	Effortful control, 24m	Internalising, 36m	.04 (.12)	.04 (.12)	-.002 (-.08, .07)

Table S3 Standardised model results of exploratory mediation analyses. NDP – nondirective parenting. SP – sensitive parenting. * $p \leq .05$, † $p \leq .06$.

5 Intervention trial supplementary analyses

Forty-three participants in the elevated likelihood (EL) group in this sample took part in a randomised controlled trial (RCT) of a parent-mediated early intervention programme (Green et al., 2015, 2017). The intervention period was between the 8 and 14 month visits. Twenty-two children were in the intervention arm of the trial. To investigate whether enrolment in the RCT - or receiving the intervention - affected the outcomes described in the Results, we conducted multiple regressions with binary variables representing participation in the RCT and receiving treatment as control variables. The results showed no significant effects of moderation in models 1-2, and this remained unchanged after adjustment for the potentially confounding effects of RCT participation or intervention receipt (see Table S4). Similarly, the finding of an indirect effect within model 3 remained unchanged after analysing the above covariates (see Table S5).

	Predicting Internalising (36 mos)				
	Predictor	β	*p*	LLCI 95%	ULCI 95%
Model 1	Infant BI, 8 months	.50	.16	-.15	1.03
	Nondirective Parenting, 14 months	.20	.32	-.35	.70
	RCT treatment receipt	-.01	.86	-.15	.13
	RCT participation	.01	.86	-.14	.12
	BI*NDP	-.42	.42	-.40	.11
Model 2	Infant BI, 8 months	.47	.14	.03	1.05
	Sensitive Parenting, 14 months	.21	.42	-.20	.62
	RCT treatment receipt	-.05	.59	-.20	.11
	RCT participation	.04	.68	-.11	.22
	BI*SP	-.39	.35	-1.12	.22

Table S4 Standardised moderation model analyses with covariates. Models 1-2 refer to hypotheses 1-2 shown in Figure 6.1; BI - behavioural inhibition; NDP – nondirective parenting; SP – sensitive parenting; BI*NDP – interaction term, behavioural inhibition x nondirective parenting; BI*SP – interaction term, behavioural inhibition x sensitive parenting; LLCI – lower limit confidence interval; ULCI – upper limit confidence interval. * $p \leq .05$.

	Predictor	Covariate	Mediator	Outcome	Total Effect (SE)	Direct Effect (SE)	Indirect Effect (95% CI Bootstrap)
Model 3	NDP, 8m	RCT treatment receipt	Effortful control, 24m	Internalising, 36m	-.21 (.14)	-.09 (.13)	-.08 (-.15, -.02)
	NDP, 8m	RCT participation	Effortful control, 24m	Internalising, 36m	-.24 (.14)	.11 (.14)	-.08 (-.16, -.02)

Table S5 Standardised model results of mediation analyses with covariates. Model 3 refers to hypothesis 3; NDP– nondirective parenting. * $p \leq .05$.

6 Effects of ASD outcome

Seventeen children in the EL group were diagnosed with ASD at 36 months. Removing children with ASD from the mediation analysis (model 3) changed the main finding such that there was no longer evidence of an indirect effect (β=-.03, 95% CI BS [-.09, .02]). Table S6 shows the effect of removing children diagnosed with ASD from the moderation models, which led to no changes to the existing (null) findings.

	Predicting Internalising (36 mos)				
	Predictor	β	*p*	LLCI 95%	ULCI 95%
Model 1	Infant BI, 8 months	.15	.69	-.42	.81
	Nondirective Parenting, 14 months	-.08	.80	-.57	.47
	BI*NDP	.10	.86	-.86	.97
Model 2	Infant BI, 8 months	.40	.19	-.04	.94
	Sensitive Parenting, 14 months	.14	.59	-.26	.58
	BI*SP	-.25	.53	-.95	.34

Table S6 Standardised model results of moderation analyses with children with ASD diagnoses excluded. Models 1-2 refer to hypotheses 1-2 shown in Figure 6.1; BI - behavioural inhibition; NDP – nondirective parenting; SP – sensitive parenting; BI*NDP – interaction term, behavioural inhibition x nondirective parenting; BI*SP – interaction term, behavioural inhibition x sensitive parenting; LLCI – lower limit confidence interval; ULCI – upper limit confidence interval. * $p \leq .05$.

7 Moderated mediation

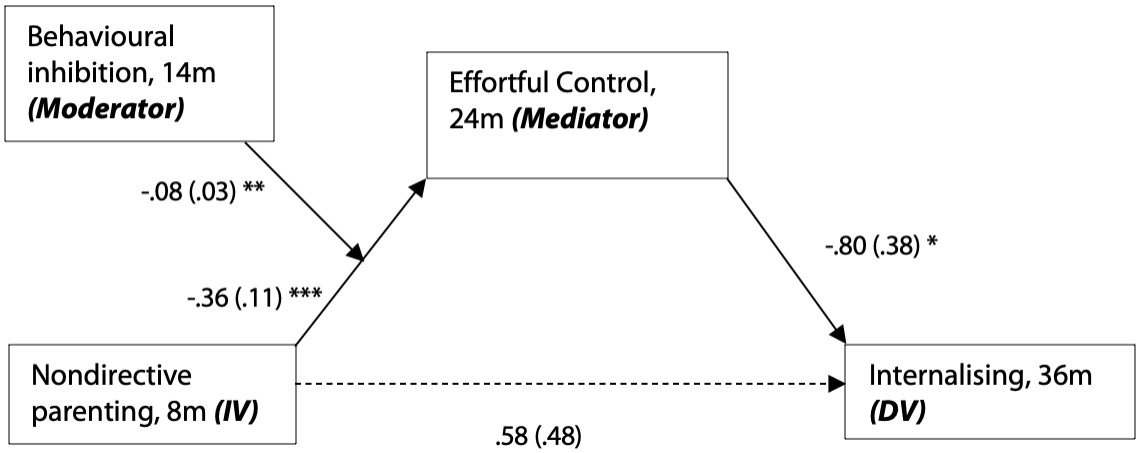

Fig. S1 Testing for moderated mediation in the relationships between nondirective parenting and child internalising behaviour (with behavioural inhibition as the moderator and effortful control as the mediator). Results of moderated mediation analysis: nondirective parenting at 8 months predicts effortful control at 24 months, with the effects moderated by behavioural inhibition. IV = independent variable; DV = dependent variable. Solid lines represent significant effects. * $p < .05$, ** $p < .02$, *** $p < .002$

	Internalising, 36m (SE)	Effortful control, 24m (SE)
Nondirective parenting, 8m	-.58 (.48)	.36 (.11) ***
Behavioural inhibition, 14m	-.01 (.46)	.12 (.11)
Nondirective parenting, 8m X behavioural inhibition, 14m	.14 (.14)	-.08 (.03) **
Effortful control, 24m	-.80 (.38) *	

Table S7 Testing for moderated mediation in the relationships between nondirective parenting and child internalising behaviour (with behavioural inhibition as the moderator and effortful control as the mediator). * $p < .05$, ** $p < .02$, *** $p < .002$.

Appendix D - Supplementary Materials for: The effect of perinatal interventions on parent anxiety, infant socio-emotional development and parent-infant relationship outcomes: a systematic review

The following supplementary materials accompany the main material presented in chapter 7, which reviews the research on perinatal interventions as they relate to reductions in parent anxiety, and improvements in infant socio-emotional functioning and the parent-infant relationship.

Of note, captions precede rather than succeed Tables S6-S19 due to their long length.

#	**Terms**
1	(parent* adj5 (mental* ill* or mental* disorder* or mental health or mood disorder* or affective disorder or anxi* or depress* or OCD or obsessive compulsive disorder or PTSD or post traumatic stress disorder or trauma)).mp.
2	exp PARENTS/ and (exp Mental Disorders/ or exp Mental Health/ or exp Mood Disorders/)
3	1 or 2
4	(intervent* or prevent* or therap* or train* or program* or treatment).mp.
5	Exp Psychotherapy/ or exp Health Services/
6	4 or 5
7	exp Parent-Child Relations/ or exp Child Rearing/ or exp Infant Behavior/ or exp Infant development/
8	((mother* or maternal) adj5 (infant* or baby or child*) adj5 (interact* or relations* or bond* or develop*)).mp.
9	7 or 8
10	3 and 6 and 9
11	randomized.mp.
12	placebo.mp.
13	randomly.mp.
14	trial.mp.
15	11 or 12 or 13 or 14
16	10 and 15

Table S1 Electronic database search terms optimised for Medline.

#	**Terms**
1	(parent* adj5 (mental disease* or mental health or mood disorder* or anxi* or depress* or obsessive compulsive disorder or posttraumatic stress disorder)).mp.
2	exp PARENT/ and (exp Mental Disorders/ or exp Mental Health/ or exp Mood Disorder/)
3	1 or 2
4	(intervent* or prevent* or therapy* or train* or health program or treatment).mp.
5	exp Psychotherapy/ or exp Health Program/
6	4 or 5
7	exp child parent relation/ or exp child rearing/ or exp child behavior/ or exp child development/
8	((mother* or maternal) adj5 (infant* or baby or child*) adj5 (interact* or relations* or bond* or develop*)).mp.
9	7 or 8
10	3 and 6 and 9
11	randomized controlled trial.mp.
12	placebo.mp.
13	11 or 12
14	10 and 13

Table S2 Electronic database search terms optimised for Embase.

#	**Terms**
1	(parent* adj5 (mental disorder* or mental health or affective disorder* or anxi* or postpartum depression or major depression or obsessive compulsive disorder or posttraumatic stress disorder or birth trauma)).mp.
2	exp PARENTS/ and (exp Mental Disorders/ or exp Mental Health/ or exp Affective Disorders/)
3	1 or 2
4	(intervent* or prevent* or psychotherap* or train* or mental health programs or treatment).mp
5	exp Psychotherapy/ or exp Intervention/
6	4 or 5
7	exp Parent Child Relations/ or exp Childrearing Practices/ or exp Infant Temperament/ or exp Infant Development/
8	((mothers or maternal) adj5 (infant* or baby or child*) adj5 (interact* or relations* or bond* or develop*)).mp.
9	7 or 8
10	3 and 6 and 9
11	Randomized controlled trials.mp.
12	placebo.mp.
13	Control Groups.mp.
14	clinical trials.mp.
15	11 or 12 or 13 or 14
16	10 and 15

Table S3 Electronic database search terms optimised for APA PsychINFO.

#	**Terms**
1	(parent* adj5 (mental* ill* or mental* disorder* or mental health or mood disorder* or affective disorder or anxi* or depress* or OCD or obsessive compulsive disorder or PTSD or post traumatic stress disorder or trauma)).mp.
2	(intervent* or prevent* or therap* or train* or program* or treatment).mp.
3	((mother* or maternal or parent or parental) adj5 (infant* or baby or child*) adj5 (interact* or relations* or bond* or develop*)).mp.
4	randomized.mp.
5	placebo.mp.
6	randomly.mp.
7	controlled trial.mp.
8	4 or 5 or 6 or 7
9	1 and 2 and 3 and 8

Table S4 Electronic database search terms optimised for MIDIRS.

1	parent* adj5 (mental* ill* or mental* disorder* or mental health or mental disease* or mood disorder* or affective disorder* or anxi* or depress* or OCD or obsessive compulsive disorder or PTSD or post traumatic stress disorder or trauma)	Limits
2	Mesh descriptor: [Parenting] in all MeSH products	MeSH
3	Mesh descriptor: [Mental Disorders] explode all trees	MeSH
4	Mesh descriptor: [Mental Health] explode all trees	MeSH
5	Mesh descriptor: [Mood Disorders] explode all trees	MeSH
6	#2 AND (#3 OR #4 or #5)	Limits
7	#1 or #6	Limits
8	intervent* or prevent* or therap* or train* or program* or treatment	Limits
9	Mesh descriptor: [Psychotherapy] explode all trees	MeSH
10	Mesh descriptor: [National Health Programs] explode all trees	MeSH
11	Mesh descriptor: [Health Services] explode all trees	MeSH
12	#9 or #10 or #11	Limits
13	#8 or #12	Limits
14	MeSH descriptor: [Parent-Child Relations] explode all trees	MeSH
15	MeSH descriptor: [Child Rearing] explode all trees	MeSH
16	MeSH descriptor: [Child Behavior] explode all trees	MeSH
17	MeSH descriptor: [Child Development] explode all trees	MeSH
18	#14 or #15 or #16 or #17	Limits
19	(mother* or maternal) adj5 (infant* or baby or child*) adj5 (interact* or relations* or bond* or develop*)	Limits
20	#18 or #19	Limits
21	#7 and #13 and #18	Limits
22	MeSH descriptor: [Randomized Controlled Trials] explode all trees	MeSH
23	MeSH descriptor: [Random Allocation] explode all trees	MeSH
24	#22 OR #23	Limits
25	#21 AND #24	Limits

Table S5 Electronic database search terms optimised for Cochrane.

Table S6 Reasons for exclusion for articles assessed at full-text. Where 'duplicate' is given as the reason for exclusion, this was because the record was not automatically excluded at an earlier screening stage due to inconsistent metadata between databases. Of note, all articles in the table below do not appear in the thesis references as all the key identifying information is recorded in each row. * = correct citation as compared to original database record containing inaccuracies.

Original ti ab classification	Title	Author(s)	Year	Reason for Exclusion
Maybe	Treating disturbances in the relationship between mothers with bulimic eating disorders and their infants: a randomized, controlled trial of video feedback	Stein et al.	2006	No parent anxiety outcome
Maybe	Randomized controlled trial of the Circle of Security-Intensive intervention for mothers with postpartum depression: maternal unresolved attachment moderates changes in sensitivity	Muhlhan et al.	2020	No parent anxiety outcome
Maybe	Prolactin, a potential mediator of reduced social interactive behavior in newborn infants following maternal perinatal depressive symptoms	Zhang et al.	2017	No parent anxiety outcome
Maybe	Mother-infant interaction: effects of a home intervention and ongoing maternal drug use	Schuler et al.	2010	No parent anxiety outcome
Maybe	Effects of preventive family service coordination for parents with mental illnesses and their children, a RCT	Wansink et al.	2015	No parent anxiety outcome

Maybe	A randomized controlled trial of a mother-infant or toddler parenting program: demonstrating effectiveness in practice	Hayes et al.	2008	Incorrect population (parental mental health problems not recruitment focus)
Maybe	A controlled clinical treatment trial of interpersonal psychotherapy for depressed pregnant women at 3 New York City sites	Spinelli et al.	2013	No parent anxiety outcome
Maybe	Attachment and Affect between Mothers with Depression and their Children: Longitudinal Outcomes of Child Parent Psychotherapy	Guild et al.*	2021	No parent anxiety outcome
Maybe	Dissemination of an evidence-based prevention innovation for aggressive children living in culturally diverse, urban neighborhoods: the Early Risers effectiveness study	August et al.	2003	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Role of home visiting in improving parenting and health in families at risk of abuse and neglect: Results of a multicentre randomised controlled trial and economic evaluation	Barlow et al.	2007	No parent anxiety outcome
Maybe	Long-term mother and child mental health effects of a population-based infant sleep intervention: Cluster-randomized, controlled trial	Hiscock et al.*	2008	No parent anxiety outcome Incorrect population
Maybe	Parenting enhancement, interpersonal psychotherapy to reduce depression in low-income mothers of infants and toddlers: a randomized trial	Beeber et al.	2013	No parent anxiety outcome
Maybe	Specificity of preventative pediatric intervention effects in early infancy	Beeghly et al.	1995	Incorrect population No parent anxiety outcome

Maybe	Can typical US home visits affect infant attachment? Preliminary findings from a randomized trial of Healthy Families Durham	Berlin et al.	2017	Incorrect population No parent anxiety outcome
Maybe	Effects of a community health worker delivered intervention on maternal depressive symptoms in rural Tanzania	Bliznashka et al.	2021	No relevant infant outcome
Maybe	The efficacy of the Triple P-Positive Parenting Program in improving parenting and child behavior: a comparison with two other treatment conditions	Bodenmann et al.	2008	Incorrect population (child age too high)
Maybe	Toward a developmentally informed approach to parenting interventions: Seeking hidden effects	Brock & Kochanska	2016	Incorrect population No parent anxiety outcome
Maybe	A Single-Session, Web-Based Parenting Intervention to Prevent Adolescent Depression and Anxiety Disorders: Randomized Controlled Trial	Cardamone-Breen et al.	2018	Incorrect population (child age too high)
Maybe	Bending the Curve: A Community-Based Behavioral Parent Training Model to Address ADHD-Related Concerns in the Voluntary Sector in Denmark	Chacko & Scavenius	2018	Incorrect population (child age too high)
Maybe	The effect of counseling with a skills training approach on maternal functioning: A randomized controlled clinical trial	Chamgurdani et al.	2020	No parent anxiety outcome
Maybe	Home Visiting and Antenatal Depression Affect the Quality of Mother and Child Interactions in South Africa	Christodoulou et al.	2019	No parent anxiety outcome

Maybe	Cognitive-behavioral depression treatment for mothers of children with attention-deficit/hyperactivity disorder.	Chronis et al.	2006	Incorrect population (child age too high)
Maybe	Development and preliminary evaluation of an integrated treatment targeting parenting and depressive symptoms in mothers of children with attention-deficit/hyperactivity disorder	Chronis-Tuscano et al.	2013	Incorrect population (child age too high)
Maybe	The efficacy of toddler-parent psychotherapy to increase attachment security in offspring of depressed mothers	Cicchetti et al.	1999	No parent anxiety outcome
Maybe	The efficacy of toddler-parent psychotherapy for fostering cognitive development in offspring	Cicchetti et al.	2000	No parent anxiety outcome
Maybe	Improving quality of mother-infant relationship and infant attachment in socioeconomically deprived community in South Africa: Randomised controlled trial	Cooper et al.	2009	Incorrect population No parent anxiety outcome
Maybe	A RCT of peer-mentoring for first-time mothers in socially disadvantaged areas (the MOMENTS Study)	Cupples et al.	2011	Incorrect population No parent anxiety outcome
Maybe	Emotional and cardiovascular reactivity to a child-focused interpersonal stressor among depressed mothers of psychiatrically ill children	Cyranowski et al.	2009	Incorrect population (child age too high)
Maybe	Chronic Maternal Depressive Symptoms Are Associated With Reduced Socio-Emotional Development in Children at 2 Years of Age: Analysis of Data From an Intervention Cohort in Rural Pakistan	De Oliveira et al.	2019	No parent anxiety outcome (parent anxiety measure too broad)

Maybe	Building Healthy Children: A preventive intervention for high-risk young families	Demeusy et al.	2021	No parent anxiety outcome
Maybe	Family connections: A program for preventing child neglect	DePanfilis & Dubowitz	2005	Incorrect population (child age too high) No parent anxiety outcome
Maybe	Impact of behavioral feeding intervention on child emotional and behavioral functioning, maternal parenting stress, and mother-child relationships	Knight et al.*	2019	Incorrect population (parental mental health problems not recruitment focus, and child age too high)
Maybe	Effect of an early perinatal depression intervention on long-term child development outcomes: Follow-up of the Thinking Healthy Programme randomised controlled trial	Maselko et al.*	2015	No parent anxiety outcome
Maybe	Couple-Focused Prevention at the Transition to Parenthood, a Randomized Trial: Effects on Coparenting, Parenting, Family Violence, and Parent and Child Adjustment	Feinberg et al.	2016	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Effects of family foundations on parents and children: 3.5 years after baseline	Feinberg et al.	2010	No parent anxiety outcome Incorrect population (parental mental health problems not recruitment focus)
Maybe	Empirical Support for a Treatment Program for Families of Young Children With Externalizing Problems	Abbott-Feinfield & Baker	2004	Incorrect population (child age too high)

Maybe	Home visiting intervention for vulnerable families with newborns: follow-up results of a randomized controlled trial	Fraser et al.	2000	No parent anxiety outcome Incorrect population (parental mental health problems not recruitment focus)
Maybe	Mental health promotion and prevention interventions in families with parental depression: A randomized controlled trial	Giannakopoulos et al.	2021	Incorrect population (child age too high)
Maybe	Behavioral Interventions for Infant Sleep Problems: A Randomized Controlled Trial	Gradisar et al.	2016	Incorrect population (parental mental health problems not recruitment focus)
Maybe	The impact of parent-delivered intervention on parents of very young children with autism	Estes et al.*	2014	No parent anxiety outcome (parent anxiety measure too broad)
Maybe	Feasibility and acceptability of an early home visit intervention aimed at supporting a positive mother-infant relationship for mothers at risk of postpartum depression	Greve et al.	2018	No parent anxiety outcome
Maybe	Relationships between parental sleep quality, fatigue, cognitions about infant sleep, and parental depression pre and post-intervention for infant behavioral sleep problems	Hall et al.	2017	No parent anxiety outcome
Maybe	Promoting Positive Mother-Infant Relationships: A Randomized Trial of Community Doula Support For Young Mothers	Hans et al.	2013	No parent anxiety outcome
Maybe	Informing Precision Home Visiting: Identifying Meaningful Subgroups of Families Who Benefit Most from Family Spirit	Haroz et al.	2019	No parent anxiety outcome

Maybe	Depressed mothers' neonates improve following the MABI and a Brazelton demonstration	Hart et al.	1998	No parent anxiety outcome
Maybe	Consistent use of bedtime parenting strategies mediates the effects of sleep education on child sleep: secondary findings from an early-life randomized controlled trial	Hatch et al.	2019	No parent anxiety outcome
Maybe	Randomised controlled trial of behavioural infant sleep intervention to improve infant sleep and maternal mood	Hiscock & Wake	2002	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Long-term mother and child mental health effects of a population-based infant sleep intervention: cluster-randomized, controlled trial	Hiscock et al.	2008	Duplicate
Maybe	Universal parenting programme to prevent early childhood behavioural problems: Cluster randomised trial	Hiscock et al.	2008	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Newborn Behavioral Observation, maternal stress, depressive symptoms and the mother-infant relationship: results from the Northern Babies Longitudinal Study (NorBaby)	Høifødt et al.	2020	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Targeting genetic and environmental risk for mental illness in the womb	Hunter et al.	2019	Full text unavailable (symposium abstract only)
Maybe	Efficacy of learning through play plus intervention to reduce maternal depression in women with malnourished children: A randomized controlled trial from Pakistan	Husain et al.	2021	No parent anxiety outcome (parent anxiety measure too broad)

Maybe	Evaluating the Incredible Years Toddler Parenting Programme with parents of toddlers in disadvantaged (Flying Start) areas of Wales	Hutchings et al.	2017	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Improving parental stress levels among mothers living with HIV: A randomized control group intervention study	Johnson et al.	2015	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Supporting insensitive mothers: The Vilnius randomized control trial of video-feedback intervention to promote maternal sensitivity and infant attachment security	Kalinauskiene et al.	2009	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Clinical overview of children with mucopolysaccharidosis type III A and effect of Risperidone treatment on children and their mothers psychological status	Kalkan Ucar et al.	2010	Incorrect population (child age too high)
Maybe	Behavioral and socioemotional outcomes through age 5 years of the legacy for children public health approach to improving developmental outcomes among children born into poverty	Kaminski et al.	2013	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Evaluation of Lay Support in Pregnant women with Social risk (ELSIPS): a randomised controlled trial	Kenyon et al.	2012	Study protocol
Maybe	Is integrated private-clinic based early child development care effective? A clustered randomised trial in Pakistan	Khan et al.	2018	No parent anxiety outcome

Maybe	Exploring differences between adolescents and adults with perinatal depression—data from the Expanding Care for Perinatal Women With Depression Trial in Nigeria	Oladeji et al.*	2019	No parent anxiety outcome
Maybe	Effect of a maternal role training program on postpartum maternal role competence in nulliparous women with unplanned pregnancy	Kordi et al.	2016	Full text in Arabic
Maybe	The protective effects of father involvement for infants of teen mothers with depressive symptoms	Lewin et al.	2015	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Effect of a family intervention on psychological outcomes of children affected by parental HIV	Li et al.	2014	Incorrect population (child age too high; parental mental health problems not recruitment focus)
Maybe	Does maternal role functioning improve with antidepressant treatment in women with postpartum depression?	Logsdon et al.	2009	No parent anxiety outcome (parent anxiety measure too broad)
Maybe	The Efficacy of Using Peer Mentors to Improve Maternal and Infant Health Outcomes in Hispanic Families: Findings from a Randomized Clinical Trial	Lutenbacher et al.	2018	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	What makes a difference: Early Head Start evaluation findings in a developmental context	Love et al.	2013	Full text unavailable (monograph abstract only)
Maybe	Home again: effects of the Mother-Child Home Program on mother and child	Madden et al.	1984	No parent anxiety outcome

Maybe	Improved child mental health following brief relationship enhancement and co-parenting interventions during the transition to parenthood	Tomfohr-Madsen et al.*	2020	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Maternal mood scores in mid-pregnancy are related to aspects of neonatal immune function	Mattes et al.	2009	No relevant infant outcome No parent anxiety outcome
Maybe	Effectiveness of an Interpersonal Psychotherapy (IPT) Group Depression Treatment for Head Start Mothers: A Cluster-Randomized Controlled Trial	Mennen et al.	2021	Incorrect population (child age too high) No parent anxiety outcome
Maybe	Does a perinatal parenting intervention work for fathers? A randomized controlled trial	Mihelic et al.	2018	Incorrect population (parental mental health problems not recruitment focus)
Maybe	The Effectiveness of an App-Based Nurse-Moderated Program for New Mothers With Depression and Parenting Problems (eMums Plus): Pragmatic Randomized Controlled Trial	Sawyer et al.*	2019	No parent anxiety outcome
Maybe	Maintaining stable parenting for young children through military life transitions	Mogil et al.	2016	Full text unavailable (presentation abstract only)

Maybe	Effect of a food supplementation and psychosocial stimulation trial for severely malnourished children on the level of maternal depressive symptoms in Bangladesh	Nahar et al.	2015	No parent anxiety outcome
Maybe	Mindfulness-based stress reduction for parents of young children with developmental delays: Implications for parental mental health and child behavior problems	Neece et al.	2014	Incorrect population (child age too high)
Maybe	Mitigating the effect of persistent postnatal depression on child outcomes through an intervention to treat depression and improve parenting: a randomised controlled trial	Stein et al.	2018	Duplicate
Maybe	The breathing bear: an intervention for crying babies and their mothers	Novosad et al.	2003	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	An intervention to decrease uncertainly and distress among parents of children newly diagnosed with diabetes: A pilot study	Page et al.	2005	Incorrect population (child age too high; parental mental health problems not recruitment focus)
Maybe	Blended Infant Massage-Parenting Enhancement Program on Recovering Substance-Abusing Mothers' Parenting Stress, Self-Esteem, Depression, Maternal Attachment, and Mother-Infant Interaction	Porter et al.	2015	No parent anxiety outcome
Maybe	Impact of ‘‘controlled crying’’ on child and parent mental health to 6 years: randomised controlled trial.	Price et al.	2010	Full text unavailable (conference abstract only)

Maybe	Effects of an infant sleep intervention at child age 6 years: randomised controlled trial	Price et al.	2011	Full text unavailable (conference abstract only)
Maybe	Inconsolable infant crying and maternal postpartum depressive symptoms	Radesky et al.	2013	No parent anxiety outcome
Maybe	Adding "Circle of Security - Parenting" to treatment as usual in three Swedish infant mental health clinics. Effects on parents' internal representations and quality of parent-infant interaction	Risholm Mothander et al.	2018	No parent anxiety outcome (only available at baseline)
Maybe	Effects of home visits by paraprofessionals and by nurses: Age 4 follow-up results of a randomized trial	Olds et al.*	2004	No parent anxiety outcome
Maybe	The efficacy of toddler-parent psychotherapy to reorganize attachment in the young offspring of mothers with major depressive disorder: A randomized preventive trial	Toth et al.*	2006	No parent anxiety outcome (only available at baseline)
Maybe	Influence of relationship skills education on pathways of associations between paternal depressive symptoms and IPV and childhood behaviors	Roopnarine et al.	2018	No parent anxiety outcome
Maybe	A community-based randomized controlled trial of Mom Power parenting intervention for mothers with interpersonal trauma histories and their young children	Rosenblum et al.	2017	Incorrect population (parental mental health problems not recruitment focus)

Maybe	Improving Maternal Representations in High-Risk Mothers: A Randomized, Controlled Trial of the Mom Power Parenting Intervention	Rosenblum et al.	2018	Incorrect population (parental mental health problems not recruitment focus)
Maybe	20.4 - Infant Mental Health Home Visiting Buffers the Adverse Impact of Maternal Adverse Childhood Experiences on Toddler and Parent Outcomes	Rosenblum et al.	2020	Full text unavailable (conference abstract only)
Maybe	A randomized controlled trial of mother-infant psychoanalytic treatment: II. Predictive and moderating influences of qualitative patient factors	Salomonsson et al.	2011	No parent anxiety outcome
Maybe	A Long-term follow-up of a randomized controlled trial of mother-infant psychoanalytic treatment: Outcomes on the children	Salomonsson et al.	2015	No parent anxiety outcome
Maybe	A long-term follow-up study of a randomized controlled trial of mother-infant psychoanalytic treatment: Outcomes on mothers and interactions	Salomonsson et al.	2015	No parent anxiety outcome
Maybe	The incredible years parents and babies program: A pilot randomized controlled trial	Pontoppidan et al.*	2016	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Effects of parental intervention on behavioural and psychological outcomes for Kurdish parents and their children	Sangawi et al.	2018	Incorrect population (child age too high)

Maybe	The Effectiveness of an App-Based Nurse-Moderated Program for New Mothers With Depression and Parenting Problems (eMums Plus): Pragmatic Randomized Controlled Trial	Sawyer et al.	2019	Duplicate
Maybe	Parent Management Training Oregon Model and Family-Based Services as Usual for Behavioral Problems in Youth: A National Randomized Controlled Trial in Denmark	Scavenius et al.	2020	Incorrect population (child age too high)
Maybe	Efficacy of the “Tuebinger-Intensiv-Programm fur Eltern” in Treating Childhood Anxieties - A Pilot Study	Schlarb et al.	2015	Incorrect population (child age too high)
Maybe	Prevention of behavior problems in a selected population: Stepping Stones Triple P for parents of young children with disabilities	Shapiro et al.	2014	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Development and pilot evaluation of an Internet-facilitated cognitive-behavioral intervention for maternal depression	Sheeber et al.	2012	Incorrect population (child age too high) No parent anxiety outcome
Maybe	A randomized-controlled trial to examine the effectiveness of the 'Home-but not Alone' mobile-health application educational programme on parental outcomes	Shorey et al.	2017	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Effectiveness of a Technology-Based Supportive Educational Parenting Program on Parental Outcomes (Part 1): Randomized Controlled Trial	Shorey et al.	2019	Incorrect population (parental mental health problems not recruitment focus)

Maybe	Multiple mediation analysis of the peer-delivered Thinking Healthy Programme for perinatal depression: Findings from two parallel, randomised controlled trials	Singla et al.	2021	No parent anxiety outcome
Maybe	New Beginnings for mothers and babies in prison: a cluster randomized controlled trial.	Sleed et al.	2013	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Effects of video feedback on early coercive parent-child interactions: the intervening role of caregivers' relational schemas	Smith et al.	2013	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome
Maybe	Does improvement in maternal attachment representations predict greater maternal sensitivity, child attachment security and lower rates of relapse to substance use? A second test of Mothering from the Inside Out treatment mechanisms	Suchman et al.	2018	Incorrect population (child age too high) No parent anxiety outcome
Maybe	Mothering from the Inside Out: results of a pilot study testing a mentalization-based therapy for mothers enrolled in mental health services.	Suchman et al.	2016	Incorrect population (child age too high) No parent anxiety outcome (parent anxiety measure too broad)
Maybe	Effectiveness of attachment based STEEP TM intervention in a German high-risk sample	Suess et al.	2016	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome

Maybe	Group psychoeducational program for mothers of children with high functional pervasive developmental disorders: A randomized controlled trial	Suzuki et al.	2012	Full text unavailable (conference abstract only)
Maybe	Opioid addiction and neonatal abstinence syndrome (NAS, also known as neonatal opioid withdrawal syndrome): Effect of drug use targeted psychotherapy (DUST) on cessation of other addictive drug use	Tabi et al.	2019	Full text unavailable (conference abstract only)
Maybe	Maternal sleep and depressive symptoms: links with infant Negative Affectivity	Tikotzky et al.	2010	No parent anxiety outcome
Maybe	The efficacy of toddler-parent psychotherapy to reorganize attachment in the young offspring of mothers with major depressive disorder: a randomized preventive trial	Toth et al.	2006	Duplicate
Maybe	Outcomes following an early parenting center residential parenting program	Treyvaud et al.	2009	Incorrect population (parental mental health problems not recruitment focus)
Maybe	In-patient psychiatric-psychotherapeutic treatment of mothers with a generalized anxiety disorder--does the co-admission of their children influence the treatment results? A prospective, controlled study	Tritt et al.	2004	Incorrect population (child age too high) No relevant infant outcomes
Maybe	A randomized controlled trial of a home-visiting intervention aimed at preventing relationship problems in depressed mothers and their infants	van Doesum et al.	2008	No parent anxiety measure
Maybe	Maternal depression and child behaviour problems. Randomised placebo-controlled trial of a cognitive-behavioural group intervention	Verduyn et al.	2003	Incorrect population (child age too high)

Maybe	Strengthening Attachment Competencies in Parents with Mental Illness: Adaptation and Pilot Testing of the Mentalization-Based Lighthouse Parenting Program	Volkert et al.	2019	No parent anxiety measure (Parent anxiety measure neither continuous nor categorical; it is qualitative data)
Maybe	Emotional Disclosure Through Journal Writing: Telehealth Intervention for Maternal Stress and Mother-Child Relationships	Whitney & Smith	2015	No parent anxiety measure
Maybe	A pilot study of a parent-education group for families affected by depression	Williams et al.	2003	Incorrect population (child age too high)
Maybe	Interruption of dysfunctional mother-child reciprocal influences associated with family therapy	Wu & Slesnick	2019	Incorrect population (child age too high)
Maybe	Intervening with Attachment and Biobehavioral Catch-Up to decrease disrupted parenting behavior and attachment disorganization: The role of parental withdrawal	Yarger et al.	2020	No parent anxiety measure
Maybe	Placentophagy's effects on mood, bonding, and fatigue: A pilot trial, part 2	Young et al.	2018	Incorrect population (parental mental health problems not recruitment focus)
Maybe	Parenting skills and emotional availability: An RCT	Yousafzai et al.	2015	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome (parent anxiety measure too broad)

Maybe	Co-Occurring Trajectory of Mothers' Substance Use and Psychological Control and Children's Behavior Problems: The Effects of a Family Systems Intervention	Zhang et al.	2018	Incorrect population (child age too high)
Maybe	Clinical Demonstration of the Potential of Parental Feedback in Reducing Deterioration During Group Psychotherapy With Children	Bitan et al.*	2020	Incorrect population (child age too high)
Maybe	Postpartum Depression Prevention through the Mother-Infant Dyad: The Role of Childhood Trauma	Berry et al.	2021	Combines data from Werner et al. (2016; included) and Scorza et al. (2020; parental mental health problems not recruitment focus)
Include	A randomized, controlled trial of nurse home visiting to vulnerable families with newborns	Armstrong et al.	1999	No parent anxiety outcome
Include	Paraprofessional-delivered home-visiting intervention for American Indian teen mothers and children: 3-year outcomes from a randomized controlled trial	Barlow et al.	2015	Incorrect population (parental mental health problems not recruitment focus)
Include	Parenting and early development among children of drug-abusing women: effects of home intervention	Black et al.	1994	No parent anxiety outcome
Include	Links between Shared Reading and Play, Parent Psychosocial Functioning, and Child Behavior: Evidence from a Randomized Controlled Trial	Canfield et al.	2019	Incorrect population (parental mental health problems not recruitment focus) No parent anxiety outcome

Include	Mums 4 Mums: structured telephone peer-support for women experiencing postnatal depression. Pilot and exploratory RCT of its clinical and cost effectiveness	Caramlau et al.	2011	Study protocol
Include	Interactions and attachment in infants of mothers with OCD	Challacombe et al.	2015	Full text unavailable (conference abstract only)
Include	Attempting to prevent postnatal depression by targeting the mother-infant relationship: a randomised controlled trial	Cooper et al.	2015	No parent anxiety outcome[18]
Include	Maternal depression trajectories in adolescent mothers living in a poor urban area and their association with parental stress, infant behavioral problems, and psychological violence	Fatori et al.	2017	Incorrect population (parental mental health problems not recruitment focus)
Include	Establishing family foundations: intervention effects on coparenting, parent/infant well-being, and parent-child relations.	Feinberg et al.	2008	Incorrect population (parental mental health problems not recruitment focus)
Include	Establishing family foundations: intervention effects on coparenting, parent/infant well-being, and parent-child relations	Feinberg et al.	2008	Duplicate
Include	Randomized controlled trial of parent-infant psychotherapy for parents with mental health problems and young infants	Fonagy et al.	2016	No parent anxiety outcome

[18]Anxiety during pregnancy is reported at baseline but not mentioned thereafter; no pre/post parent anxiety outcome measure.

Include	Effective treatment for postpartum depression is not sufficient to improve the developing mother-child relationship	Forman et al.	2007	No parent anxiety outcome
Include	The efficacy of parent training for promoting positive parent-toddler relationships.	Gross et al.	1995	No parent anxiety outcome
Include	Long-term effects of a home-visiting intervention for depressed mothers and their infants	Kersten-Alvarez et al.	2010	No parent anxiety outcome
Include	Treatment of severe fear of childbirth with haptotherapy: Design of a multicenter randomized controlled trial	Klabbers et al.	2014	Study protocol
Include	Parent-Child Interaction Therapy with Toddlers: A Community-based Randomized Controlled Trial with Children Aged 14-24 Months	Kohlhoff et al.	2020	No parent anxiety outcome
Include	Effect of home-based peer support on maternal-infant interactions among women with postpartum depression: A randomized, controlled trial.	Letourneau et al.	2011	No parent anxiety outcome
Include	Video feedback compared to treatment as usual in families with parent-child interactions problems: A randomized controlled trial	Lydersen et al.	2015	No parent anxiety outcome
Include	Effectiveness of a peer-delivered, psychosocial intervention on maternal depression and child development at 3 years postnatal: a cluster randomised trial in Pakistan.	Maselko et al.	2020	No parent anxiety outcome

Include	A randomised controlled trial on intranasal oxytocin as an adjunct to interaction coaching to improve maternal bonding in women with mild postpartum depression	McErlean et al.	2011	Full text unavailable (conference abstract only)[19]
Include	Outcomes of a Randomized Trial of a Cognitive Behavioral Enhancement to Address Maternal Distress in Home Visited Mothers	McFarlane et al.	2017	No parent anxiety outcome
Include	Cumulative environmental risk in substance abusing women: early intervention, parenting stress, child abuse potential and child development.	Nair et al.	2003	No parent anxiety outcome[20]
Include	Infant outcomes following treatment of antenatal depression: Findings from a pilot randomized controlled trial	Netsi et al.	2015	No parent anxiety outcome
Include	Effects of lay support for pregnant women with social risk factors on infant development and maternal psychological health at 12 months postpartum.	Popo et al.	2017	No parent anxiety outcome
Include	Maternal patterns of antenatal and postnatal depressed mood and the impact on child health at 3-years postpartum.	Rotheram-Fuller et al.	2018	No parent anxiety outcome
Include	A randomized controlled trial of mother-infant psychoanalytic treatment: I. Outcomes on self-report questionnaires and external ratings	Salomonsson & Rolf	2011	No parent anxiety outcome

[19]Could not identify full report of this study so contacted the authors and received following response: 'Due to having null findings the first author didn't pursue publication. So unfortunately it's a file drawer null effect.' (Prof Mark Dadds; personal communication; 10 June, 2021).

[20]The Brief Symptom Inventory (BSI; Derogatis & Melisaratos, 1983) probes anxiety as one of nine psychological wellbeing dimensions at baseline, but this is not reported and there is no post-intervention anxiety measure.

Include	Oxytocin in postnatally depressed mothers: Its influence on mood and expressed emotion	Mah et al.	2013	No parent anxiety outcome
Include	Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women.	Spinelli et al.	2003	No parent anxiety outcome
Include	A pilot randomised controlled trial to evaluate the feasibility and acceptability of the Baby Triple P Positive Parenting Programme in mothers with postnatal depression.	Tsivos et al.	2015	No parent anxiety outcome
Include	The effects of a music and singing intervention during pregnancy on maternal well-being and mother-infant bonding: a randomised, controlled study	Wulff et al.	2021	No parent anxiety outcome
Hand sought	Lay support for pregnant women with social risk: a randomised controlled trial	Kenyon et al.	2016	No parent anxiety outcome
Hand sought	What makes a difference: Early Head Start evaluation findings in a developmental context: III. Impacts of Early Head Start participation on child and parent outcomes at ages 2, 3, and 5	Vogel et al.	2013	No parent anxiety outcome
Hand sought	A Trauma-Informed, Family-Centered, Virtual Home Visiting Program for Young Children: One-Year Outcomes	Mogil et al.	2021	Incorrect population (child age too high)
Hand sought	Outcomes at six years of age for children with infant sleep problems: longitudinal community-based study	Price et al.	2012	Incorrect population (parental mental health problems not recruitment focus)

Hand sought	A failure to confirm the effectiveness of a brief group psychoeducational program for mothers of children with high-functioning pervasive developmental disorders: a randomized controlled pilot trial	Suzuki et al.	2014	Incorrect population (child age too high)
Hand sought	Opioid addiction/pregnancy and neonatal abstinence syndrome (NAS): A preliminary open-label study of buprenorphine maintenance and drug use targeted psychotherapy (DUST) on cessation of addictive drug use.	Tabi et al.	2020	No parent anxiety outcome
Hand sought	Maternal Parenting Electronic Diary in the Context of a Home Visit Intervention for Adolescent Mothers in an Urban Deprived Area of São Paulo, Brazil: Randomized Controlled Trial	Fatori et al.	2020	Incorrect population (parental mental health problems not recruitment focus)
Hand sought	Haptotherapy as a new intervention for treating fear of childbirth: a randomized controlled trial. Journal of Psychosomatic Obstetrics & Gynecology, 40(1), 38-47.	Klabbers et al.	2019	No infant outcome
Hand sought	Preventing maternal mental health disorders in the context of poverty: pilot efficacy of a dyadic intervention	Scorza et al.	2020	Incorrect population (parental mental health problems not recruitment focus)
Key expert suggestion	Changes in infant emotion regulation following maternal cognitive behavioral therapy for postpartum depression	Krzeczkowski et al.	2021	No parent anxiety outcome (baseline co-morbid anxiety available only)

Hand sought	Effectiveness of a psycho-educational intervention for expecting parents to prevent postpartum parenting stress, depression and anxiety: a randomized controlled trial	Missler et al.	2020	Incorrect population (parental mental health problems not recruitment focus)
Hand sought	A randomized controlled trial of 'MUMentum Pregnancy': Internet-delivered cognitive behavioral therapy program for antenatal anxiety and depression	Loughnan et al.	2019	No relevant infant outcome (fetal rather than infant outcomes)
Maybe	Teaching attachment behaviors to pregnant women: a randomized controlled trial of effects on infant mental health from birth to the age of three months	Akbarzadeh et al.	2017	Unreliable reporting (discrepancies regarding main findings and nature of intervention, among other inconsistencies)
Hand sought	Relationship and mother-infant bonding outcomes following a psychological intervention for antenatal anxiety	Thompson-Booth	2017	Unpublished thesis without peer review

Table S7 Reasons for inclusion for articles assessed at full-text

Original ti ab classification	Title	Author(s)	Year	Parent outcome measure (pre/post intervention)	Infant/parent-infant outcome measure (pre/post intervention)	All other eligibility criteria met (Y/N)
Maybe	PREPP: postpartum depression prevention through the mother-infant dyad	Werner et al.	2016	Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959)	Average daily frequency of fuss/cry episode; Baby's Day Diary (Barr et al., 1988)	Yes
Include	Effects of psychological treatment of mental health problems in pregnant women to protect their offspring: Randomised controlled trial	Burger et al.	2020	Brief State-Trait Anxiety Inventory (Brief STAI; Marteau & Bekker, 1992)	CBCL (Internalising/Externalising; Rescorla, 2005); and Postpartum Bonding Questionnaire (PBQ; Brockington et al., 2006)	Yes
Include	A pilot randomized controlled trial of time-intensive cognitive-behaviour therapy for postpartum obsessive-compulsive disorder: effects on maternal symptoms, mother-infant interactions and attachment.	Challacombe et al.	2017	Yale–Brown Obsessive–Compulsive Scale (YBOCS; Goodman et al., 1989)	Numerous (x8 measures) including: Bates Infant Temperament Questionnaire (ITQ; Bates et al., 1979) and Ainsworth sensitivity/intrusiveness measures (Ainsworth et al., 1978)	Yes

Include	A therapeutic playgroup for depressed mothers and their infants: feasibility study and pilot randomized trial of community HUGS	Ericksen et al.*	2018	Depression, Anxiety and Stress Scale (DASS; Lovibond & Lovibond, 1995)	Paediatric Infant Parent Exam (PIPE; Fiese et al., 2001)	Yes
Hand sought	Feasibility study and pilot randomised trial of an antenatal depression treatment with infant follow-up	Milgrom et al.*	2015	Beck Anxiety Inventory (BAI; Beck & Steer, 1991)	Numerous, including: Ages and Stages Questionnaire Social Emotional (ASQ:SE: Squires et al., 2002) and Infant Behaviour Questionnaire Short Form (IBQ- R: Gartstein and Rothbart, 2003; Putnam et al., 2014)	Yes
Maybe	Improving the mother-infant relationship following postnatal depression: a randomised controlled trial of a brief intervention (HUGS)	Holt et al.*	2021	Beck Anxiety Inventory (BAI; Beck & Steer, 1991)	Numerous, including: ASQ-SE (Squires et al., 2002); PBQ (Brockington et al., 2006)	Yes
Include	Perinatal Dyadic Psychotherapy for postpartum depression: a	Goodman et al.	2015	State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970)	Coding Interactive Behavior manual (CIB; Feldman, 1998): maternal sensitivity,	Yes

	randomized controlled pilot trial			Anxiety disorder measured by the Structured Clinical Interview for DSM-IV-R for Axis I disorders (SCID-IV-R; First et al., 1998)	dyadic reciprocity, infant involvement	
Include	Lessons learned from a pilot randomized controlled trial of dyadic interpersonal psychotherapy for perinatal depression in a low-income population	Lenze et al.	2020	Brief State-Trait Anxiety Inventory, State Scale (Berg et al., 1998)	Numerous including: the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter et al., 1999); Coding Interactive Behavior manual (CIB; Feldman, 1998)	Yes
Maybe	Postnatal depression and mother and infant outcomes after infant massage	O'Higgins et al.	2008	Spielberger State Anxiety Inventory (SSAI; Spielberger et al., 1970)	Numerous including: Global Ratings for Mother–Infant Interactions (see Murray et al., 1996)	Yes
Hand sought	Netmums: a phase II randomized controlled trial of a guided Internet behavioural activation treatment for postpartum depression	O'Mahen et al.	2014	Generalised Anxiety Disorder 7-item screening tool (GAD-7; Spitzer et al., 2006)	Postnatal Bonding Questionnaire (PBQ; Brockington et al., 2006)	Yes

Maybe	Mitigating the effect of persistent postnatal depression on child outcomes through an intervention to treat depression and improve parenting: a randomised controlled trial.	Stein et al.	2018	Generalised Anxiety Disorder (and Posttraumatic Stress Disorder) as measured by the Structured Clinical Interview for DSM-IV-R for Axis I disorders (SCID-IV-R; First et al., 1998)	Numerous including CBCL and child emotion-regulation assessed with the barrier paradigm from the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith & Rothbart, 1996)	Yes
Hand sought	An exploratory parallel-group randomised controlled trial of antenatal Guided Self-Help (plus usual care) versus usual care alone for pregnant women with depression: DAWN trial	Trevillion et al.	2020	Proportion meeting Generalized Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006) criteria for anxiety (i.e., score of ≥8)	Postnatal Bonding Questionnaire (PBQ; Brockington et al., 2006)	Yes

Table S8 Risk of bias assessment – Burger.

Unique ID	BURGER	**Study ID**	CSPASR01_BURGER	**Assessor**	Consensus: CS/DJ
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	CBT	**Comparator**	CAU	**Source**	Journal article(s); Trial protocol; Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	CBCL Internalising - 18 months postpartum	**Results**	Mean difference 0.76 (95% CI -0.11,1.63), T = 1.73, p = 0.085	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1-1.2), yes. 'Eligible women were randomised 1:1 to either CBT or CAU by an independent assistant after baseline assessments using a computer-generated list created by a central service...' (p. 183).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3), probably no. There are differences related to prognostic factors but these are compatible with chance (e.g., the CBT group has a higher prevalence of single diagnosis while CAU group has a higher prevalence of co-morbidity). 'The randomised groups... were comparable on most baseline variables, though anxiety, PTSD and depression as single disorders were more prevalent in the CBT group, and a diagnosis of comorbid depression and an anxiety disorder or PTSD was more prevalent in the CAU group' (p. 184).

	Risk of bias judgement	**Low**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PY	Regarding (2.1), probably yes as participants are not specified as being masked. 'The trial is a ... CONSORT-compliant parallel-group assessor-masked multicentre RCT…' See also reference to trial registry: 'single masking'. Regarding (2.2), probably yes. Given the nature of intervention and comparator, it is unlikely participants and clinicians would be unaware of their assigned intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PY	Regarding (2.3), probably yes. See discrepancy between session delivery; listed as 'once a week' in the trial registry vs. irregular in the final report ('the exact timing of the sessions was planned on the basis of shared decision-making with the participant'). This deviation presumably arose from the trial context, perhaps as irregular sessions made the intervention easier to engage with for participants.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	PN	Regarding (2.4), probably no. The intervention will have taken place in the same time period for all women regardless, though sessions may have been concentrated at certain time points for different women. (i.e., '10-14 individual sessions, of which 6-10 were intended to be delivered during pregnancy. Sessions were scheduled from 20 weeks' gestation up to 3 months postpartum; the exact timing of the sessions was planned on the basis of shared decision-making with the participant' (p. 183).
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes. 'Analyses were primarily performed according to the intention-to-treat principle' (p. 183).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Some concerns**	--

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	N	Regarding (3.1), no. Rather, 46 (CBT group) and 44 (CAU group) participants were missing (see Table 3, p.187).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Regarding (3.2), probably yes. 'Because neither MAR nor MCAR can be proved, we added complete case analyses as a sensitivity analysis' (p. 184) ... 'In all analyses, adjustment for baseline diagnosis or following a complete case approach did not materially affect the results' (p. 186).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Regarding (4.1), probably no. 'The primary outcome was the... behavioural and developmental problems in the child at 18 months of age, assessed using the validated, parent-report Child Behavior Checklist for Ages 1.5-5 (CBCL/1.5-5)' (p. 183). I am unable to comment on whether important ranges of outcome values fall outside levels that are detectable using this measure.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no. The CBCL measure was only collected at '18 months of age' (p. 183) – the exact procedure for the 18 month visit is not specified at the group-level, but this is likely due to word limit constraints only.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Regarding (4.3), yes. The measure is partly parent-report, and the guidance indicates that, for participant-reported measures, the assessor is the study participant. Study participants do not appear to be blinded/masked in this study (see answers to Domain 1).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.4), probably yes. The CBCL requires parental judgement of child behaviour. The intervention was not directly focused on managing the infant relationship (the 'overall focus was on identifying and changing dysfunctional

	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	beliefs', p. 183) but did address 'pregnancy-related cognitions and attitudes', which might have included thoughts about the fetus/unborn infant. Therefore, it is plausible that knowledge of the intervention informed the participant's judgement of the outcome. However, regarding (4.5), there are unlikely to be strong levels of belief in either beneficial or harmful effects of the CBT intervention on the part of the participant. That is, there is no reason that they should have 'therapy allegiance'; they were women 'recruited in 109 midwifery practices and 9 obstetrics and gynaecology departments...' (p. 183).
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalised before unblinded outcome data were available for analysis?	PN	Regarding (5.1), probably no. While the protocol and journal article agree that analyses will be carried out according to 'the intention-to-treat-principle' (p. 6 of protocol; p. 183 journal article), they differ with respect to the analysis for the CBCL. The trial protocol states the CBCL will be analysed using 'unpaired t-tests' (see p. 6) yet the journal article states that linear regression models were used for analysis (see Table 3, caption a).
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Regarding (5.2), probably no. Note that there is a 'Caregiver-Teacher Report Form (C-TRF) that is averaged with the parent-report (p. 183) and scores for these are not given separately. However, the decision to present this as an average may be a product of the scoring system. Note also in the trial protocol that the CBCL 'provides ratings of seven syndrome scales' in addition to 'internalising, externalising, and total problems' (p. 5), and it is not stated which of these will be measured specifically in the final report. However, the result is null; it is unlikely to have been selected on the basis of 'noteworthy' results.
	5.3 ... multiple eligible analyses of the data?	PN	Regarding (5.3), probably no. Though there is insufficient detail on which measures of the CBCL were intended to be analysed, the result is null; it is unlikely the numerical result has been selected on the basis of the result.
	Risk of bias judgement	**Some concerns**	--

Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S9 Risk of bias assessment – Challacombe.

Unique ID	CHALLACOMBE	**Study ID**	CSPASR01_CHALLA	**Assessor**	CS
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	iCBT	**Comparator**	TAU	**Source**	Journal article(s)
Outcome	Maternal vocalisations - 12 months postpartum	**Results**	F (2, 69) = 2.16, p = .12	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1-2) yes. 'A random sequence of the two treatment categories was generated in blocks of six (www.randomization.com). A person unconnected with the study sealed cards with each category in numbered individual envelopes. The researcher and participants were blind to group allocation until the envelope was opened at the end of the baseline assessment' (p. 1482).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PY	Regarding (1.3), possibly yes. 'The TAU group was significantly higher in dimensionally measured anxiety on the DASS scale' (p. 1481). Anxiety was likely to be a relevant prognostic factor in this study.
	Risk of bias judgement	**Some concerns**	--

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Regarding (2.1-2), yes. 'The researchers and participants were blind to group allocation until the envelope was opened at the end of the baseline assessment' (p. 1482). Note that the intervention provider, FLC, was the lead author, i.e., a member of the research team (see p. 1482).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NI	Regarding (2.3), inadequate detail is available on the intended intervention so it is not possible to make a judgement.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes. 'Analyses were 'intention to treat' and outcome data were available for all participants' (p. 1481).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Some concerns**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	Y	Regarding (3.1), yes. Only one participant was missing from each group. This was calculated from the total number of participants indicated in the abstract (p. 1478) minus the number of participants with data available according to Table 3 (p. 1484).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	

	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	Regarding (4.1), there is insufficient detail regarding this measure available to make a judgement.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), though there is limited detail available on the data collection procedure, it appears that the data collection process was consistent between groups (see Table 3, p. 1484) and lack of clarity on this point is likely due to word limits in the journal article.
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Regarding (4.3), no. 'The outcome/12 month assessment was conducted by a researcher who was blind to group allocation and was not in any way involved in the therapy ... Video coding of interactions was conducted by a further researcher blind to group…' (p. 1482).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalised before unblinded outcome data were available for analysis?	NI	Regarding (5.1), inadequate detail available about intended analyses precludes a judgement of this.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Regarding (5.2), inadequate detail available about intended analyses precludes a judgement of this.

	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), inadequate detail available about intended analyses precludes a judgement of this.
	Risk of bias judgement	**No information**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S10 Risk of bias assessment – Ericksen

Unique ID	ERICKSEN	**Study ID**	CFPASR01_ERICKSEN	**Assessor**	CS
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	CHUGS	**Comparator**	Wait-list control	**Source**	Journal article(s); Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	PSI - difficult child - 10 weeks post-randomisation	**Results**	Wald x^2[1] = 6.82, p = .01	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	Regarding (1.1-2), yes. 'A computer-generated permuted blocks randomised treatment allocation schedule produced by an independent researcher and administered by a hospital administrator was used and remained double-blinded until the point of allocation' (p. 401).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PY	Regarding (1.3), potentially/probably yes, insofar as a key prognostic factor (quantity of children) was imbalanced: 'the number of women with only one child was approximately one and a half times higher in the intervention group, a potentially important imbalance' (p. 404). Note that authors conducted 'independent samples t-tests comparing participants with one child with those with two[+] children [and this showed] no significant differences' (p. 404). Note also that the guidance document suggests that 'to remove the risk of bias caused by problems in the randomisation process, it would be necessary to know, and measure, all the prognostic factors that were imbalanced at baseline. It is unlikely

			that all important prognostic factors are known and measured, so such analyses will at best reduce risk of bias' (p. 18).
	Risk of bias judgement	**Some concerns**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PY	Regarding (2.1-2), probably yes as the trial registration indicates 'masking not used', presumably with the exception of allocation concealment (see answers to 1.1-2).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	Regarding (2.3), probably no. The trial registration record and the journal article have high levels of consistency. The trial registry record describes a 'specialised 10-week therapeutic playgroup to promote the relationship between mother and infant ... sessions are delivered in group format with facilitators following a detailed manual. Sessions last approximately one hour (once a week for 10 weeks) and are followed by an informal chat and refreshments.' This accords with the journal article protocol: 'Weekly playgroups were run ... participants completed... 10 weekly sessions lasting approximately 60 to 90 min each, and the content of each module focused on areas of difficulty within the mother-baby interaction...' (p. 400).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes. 'Data from [this study] were analysed on an intention-to-treat (ITT) basis' (p. 401).

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Low**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	PN	Regarding (3.1), probably no. It appears from the participant flow diagram (p. 403) that 16 participants were randomised to CHUGS but post-treatment data were only available for 13 participants (i.e., three missing) and 15 were randomised to the wait-list control but post-treatment data were only available for 13 participants (i.e., two missing). A further participant was missing from the WL control for this outcome measure at post-treatment (see footnote 'a', Table 3). This represents 18.75% of missing data (CHUGS & WL control). See p. 403 for participant flow diagram and p. 404 for Table 3.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Regarding (3.2), probably yes insofar as authors could show missing data were MCAR. See analytical plan detailing imputation of missing data assuming 'data were missing completely at random' (Little's MCAR test statistics given). Note also that analyses were executed a second time 'using observed data' and 'for between group comparisons, continuous outcomes were fitted in generalised estimating equations that accounted for the clustering of groups and baseline scores.' (p. 401).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Regarding (4.1), no. 'The Parenting Stress Index Short Form' (PSI/SF, Abidin, 1995) has adequate validity, including in high-risk samples (Barroso et al., 2016). Note, this is not stated in the journal article but is identifiable in the wider literature.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no. Data collection is reported to be similar, e.g., 'outcome data were collected at two points in ... the... pilot RCT: at baseline (completed before Session 1) and post-treatment (completed either after Session 10 of the program or contemporaneously in the RCT wait-list control group)' (p. 400). Note that the trial registry record indicates that the 6-month outcome was only measured for the intervention group, but as the outcome of interest is the post-treatment effect (not 6-month outcome), this is not relevant.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Regarding (4.3), probably yes as the PSI/SF is a parent-report measure, and the participants were likely aware of their intervention assignment (see answers to question 2.1).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.4), probably or potentially yes. The intervention was 'specifically target[ing] the mother-infant relationship' (p. 399) and the outcome measure involves individual judgement. However, regarding (4.5), probably no, as the population recruited are not known to have preconceived beliefs about the benefits or harms of the intervention ('women were included if they had a child less than 1 year old and had recently consulted with a health professional about their mental health;' p. 401).
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), there is insufficient detail in the trial registry record to make an assessment.

	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Regarding (5.2), there is insufficient detail in the trial registry record to make an assessment.
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), there is insufficient detail in the trial registry to make an assessment.
	Risk of bias judgement	**No information**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S11 Risk of bias assessment – Goodman

Unique ID	GOODMAN	**Study ID**	DJPASR01_GOODMAN	**Assessor**	CS
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Perinatal Dyadic Psychotherapy	**Comparator**	'Control'	**Source**	Journal article(s); Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	CIB - infant involvement - 3 months follow-up	**Results**	Coefficient: .01, z = .07, p = .95 (95% CI, -.29, .31)	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	Regarding (1.1), probably yes. 'Mother-infant dyads were randomised to intervention or control groups by the study coordinator using consecutively numbered, sealed, opaque envelopes containing randomly generated numbers' (p. 5). Regarding (1.2), probably yes. See above quote regarding envelopes. Also: 'randomisation occurred without coordinator's knowledge of or access to baseline data' (p. 5).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PY	Regarding (1.3), probably yes given an imbalance in key prognostic factors. 'There was a statistically significant difference on state anxiety score, with the intervention group (M = 43.62, SD = 9.47) showing significantly higher baseline state anxiety than controls (M = 36, SD = 10.39, p = 02) [independent samples t-test].' See Table 2 and p. 9.
	Risk of bias judgement	**Some concerns**	--

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PY	Regarding (2.1), probably yes. The trial registry record refers to 'single' masking for 'outcomes assessor' but not participants. In addition, the journal article states that the research assistants were 'blind to psychiatric status and group assignment' (p. 6) but participant masking is not mentioned. It is likely that participants would be aware of their assignment given the nature of the intervention. Similarly, the intervention providers would be aware of the assignment given its qualitative difference from the control group (p. 5).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Regarding (2.3), no. The trial registration and journal article information about the intervention and control group have high consistency. Compare paragraph two of p. 5 (journal article) with 'Study arms' bullet points in tabular format (trial registration).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Regarding (2.6), probably yes. Though ITT principles are not stated, the analyses are nonetheless appropriate for estimating effect of assignment on the basis that there 'was no attrition from the study for either the intervention or control groups' (pp. 9-10).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	Y	Regarding (3.1), yes. 'There was no attrition from the study for either the intervention or control groups' (pp. 9-10).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	

	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Regarding (4.1), no. 'Recordings were analysed using the Coding Interactive Behavior manual (CIB: Feldman, 1998), a well-validated method for measuring parent-infant interactions that has demonstrated sensitivity to... psychiatric risk and intervention effects' (p. 8).
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no as the journal article suggests outcome data was collected at the same time in the same way by research assistants regardless of group: 'post-intervention and follow-up outcome data were collected at home visits by RAs blind to psychiatric status and group assignment' (p. 6).
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Regarding (4.3), no: 'mother-infant interaction videotapes were coded by two RAs... blind to participant group status' (p. 6).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), there is inadequate detail in the trial registration to make a judgement on this point.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Regarding (5.2), analysis intentions are not available in detail from the trial registration so it is not possible to make a judgement on this. It is plausible that the study authors could have chosen to analyse the measures differently

			but they have reported all the key composites from the coding scheme across numerous timepoints, virtually all of which are non-significant (including the numerical result under assessment here) so it is unlikely the numerical result was selected on the basis of the results.
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), there is not sufficient detail available from the trial registration to judge this.
	Risk of bias judgement	**Some concerns**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S12 Risk of bias assessment – Holt

Unique ID	HOLT	**Study ID**	CSPASR01_HOLT	**Assessor**	Consensus: CS/DJ
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	PND program + HUGS	**Comparator**	PND program + control playgroup	**Source**	Journal article(s); Trial protocol; Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	ERA Factor I - 6 months follow-up	**Results**	F[1, 47] = 4.96, p = .03, partial eta squared = .10	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1), yes. See journal article: 'women were randomised in a 1:1 ratio prior to the PND program. A computer-generated permuted blocks... randomised treatment allocation schedule, stratified by treatment site, was produced by an independent researcher and administered by a hospital administrator, double blinded until the point of allocation. The hospital administrator sequentially allocated each new participant from an ID number and corresponding A or B allocation from the pre-generated list. The hospital administrator was blind to the representation of A (HUGS) and B (control playgroup). The researcher informed the participant of their allocation' (p. 4).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PY	Regarding (1.3), probably yes due to there being a 10% higher frequency of major depressive episodes in the HUGS intervention group vs. control group (see Table 2,

			p. 6), which the authors note is a 'potentially important imbalance' (presumably as it is a prognostic factor).
	Risk of bias judgement	**Some concerns**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	N	Regarding (2.1), no. The journal article states: 'participants were blind to treatment allocation as both conditions were presented as potentially beneficial playgroups that were being compared. The women had consented to be randomised to one of two playgroups' (p. 5). Regarding (2.2), probably yes as the people delivering the intervention were not involved in the control playgroup: 'facilitators were ... trained to deliver the intervention and were not involved in the control playgroup' (p. 3).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	The trial protocol and journal article are consistent in the description of both the HUGS and control playgroup. There was also no way that informed consent could have influenced intervention effects due to the randomisation method (see response to question 2.1).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes as analyses were ITT: 'Primary outcomes were analysed on an intention-to-treat basis' (p. 5).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Low**	--

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	N	Regarding (3.1), no. Data were available from 23/38 HUGS participants and 28/39 control playgroup participants (see Fig. 1).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Regarding (3.2), unclear but probably yes. The authors conducted analyses to correct for bias (‘baseline depression was controlled for in all analyses,’ p. 5). Also, analyses were conducted twice: 'once using observed data and once after imputing missing values' (p. 5) According to the guidance document, a multiple imputation approach ‘based only on the intervention group’ is insufficient evidence for unbiased results (p. 45). However, in this instance ‘all available data from both participants were analysed in their allocated conditions’ (p. 5), indicating this was not the case.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PY	Regarding (3.3), probably yes, due to baseline imbalances involving a prognostic factor (i.e., number of MDD episodes, see Table 2), and on the basis that reasons for participants dropping out were not documented. However, regarding (3.4), no, as the analyses accounted for participant characteristics likely to explain missingness in the outcome and its true value (see answer to question 3.2).
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Regarding (4.1), no due to the validity of the measure and its suitability for both normative and high-risk samples: 'the validity and reliability of the ERA have been established in high-risk and normative samples' (p. 4, Table 1).
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no as the groups were matched for duration/frequency (HUGS: 'four, weekly 1.5h group sessions'; control: 'four, weekly 1.5h ... group sessions, p. 3). In addition, on Table 1 of the trial protocol, the authors express the third timepoint as 'Post-HUGS/Playtime' (p. 5), indicating measures would be collected after both groups had finished. Lack of explicit comment on comparable measurement in the journal article is likely an effect of word count limits.
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Regarding (4.3), no. The outcome assessors were blinded: 'Coders using the ERA were also blind to treatment allocation and time point of video-taped segment' (p. 5).

	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Regarding (5.1), probably yes. The trial protocol 'analyses' section includes reference to 'controlling for baseline values' (p. 4), 'intention-to-treat' principles (p. 5), and the analysis of 'observed data' and data using 'multiple imputation methods' as well as assessors who are 'blind to treatment' (p. 5). This is all consistent with what is reported in the journal article (see quotations given in answers for Domains 2-3). The authors do not document the use of 'ANCOVA' in the trial protocol, which is what is used in the journal article (p. 5); this is one discrepancy.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PY	Regarding (5.2), probably yes. The trial protocol indicates that the ERA was due to be measured at the post-PND programme time point (p. 5, Table 1), but it was not shown to have been measured in the final paper, and no explicit justification was provided for this (p. 4, Table 1). The guidance document notes that an answer of 'no' or 'probably no' can only be assigned to this RoB question if 'there is clear evidence (…) that all eligible reported results for the outcome domain correspond to all intended outcome measurements' (p. 63). Possibly the ERA was not measured at the post-PND programme time point as its effects are not likely to be detected until a mother-infant intervention has been carried out, as suggested by the text describing ERA Factor I in Table 1: '[ERA FI] was selected a priori, based on previous research that showed significant improvements in this domain following mother-infant intervention' (p. 5). However, this argument is not made explicit and does not explain why the trial authors stated that the measure would be collected at the post-PND programme in the original protocol.

			When reviewing the Figures in the journal article for the PBQ, PSI and ERA Factor I, the absence of the post-PND programme timepoint for ERA Factor I is particularly apparent. There is a possibility that data from the post-PND programme timepoint was measured (as indicated by the trial protocol) but not reported. This is a cause for some concern and should be highlighted in the review.
	5.3 ... multiple eligible analyses of the data?	PN	Regarding (5.3), probably no. The trial protocol analyses are consistent with the journal article statistical analyses (with the exception noted in response to question 5.1, above).
	Risk of bias judgement	**High**	
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S13 Risk of bias assessment – Lenze

Unique ID	LENZE	**Study ID**	CFPASR01_LENZE	**Assessor**	CS
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	IPT-DYAD	**Comparator**	ETAU	**Source**	Journal article(s); Trial protocol
Outcome	CIB - parent sensitivity - 6 months postpartum	**Results**	IPT-Dyad: estimate 0.21 (SE .08), F = 7.13, p =.02 (95% CI, -.39, -.04); ETAU: estimate -.17 (SE .09), F = 4.06, p = .06 (95% CI -.36, .08)	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1-2), yes. See: 'eligible participants were randomised by a statistician using a computer generated permuted block design to IPD-Dyad... or ETAU ... The PI and study staff were blinded to the randomization grid and assignments were stored in opaque, sealed envelopes opened by participants after signing consent' (p. 287).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3), no. 'There were no significant differences between IPT-Dyad and ETAU on demographic variables at baseline' (p. 288).
	Risk of bias judgement	**Low**	--
Bias due to deviations from	2.1.Were participants aware of their assigned intervention during the trial?	Y	Regarding (2.1), yes. 'Assignments were stored in opaque, sealed envelopes opened by participants after signing consent' (p. 287).

intended interventions	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	NI	Regarding (2.2), unclear. The journal article states that 'the PI and study staff were blinded to the randomization grid' (p. 287) but, later on it states that study staff (e.g. 'SL') delivered the intervention, with 'all sessions [...] video-taped and reviewed during weekly team meetings (including SL, JL, and JR or MAP) and individual supervision sessions with the PI (p. 288).
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	Regarding (2.3), probably not. The trial registration is consistent with the journal article (NB: no trial protocol available). The trial registration states that the intervention consists of a 'brief psychotherapeutic intervention, during pregnancy. Interpersonal psychotherapy focuses on improving social relationships and interpersonal communication to improve mood. The postpartum phase also utilises developmentally appropriate strategies to improve the mother-infant relationship.' This is compared with the journal article, which refers to brief-IPT ‘during pregnancy’ and ‘postpartum sessions.’ These have a ‘dual focus’ - the ‘mother's IPT problem area and [...] the mother-infant dyad’ (p. 287).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes. The authors 'follow[ed] intent to treat principles' and 'included all randomised participants in the models' (p. 288).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Low**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	N	Regarding (3.1), no. In the intervention group, 7/21 [~33%] participants' data were missing, and in the control group, 6/21 [~29%] participants' data were missing (compare Table 1, p. 289 and flow diagram, p. 290).

	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Regarding (3.2), probably yes as the authors elected to use 'linear mixed models, which are less sensitive to missing data time-points than repeated measures ANOVA … We used unstructured, repeated and Kenward-Rogers specifications for the outcome measures that were collected at four or more timepoints' (p. 288). Though note this means that the results indicate within group rather than between group significance.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Regarding (4.1), no. The CIB scheme, from which this outcome measure is drawn, has been validated on several high and low-risk samples (Feldman et al., 1997, Feldman et al., 2004).
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Regarding (4.2), no. The journal article states: '... outcomes were measured [at] 3 months, 6 months, 9 months and 12 months postpartum in both IPT-Dyad and ETAU groups unless otherwise indicated below' (p. 288).
	4.3 Were outcome assessors aware of the intervention received by study participants?	NI	Regarding (4.3), unclear; though the authors state that 'study staff were blinded to the randomization grid', in the trial registration the 'masking' question is answered as 'None (Open label)'.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NI	Regarding (4.4), unclear for reasons given in response to (4.3). Regarding (4.5), it is difficult to judge whether the assessment of the outcome was influenced by the knowledge of intervention received as the measure was collected by the 'research team' (p. 288) rather than the intervention providers (i.e., 'clinical psychologist or... professional counsellors', p. 287). Regardless of whether the research team were blinded or not, they are less likely than intervention providers to hold beliefs about the efficacy of the
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NI	

			intervention. However, it is possible the research team could have 'therapy allegiance.' Such information is rarely included in journal articles.
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), insufficient detail in the trial registration precludes a judgement on this point. In addition, no trial protocol was available.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Regarding (5.2), probably no as the journal article reports all scales measured at all timepoints (compare p. 288 with p. 289, Table 1).
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), insufficient detail is available to judge analysis intentions.
	Risk of bias judgement	**Some concerns**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S14 Risk of bias assessment – Milgrom

Unique ID	MILGROM	**Study ID**	CSPASR01_MILGROM	**Assessor**	CS
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Beating the Blues Before Birth	**Comparator**	Usual care	**Source**	Journal article(s); Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	ASQ:SE - Self-regulation - 9 months postpartum	**Results**	Cohen's d = .83, F = 2.22, p = .04 (95% CI 0.41, 1.24)	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	Regarding (1.1-2), probably yes; a random element is stated and it seems participants provided consent in advance of allocation. 'Consenting, eligible women were allocated to treatments at random in a 1:1 ratio. A variable-length permuted block randomisation schedule was generated by an independent person prior to commencement of the trial and was centrally administered by a hospital administrator blind to treatment coding' (p. 723).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3), probably no. There are no incompatibilities that seem to be above chance (see Table 5, p. 725). Also see author statement: 'the groups appeared broadly comparable' (p. 724).

	Risk of bias judgement	**Low**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Regarding (2.1-2.2), yes/probably yes as the trial registry record indicates 'masking not used' and 'open'.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	Regarding (2.3), probably no (though uncertain). The information in the trial registry record is consistent with the journal article description of the intervention. The trial registry record states that the intervention group has '8 sessions of a cognitive behavioural therapy group program... each weekly session runs for an hour and a half ...' The journal article refers to 'pregnancy-specific CBT' and an 'eight-session programme' where each session runs 'for approximately an hour' (p. 723). However, there is a discrepancy between the medium of delivery (indicated to be a group format in trial registration and 'one-to-one' in the journal article). This is justified by the authors: 'the feasibility study suggested that individual delivery was an acceptable format for the [intervention].' This indicates that deviation from the intended intervention was due to empirical evidence of acceptability rather than the trial context.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Regarding (2.6), probably yes as it seems like the authors used a modified ITT approach in which participants with missing outcome data were excluded. ‘Only the main maternal outcomes (post-treatment depression and anxiety) in the pilot RCT were analysed by intention-to-treat. All other statistics are based on observed-case analysis' (p. 724).

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Low**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	N	Regarding (3.1), no. In the intervention group, 11/27 participants' data were missing, with 14/27 in the control group. This amounts to approx. 46% of attrition (see p. 725).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Regarding (3.2), probably yes. The authors state that they used 'univariate logistic regression to determine any prognostic baseline variables that predicted the return or non-return of follow-up data' (p. 724).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Regarding (4.1), probably no. Though the journal article does not state this, the ASQ:SE measure is validated for both low and high-risk samples (see Squires et al., 2004).
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably not as it appears the two groups followed the same data collection schedule. 'Following treatment (9 weeks after randomisation for both conditions), participants completed [other outcome measures] which were administered again at the infant follow-up (9 months postpartum)' (p. 722).
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Regarding (4.3), probably yes as the ASQ:SE measure is a self-report tool and the participants were likely aware of their group allocation (see response to question 2.1).

	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.4), possibly yes as the intervention involved some focus on parental expectations ('unrealistic expectations of parenting', p. 723), and knowledge of this could affect answers to the ASQ:SE, which involves individual judgement. However, regarding (4.5), probably not as the population recruited are not known to have preconceived beliefs about the benefits or harms of this intervention ('pregnant women aged 18 years and over, less than 30 weeks pregnant with a depressive disorder', p. 721).
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), there is inadequate detail on the intended analyses in the trial registry record to make an assessment.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Regarding (5.2), there is inadequate detail on the intended analyses in the trial registry record to make an assessment (indeed, the ASQ:SE is not mentioned specifically in the trial registry record).
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), there is inadequate detail about the intended analyses in the trial registry record to make an assessment.
	Risk of bias judgement	**No Information**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S15 Risk of bias assessment – O'Higgins

Unique ID	OHIGGINS	**Study ID**	CSPASR01_OHIGGINS	**Assessor**	CS
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	Infant massage	**Comparator**	Support group control	**Source**	Journal article(s)
Outcome	Maternal sensitivity - 12 months postpartum	**Results**	F = 4.95 (2), p = .08	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	NI	Regarding (1.1-2), there is limited detail available on this due to the format of the journal article ('brief report') and its strict word count - but it is likely the trial met these standards.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3), probably no: 'at baseline, the two depressed groups were similar to each other...' (p. 191).
	Risk of bias judgement	**Some concerns**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PY	Regarding (2.1-2), probably yes because of the qualitatively different nature of the interventions, and because specialists ran the infant massage group while researchers ran the control group. See 'classes were run by trained members of the [IAIM]' (p. 191) vs. 'the [support group] was run by an experienced research team member' (p. 191).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	

	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NI	Regarding (2.3), it is not possible to make an assessment due to inadequate detail available about the intended intervention.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PN	Regarding (2.6), insufficient detail is available regarding analysis. The authors state: 'any mother who completed four sessions or more as well as the outcome measures was included in the analysis.'
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NI	Regarding (2.7), insufficient detail is available, though this is very likely to be a product of strict word limits.
	Risk of bias judgement	**Some concerns**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	NI	Regarding (3.1), it is not possible to judge this as there is insufficient detail on the number of participants' data available.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PN	Regarding (3.2), there is not enough detail in the journal article to make a judgement, though there is no 'no information' response available so I have selected 'probably no.'
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NI	Regarding (3.3-4), there is inadequate information available to make an assessment of whether missingness in the outcome depended on its true value. The lack of detail is more likely to depend on the word limits than issues with the study so a judgement of 'some concerns' rather than 'high risk' has been selected here.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NI	
	Risk of bias judgement	**Some concerns**	--

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Regarding (4.1), probably not due to the well-established use of Murray's Global Rating scales in similar interaction contexts (Murray et al., 1996). Though note, no formal validation paper is available.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no. See: 'mothers were asked to attend six sessions of their assigned intervention after which they completed questionnaires and were filmed interacting with their infant again at infant age 19 weeks' (p. 190).
	4.3 Were outcome assessors aware of the intervention received by study participants?	N	Regarding (4.3), no. The outcome was assessed by a 'blinded, trained rater' (p. 190).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), there is insufficient detail on the subject of the intended analyses to make a judgement.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Regarding (5.2), see answer to (5.1).
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), see answer to (5.1).
	Risk of bias judgement	**No information**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S16 Risk of bias assessment – O'Mahen

Unique ID	OMAHEN	**Study ID**	DJPASR01_OMAHEN	**Assessor**	Consensus: CS/DJ
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	NetmumsHWD	**Comparator**	TAU	**Source**	Journal article(s)
Outcome	PBQ - postnatal bonding - 17 weeks post-randomisation	**Results**	Effect size (Cohen's d) [imputed]: .247 (95% CI -0.185, 0.679), p = .69	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1), yes due to a random component being used. 'The minimisation algorithm included a stochastic element to inform the allocation process and was administered using a computer generated code to ensure concealment.' (p. 1677). Regarding (1.2), yes; see remote administration method above. Also 'eligible women were sent an electronic link to a webpage where they could learn their randomization assignment' (p. 1677).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Regarding (1.3), no due to minimal imbalances: 'there were no differences between those who... were randomised [to the intervention group] ... and those who [were not] on baseline measures ...' (p. 1680).

	Risk of bias judgement	**Low**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Regarding (2.1), yes. '... women were sent an electronic link to a webpage where they could learn their randomization assignment' (p. 1677). As such, people delivering the intervention were likely aware of the participants' assignment (especially as the control condition was TAU).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	NI	Regarding (2.3), a trial protocol or registration document is not available, so it is not possible to judge this.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	NA	
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Regarding (2.6), probably yes. The main report notes that 'all clinical outcome data [were analysed] on an intention-to-treat basis' (p. 1680). It is not clear whether this refers to the PBQ measure, but the authors also describe analysis methods fitting with ITT principles: 'We examined the effect of missing data by imputing missing follow-up data...' (p. 1680) and this is reflected in the PBQ results reported in Table 4 - though the labelling is unclear.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	
	Risk of bias judgement	**Some concerns**	--
	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	N	Regarding (3.1), no. Ten participants' data were missing from the intervention group, with 14 missing from the control group (see p. 1681, Fig 1 for overall participant numbers at 17 weeks ['post-

			treatment follow up’] and p. 1684, Table 4 for available N at 17 weeks).
Bias due to missing outcome data	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PN	Regarding (3.2), probably no though uncertain. Analyses are adjusted for baseline scores ('we used analysis of covariance to compare outcomes between groups at 17 weeks adjusting for baseline scores', p. 1680). However, the multiple imputation strategy does not appear to include a sensitivity analysis showing that results are little changed under a range of plausible assumptions about the relationship between missingness in the outcome and its true value. The chained equation MI model (White, Royston, et al., 2011) only functions under a correct assumption of MAR (data missing at random; 'the probability of data being missing does not depend on the unobserved data, conditional on the observed data, p. 377 of White, Royston, et al., 2011).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NI	Regarding (3.3), there is limited information on the reasons for loss to follow-up at the timepoint identified above. In the intervention group, 3/10 participants dropped out for identifiable reasons and in the control group 8/14 participants dropped out for identifiable reasons ('withdrew' or 'unable to contact', p. 1681). Reasons are not specified for why the remaining participants dropped out. Regarding (3.4), no, as the analyses account for participant characteristics that would be likely to explain the relationship between missingness in the outcome and its true value. The authors state: 'we assessed participants' mood symptoms at baseline' (p. 1679) and 'we used analysis of covariance... adjusting for baseline scores' (p. 1680).
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N	
	Risk of bias judgement	**Some concerns**	--

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Regarding (4.1), no, due to its validity and suitability for use in intervention trials. 'The PBQ has adequate... validity and is sensitive to changes in treatment' (p. 1680).
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	NI	Regarding (4.2), this is difficult to judge as there is limited information available on the procedure for data collection at post-17 weeks randomisation, though the Tables in the journal article indicate that the outcome measurement occurred at the same time (see Table 4, p. 1684).
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Regarding (4.3), yes, as the PBQ is a self-report measure and the participants were aware of their group allocation (see answer to question 2.1).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.4), probably yes as the intervention could influence participants' views of their infant or themselves (see Table 1, e.g., 'being a good enough mother'; 'attachment and bonding with my baby', p. 1678), and because the PBQ is a self-report measure involving individual judgement. Regarding (4.5), probably no as there is no indication that the participants held beliefs about the efficacy of the intervention (see 'Participants' section, p. 1677).
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), we were not able to identify any trial registration or trial protocol for this specific study, and therefore do not have information available to make a judgement on this point.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Regarding (5.2), it is not possible to make an assessment due to insufficient detail regarding intended analyses and measurement; see answer to 5.1.
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), analyses intentions are not available. See 5.1.

	Risk of bias judgement	**No information**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S17 Risk of bias assessment – Stein

Unique ID	STEIN	**Study ID**	CSPASR01_STEIN	**Assessor**	Consensus: CS/DJ
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	CBT + VFT	**Comparator**	CBT + PMR	**Source**	Journal article(s); Trial protocol; Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	CBCL externalising - 2 years postpartum	**Results**	Mean difference: -1.77 (95% CI: -4.39, 0.86), p = .19	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1) and (1.2), yes. Allocation had a random component and was administered centrally/remotely: 'participants were allocated to the VFT or PMR treatment group through a centralised randomisation service provided through the Oxford Health and Neuroscience Clinical Trials Unit. A random-deterministic minimisation algorithm was used...' (p. 136)
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3), probably no. The groups were 'generally well balanced.' The authors report that the number of participants taking antidepressants was '... 25% in the VFT and 15% in the PMR group' (p. 139).
	Risk of bias judgement	**Low**	--
Bias due to deviations	2.1.Were participants aware of their assigned intervention during the trial?	PY	Regarding (2.1-2), probably yes, as in both the trial protocol and journal article there is reference to only the research assessors being masked/blinded (see p. 26 of

from intended interventions	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	protocol; p. 136 of journal article). In addition, VFT and PMR are qualitatively different therapies so group allocation would be clearly apparent to the participant and the person delivering the sessions.
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PY	Regarding (2.3), probably yes. There are discrepancies in the quantity and structure of sessions in the trial protocol and journal article. - Protocol: 'There will be *five* weekly sessions to begin with between 6-8 months, followed by five fortnightly sessions around 8-12 months, and then by two booster sessions at 16 and 20 months', p. 28). - Journal article: '*six* weekly sessions were followed by five fortnightly sessions, and two booster sessions between 6-10 months after the end of therapy' (p. 136). The protocol also suggests 'CBT and VFT/PMR [occurs together] at every therapy session' (p. 28) whereas the journal article states that 'the first session was CBT, the second was either VFT or PMR, and all subsequent sessions were equally divided between [CBT and VFT/PMR]' (p. 136). It is plausible that the trial context affected the quantity and nature of sessions, as the additional session/sessions focused exclusively on VFT or PMR could have been included to increase engagement. These discrepancies may have developed for non-trial context reasons, however.
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	PY	Regarding (2.4), yes if it is true that the discrepancies recorded above were indeed a product of the trial context, but not otherwise.
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	Y	Regarding (2.5), yes, the deviation from the intended intervention described above affects both groups equally (see above for quotations).
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes. 'All analyses were done according to the intention-to-treat principle' (p. 134).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	

	Risk of bias judgement	**Some concerns**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	PN	Regarding (3.1), probably no. In the VFT group, 8/72 participants' data were missing [approx. 11.1%]; in the PMR group 4/72 participants' data were missing [approx. 5.5%] (see trial profile Figure, p. 139).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	Y	Regarding (3.2), yes. Sensitivity analyses were conducted to show this. 'Departure from the MCAR assumption was considered in a separate sensitivity analysis of the primary outcomes' (p. 138).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Regarding (4.1), no. See: 'this widely used measure has good discriminant validity' (p. 137).
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no. There is no indication in the (detailed) trial protocol that there was any difference in how the outcome was measured; see 'study assessments' (6.4.3, p. 26, trial protocol). In addition, the protocol emphasises that coders/assessors would be 'blind to therapy arm', suggesting collection of data occurred in the same way for both therapy arms.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Regarding (4.3), probably yes. The CBCL is a parent-report measure, and the participants were likely aware of their group status (see answers to Domain 2, questions 2.1-2).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.4), probably yes, as one of the groups focuses more on the infant and parent-infant relationship (VFT, 'aimed to... enhance parenting skills', p. 136) whereas the other does not (PMR: 'commonly used for stress management, but

	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	which does not target parenting practices or the mother-infant interaction', p. 139). The CBCL requires individual judgement so the intervention assignment could have informed this. However, regarding (4.5), probably no, as it is unlikely the participants held any beliefs/allegiances towards either therapy due to the nature of recruitment (the trial involves a community sample of mothers with major depression disorder who were not receiving psychological therapy; p. 136).
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PN	Regarding (5.1), probably no. There is a slight discrepancy between the model used in the trial protocol and the one mentioned in the journal article. Trial protocol: 'to test [whether VFT will lead to... fewer behavioural problems] ... ANOVAs will be conducted' (p. 32). Journal article: 'The analysis for each primary outcome utilised an ANCOVA model' (p. 138). Of note, the trial protocol specifies ANCOVA models for secondary outcome variables ('parenting capacities') but not behavioural problems (p. 32).
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Regarding (5.2), probably no. See the consistency between: Trial protocol: - the CBCL externalising scale at 24 months is one of the 'principal outcome variables at 24 months' (p. 21) - 'behaviour problems will be assessed by the ... CBCL ... the principal outcome will be the externalising scale' (p. 21). Journal article: 'the principal outcome was the externalising scale [of the CBCL]' (p. 137). Note that 'at the second assessment visit (child 12 months old) ... the CBCL will be conducted' (Trial protocol, p. 26). This is not reported in the journal article. But as

			all infant outcomes that are reported are non-significant, it is unlikely the two-year CBCL externalising outcome has been biased by selective reporting.
	5.3 ... multiple eligible analyses of the data?	PN	Regarding (5.3), probably not. Despite the discrepancy in analysis model noted in the trial protocol and journal article (see above), the result reported is a null finding rather than a positive or 'noteworthy' one. It is therefore unlikely to have been selected on the basis of multiple eligible analyses.
	Risk of bias judgement	**Some concerns**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	--

Table S18 Risk of bias assessment – Trevillion

Unique ID	TREVILLION	**Study ID**	CSPASRR01_TREVILLION	**Assessor**	Consensus: CS/DJ
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	GSH with usual care	**Comparator**	Usual care	**Source**	Journal article(s); Trial protocol; Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	PBQ - post-delivery bonding - 3 monthd postpartum	**Results**	Effect size 0.42 [95% CI -0.15, 0.97, p = 0.14	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding questions (1.1-2): yes - a random component was used in the sequence generation, and the trial used a centrally administered system: 'A central randomisation system, provided by the UK Clinical Research Collaboration... allocated participants to either... GSH or to usual care alone. Randomisation ... was applied using computer-generated, block-randomisation of varying sizes, with a 1:1 allocation. Trial researchers responsible for collection of outcome data and trial statisticians were blind to treatment allocation' (p. 188, main report).
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3): probably no – there is only one difference that is likely significant (annual income). This is unlikely to be a prognostic factor, though financial income could have an impact on parent wellbeing. 'Overall the two groups had similar characteristics, except for annual income; the usual care arm had considerably

			higher annual incomes than the intervention arm (annual income ≥ £46,000 of 70% versus 24%, respectively)' (main report, p. 191).
	Risk of bias judgement	**Low**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	PY	Regarding (2.1), probably yes, as the trial protocol implies participants are aware of their allocation. Regarding (2.2), probably no: 'the researcher will ask the participant not to mention to which group she was allocated' (p. 6).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PN	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PY	Regarding (2.3), probably yes. There is a session separate from the core 8-week intervention programme that occurs at 6-8 weeks post-delivery; in the trial protocol this is recorded as an 'additional session' separate to the initial eight sessions of the intervention (p. 5), whereas in the main report the authors write that this session was a 'check-in' and 'did not form part of the therapeutic programme' (p. 189). There are potential concerns here about the possibility of this postpartum session not being implemented as a therapeutic session at 6-8 weeks post-delivery (as the trial protocol appears to suggest).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	PN	Regarding (2.4), probably no. The intervention is not primarily focused on postpartum bonding. While 'parenthood' is mentioned this is not the predominant theme. See intervention description: 'psychoeducation on antenatal depression; managing relationships; planning for parenthood; health and lifestyle factors' (p. 189).
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes: 'Analysis will be by intention to treat; missing data will be imputed' (trial protocol, p. 7).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to	NA	

	analyse participants in the group to which they were randomised?		
	Risk of bias judgement	**Some concerns**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	PN	Regarding (3.1), probably no. Outcome data were available for 2/26 and 2/27 participants in the intervention and comparison group respectively (p. 193, participant flow diagram). This amounts to ~93% of data availability, which is close but does not meet the 95% threshold suggested in the guidance document.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Regarding (3.2), no because, while imputation was performed for ≤30% missing data, it is not clear how bias was corrected other than by imputation (p. 190).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N	Regarding (3.3), no because the 'lost-to-follow-up' reasons do not appear to be linked to the participants' health status (p. 193, Figure 1).
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Regarding (4.1), probably no. The PBQ measure is validated (Brockington et al., 2006) despite the validity of this measure not being stated in the journal article. It is also unlikely that this measure would be insensitive to plausible intervention effects.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Regarding (4.2), probably no. There is no indication that participant measures were collected differently according to group. The journal article states: 'participant data were collected at ... 3 months post-delivery' (p. 189) and this is confirmed in Table S2 of the trial protocol appendix.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Regarding (4.3), probably yes, as the PBQ is a parent-report measure, and the parents were likely aware of their allocation (see Domain 2). See guidance document (i.e., 'for participant-reported outcomes, the outcome assessor is the study participant). The PBQ is described in the trial protocol as 'a 25 item self-

			administered measure' (Table S2). Note that the authors are aware of this limitation ('this approach was necessary due to these data being unavailable from another single source', p. 195 of main report).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.3), it is probably the case that participants' awareness of intervention allocation could have influenced participant-reported outcomes, as the PBQ measure involves a degree of judgement. However, regarding (4.4), it is probably not the case that the 'assessor' (participant) had high levels of belief in either beneficial or harmful effects of the intervention, since the participants were not from a population known to have specific beliefs about this type of intervention (see 'eligibility criteria', section 2.4, p. 189).
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), this has been marked as 'No Information.' This is because information on how 'parenting stress'/the PBQ was intended to be analysed is not available in the trial protocol.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Regarding (5.2), this has been marked as 'No Information.' In the trial protocol (Table S2) it states that the 'CARE index' was used to measure mother-infant interactions at 3 months post-delivery, which would produce a measure of 'sensitivity' or 'unresponsiveness' that would have been comparable to the PBQ score. In addition, Table S2 of the trial protocol indicates that 'analysis of the [PBQ] scale includes both its total and its subscales', while only a total score is reported in the journal article. However, the analysis intentions for these measures were not reported in sufficient detail to enable an assessment. The guidance document therefore recommends this should be marked as 'No Information.'
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), this has been marked 'No Information,' as analysis intentions for this measure were not reported in sufficient detail in the trial protocol, and there is more than one way in which the outcome measurement could have been analysed (e.g., subscales vs. total score).

	Risk of bias judgement	**No information**	--
Overall bias	**Risk of bias judgement**	**Some concerns**	

Table S19 Risk of bias assessment – Werner

Unique ID	WERNER	**Study ID**	CSPASR01_WERNER	**Assessor**	Consensus: CS/DJ
Ref or Label		**Aim**	assignment to intervention (the 'intention-to-treat' effect)		
Experimental	PREPP	**Comparator**	ETAU	**Source**	Journal article(s); Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
Outcome	Infant fuss/cry behaviour - 6 weeks/average postpartum	**Results**	PREPP (m = 4.07, SD = 2.5); ETAU (m = 6.30, SD = 2.63), F [1, 28] = 5.68, p = .02	**Weight**	1

Domain	**Signalling question**	**Response**	**Comments**
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Regarding (1.1), yes and regarding (1.2), probably yes though slightly unclear. See: 'potential participants came to the laboratory to provide informed consent and complete mood questionnaires ... they also met with a clinical psychologist who informed them of their treatment group assignment dictated by a computer-generated random assignment schedule' (p. 5). It is unlikely the clinical psychologist was the enrolling investigator as the women 'were recruited and screened for study eligibility by telephone' (p. 5), which appears to be a separate event.
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Regarding (1.3), probably no. Though the subsample for which the outcome measure was available differed significantly on their PHQ-9 scores (see p. 11), overall, the groups 'did not differ significantly from one another on any of the variables' post-randomisation (p. 9).

	Risk of bias judgement	**Low**	--
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Regarding (2.1), yes. See answer to signalling question (1.1). Regarding (2.2), probably yes. The trial registration selects 'none' in answer to the question of masking, as it is 'open label' (see 'Study Design,' trial registration).
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PY	Regarding (2.3), probably yes. It is not clear whether the following deviations arose due to the trial context (i.e., a desire to keep participants engaged postpartum) but it is possible. The trial registration and journal article are comparable except that the journal article mentions the use of a telephone call for the PREPP group whereas the trial registration does not: 'the psychologist also contacted participants by telephone at 2 weeks postpartum, and, using motivational interviewing, encouraged the use of PREPP skills and answered specific participant questions' (p. 7, journal article).
	2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	PY	Regarding (2.4), probably yes due to the use of 'motivational interviewing' to sustain engagement with the intervention (p. 7), which included 'a number of infant behavioural interventions and targeted psychotherapy techniques' (p. 7); this could have affected the outcome.
	2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	PY	Regarding (2.5), yes. The ETAU group also received a telephone call. 'At two weeks postpartum... those in the ETAU group received a brief check-in call from the research assistant' (p. 5).
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Regarding (2.6), yes. 'All analyses .... adhered to intention-to-treat principles' (p. 8).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomised?	NA	

	Risk of bias judgement	**Some concerns**	--
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomised?	N	Regarding (3.1), no. Fifty-four participants were randomised in total (see abstract, p. 1). By contrast, 'data from the baby day diary' - the measure of interest – 'was available in a subset of participants enrolled in the current study, n = 30' (p. 11).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PN	Regarding (3.2), there is insufficient information to adequately judge this, but since 'no information' is not available from the drop-down menu, I have selected 'probably no.' There are no sensitivity analyses - the only reference to a missing data strategy is in reference to ITT principles (see response to question 2.6).
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PY	Regarding (3.3), probably yes because those who completed the Baby Day Diary (n=30) scored significantly higher on the PHQ-9 prior to randomisation than those who did not complete it (n = 24; p. 11). It is therefore possible that those with greater depression struggled more with infant behaviour and were more likely to fill out the diary as a result. Regarding (3.4), probably yes. The circumstances of the trial make it likely that missingness in the outcome depends on its true value, as this is a sample at risk of depression who give birth at the beginning of the intervention; trial drop out due to difficulty managing the new-born period could be a reason for missing data.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	
	Risk of bias judgement	**High**	--
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Regarding (4.1), probably no due to validity: 'This measure has been well validated, as evidenced by high correlation between its metrics and audio recordings of fussing and crying' (p. 7). I am unable to comment on whether this measure would be sensitive to plausible intervention effects with surety, but it seems likely.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	NI	Regarding (4.2), there is inadequate detail available to make a judgement on how the data collection varied by group.

	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Regarding (4.3), yes. The outcome assessors were the participants, as this was a self-report measure (p. 7), and the participants were aware of the assignment (see answer to signalling questions 1.1/2.1).
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Regarding (4.4), probably yes. The intervention was focused on 'specific infant behavioural techniques... aimed at reducing infant fuss/cry behaviour' (p. 7) and the outcome measure involves a degree of judgement, so the assessment of outcome could plausibly have been influenced by the knowledge of intervention received. However, regarding (4.5), it is unlikely that this is the case as the sample information contains no details indicating they were likely to have held beliefs about the benefits/harms of the intervention (see 'inclusion criteria', trial registration).
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
	Risk of bias judgement	**Some concerns**	--
Bias in selection of the reported result	5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Regarding (5.1), it is not possible to assess this. We were not able to identify a trial protocol for this study, and the trial registration that we were able to source did not contain any analysis intentions.
	5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PY	Regarding (5.2), possibly yes due to the discrepancy in timepoint reporting. In the trial registration, the authors state: 'the investigators will... evaluate infant behaviour at 6 and 14 weeks' (i.e., two timepoints). However, in the final report/journal article, only a 'four day' average was reported (p. 7) with no reference to timepoint other than in the Discussion, where the authors state that 'reductions in distressed mood and infant fuss/cry behaviours both occurred at 6 weeks' (p. 12, main report). Given that the result is significant, it is possible that it was selectively reported. The authors justify their use of the four-day average by stating that they are 'following previously published reports using this measure' (p. 7), which suggests that the aggregate/averaging approach is standard for this measure. However, this approach still appears to be somewhat contradictory to the trial

			registration information, which mentions two timepoints yet no aggregate/averaging intention.
	5.3 ... multiple eligible analyses of the data?	NI	Regarding (5.3), there is not sufficient detail in the trial registration of the pre-specified analysis plan for this outcome measure (there is no mention, for instance, of the decision to use a 'four day' average approach).
	Risk of bias judgement	**High**	--
Overall bias	**Risk of bias judgement**	**High**	--

1 Intervening for perinatal anxiety *v.* intervening for broad risk or transdiagnostic symptoms

Before beginning a review of interventions for perinatal anxiety, it was necessary to consider what population should be within scope. Perinatal anxiety, like the umbrella term 'anxiety,' may be operationalised in myriad ways. It can refer to an observable response (state anxiety) or a propensity towards anxiety (trait anxiety; Reiss, 1997; Spielberger, 1985). It may refer to a range of cut-offs on a dimensional scale ('severe', 'moderate', 'mild'), or a series of conditions classified in a diagnostic manual ('generalised anxiety disorder', 'social anxiety disorder', 'panic disorder'). Some cognitive and physiological features of anxiety are thought to be common to other psychiatric diagnoses (Faustino, 2021; Grisanzio et al., 2018), and there is further overlap between the constructs of stress and anxiety (though stress is considered more specific and less diffuse; Epel et al., 2018). Perinatal anxiety risk is also likely to increase in the context of a broad range of socio-economic circumstances and environmental stressors (Furtado et al., 2018; Leach et al., 2017), though over half of individuals who go on to later develop mental health or developmental conditions do not have identifiable risk factors (Hiscock et al., 2008; Offord et al., 1998). In the present review, we took a clinical, rather than risk-based or universal approach to determining the scope of the population. We recognised both dimensional and categorical conceptualisations of perinatal anxiety, as well as a broad range of anxiety diagnoses. We also acknowledged that perinatal anxiety would often be studied alongside other co-occurring conditions (especially depression).

2 Rationale for RoB assessment: numerical result selection

The Risk of Bias (RoB) 2 tool requires that bias assessments be conducted on a specific outcome measure and numerical result (Sterne et al., 2019). Wherever possible, we selected a significant between group effect as the result on which to base the RoBs. We selected an infant or dyadic outcome given the thesis's principal orientation towards child development. We did not elect to conduct RoB assessments on parent anxiety measures as not all studies calculated inferential statistics on parent anxiety outcome measures (e.g., Stein et al., 2018). Only participants belonging to groups that were randomised were considered in the RoB assessments. We prioritised between group effects as these are most likely to detect differences in the outcome according to the intervention (rather than, for instance, effects of study engagement or the 'dodo bird' effect; Enck & Zipfel, 2019). We prioritised significant over non-significant results as positive findings are more likely to be biased than null findings (Sterne et al., 2019). Preference was then given to primary over secondary outcome results; if multiple results were significant, we made our selection from these results at random. Note that for Lenze et al. (2020), a within group effect was selected as no between group analyses were conducted. For Goodman et al. (2015), a non-significant between group effect was selected rather than a significant within group effect.

	Small	Medium	Large
Hedges *g*/Cohen's *d*	~ .2	.3-.7	>.8
Odds Ratios	~ 1.5	1.6-3	> 5

Table S20 An approximate guide to interpreting the strengths of associations represented by Hedges *g*/Cohen's *d*, as well as odds ratios (Chen et al., 2010).

3 Component-by-component breakdown of adult-focused interventions

Of the five adult-focused interventions, three were delivered postnatally (Challacombe et al., 2017; O'Mahen et al., 2014) while three were delivered prenatally (Burger et al., 2020; Milgrom et al., 2015; Trevillion et al., 2020). All interventions were delivered via individual rather than group sessions. Interventions evaluated by Trevillion et al. (2020) and O'Mahen et al. (2014) used a CBT-based, guided self-help model, i.e., low-intensity treatment involving the support of a health professional to guide the use of a self-help manual or e-resource (Coull & Morris, 2011). One intervention was delivered via an intensive model whereby hours were compressed into a relatively short treatment period (Challacombe et al., 2017).

All of the interventions in this grouping incorporated techniques from CBT. Three interventions included CBT strategies for anxiety-related conditions, including elements such as exposure, response prevention, and/or cognitive-restructuring (Burger et al., 2020; Challacombe et al., 2017; O'Mahen et al., 2014). This involves controlled exposure to fear-provoking stimuli, resisting 'escape behaviour' when in anxiety-inducing situations, and reappraising 'maladaptive' thoughts and beliefs that maintain psychological distress (Bolton & Perrin, 2008; Clark, 2013). Three interventions also included CBT strategies for mood-related conditions, such as depression; for example, cognitive-restructuring and problem-solving exercises (Burger et al., 2020; Milgrom et al., 2015; Trevillion et al., 2020). Two studies also explicitly focused on or emphasised the use of behavioural activation (Burger et al., 2020; O'Mahen et al., 2014). Behavioural activation draws on behavioural aspects of CBT while omitting its cognitive features (Ekers et al., 2014). It draws on the principles of operant conditioning and other functional analytical approaches, and has been found to be as effective as standard CBT for managing depression (Richards et al., 2016). One study used CBT techniques specific to PTSD (Burger et al., 2020).

Independent of the CBT strategies, three studies in this grouping incorporated intervention components related to supporting participants with: (a) establishing a more healthy lifestyle and (b) managing their social networks to maximise support available (Milgrom et al., 2015; O'Mahen et al., 2014; Trevillion et al., 2020). Milgrom et al. (2015) also included a component related to relaxation

training. In addition to the adult-directed components, some of the studies in this grouping also incorporated a small number of components relating more specifically to the infant or dyad (see components 1-10; Table 3).

4 Component-by-component breakdown of infant or dyad-focused interventions

Of the seven infant or dyad-focused interventions, all were delivered predominantly postnatally, with one exception that split a roughly equal number of sessions over the prenatal and postnatal period (Lenze et al., 2020). Four interventions were delivered using individual sessions (including the infant; Goodman et al., 2015; Lenze et al., 2020; Stein et al., 2018; Werner et al., 2016), while three operated via group format (Ericksen et al., 2018; Holt et al., 2021; O'Higgins et al., 2008).

Six out of seven of the interventions in this grouping incorporated elements of interaction coaching, including support with how to read, understand or respond to infant cues (exception: Werner et al., 2016). Three interventions included an attachment-based exploration of the parent-infant relationship (Ericksen et al., 2018; Lenze et al., 2020; Stein et al., 2018), while three provided information on infant temperament or developmental stages (Ericksen et al., 2018; Goodman et al., 2015; Lenze et al., 2020). Four interventions incorporated therapeutic approaches examining the parent's patterns of relating to others, including, for example, how the mother's own memories of childhood or representation of her child informs the dyadic relationship (Goodman et al., 2015; Holt et al., 2021; Lenze et al., 2020; Werner et al., 2016). Two interventions incorporated elements of play therapy or sensory activities (Ericksen et al., 2018; Holt et al., 2021), and three incorporated infant massage (Ericksen et al., 2018; Holt et al., 2021; O'Higgins et al., 2008). One intervention explicitly conceptualised the infant as a psychological agent (Stein et al., 2018), one provided practical support focused on infant behaviours such as fussing, feeding and sleeping (Werner et al., 2016), one included 'good enough' parenting principles (Holt et al., 2021), and one provided explicit support with the transition to parenthood (Goodman et al., 2015).

Of note, two of the infant-focused interventions included a prefatory CBT programme before the 'main' intervention; however, both intervention and active control groups attended the CBT programme, reducing the potential to detect CBT-specific between group effects (Holt et al., 2021; Stein et al., 2018).

Appendix E – Power calculations

The following section outlines issues related to statistical power that concern the empirical studies presented in this thesis.

1 A priori versus post hoc power estimates

The studies presented in this thesis were attached to broader 'parent' projects focused on separate hypotheses. While a priori power estimates were calculated for these parent projects, no such calculations were made for the thesis studies. This limitation is described in Chapter 8.

To address this gap, post hoc or 'observed' power calculations were considered. Observed power refers to the statistical power of the performed test, based on an effect size estimate from the data that has been collected; this is in contrast to statistical power, the probability of finding a statistical difference from 0 in the test (Lakens, 2014; Zhang & Wang, 2019). Observed power calculations are spurious as they assume that the estimated effect size from the data is the true effect size. Statisticians argue that power analyses should only be based on a scientifically-grounded, assumed effect size, and not the effect size observed in the study (Gelman, 2019). The decision was therefore taken to eschew calculations of observed power.

2 A priori power estimates for parent projects

For the sake of transparency, the original power calculations for the parent projects are given here. It must be emphasised that these calculations were made by the original grant holders, and the estimates bear little relation to the thesis hypotheses. For instance, the following passage is excerpted from the original grant for the BLAISE study (ESRC grant number ES/N017560/1), from which Chapters 4 and 5 of this thesis are derived:

> 'A relationship between stress reactivity and learning in 12-month-old infants was reported in a previous study, with an effect size of 0.69 (de Barbaro et al., 2016). Allowing for 25% attrition in the present sample of 80 will, therefore, give 88% power for two-tailed significance of 0.05.'

In addition, the following passage represents a paraphrased section of the original grant for the BASIS study (UK Medical Research Council G0701484 & MR/K021389/1) from which Chapter 6 of this thesis is derived:

> 'Power was intended to be maximised by use of repeated continuous measures and joint modelling of high and low risk groups according to growth curve models. … To estimate power, summary statistics were constructed from the literature. The power of the test was obtained from non-central chi-square distributions, where the test chi-square values were used as non-centrality parameters ... An 80% retention rate has been assumed corresponding to 208

elevated likelihood (EL) and 97 typical-likelihood (TL) infants, followed up at age seven years. Using the observed correlations in the Autism Observation Scale for Infants (AOSI) and Autism Diagnostic Observation Schedule (ADOS) total scores reported in the supplementary materials of Green et al. (2017) as an example, the full intended sample size gives 84% power to detect an EL/TL effect size difference of 0.2 sustained across measures.'

3 A priori power estimate for the Heart 2 Heart study

To illustrate how statistical power can be estimated for studies with hypotheses similar to those of this thesis, a further power calculation is described below. This passage is adapted from the application submitted for ethical approval for the Heart 2 Heart study (London Queen Square Research Ethics Committee, UK; IRAS 263692). The Heart 2 Heart study is described on page 5.

'The primary hypothesis for the Heart 2 Heart study is that the physiological activity of dyads with more severe anxiety will be characterised by greater synchrony (compared to infants and parents with less severe anxiety). The sample size for the Heart 2 Heart study was calculated using existing comparable data on the primary outcome: level of parent-infant physiological synchrony. The data came from a previous study using the same protocol in a community sample (Smith, Jones, Charman, et al., 2021). Previous analyses examined differences of infants grouped by higher/lower parental anxiety, based on a median split of the GAD-7 screening tool (Spitzer et al., 2006). Using dyadic cross-correlation of arousal as the primary outcome measure, Cohen's *d* was calculated to be .53. The sample size for the present study was determined through a power analysis using G*power, which indicated that, for one-tailed significance of .05, eighty participants were needed to detect $d = .53$ with 70% power.'

'Seventy percent power was judged to be acceptable given the effect size is likely to be higher among clinical populations. Clinical samples are likely to exhibit greater anxiety severity than community samples, and research indicates that greater anxiety associates with greater synchrony (Granat et al., 2017). In addition, as the Heart 2 Heart study ($N = 80$) is a replication of the aforementioned community study ($N = 80$), and both include a dimensional measure of anxiety, it will be possible to conduct group difference analyses across the studies that will be amply powered.'

Appendix F – Ambivalence and research waste: an auto-ethnographic perspective on conducting quantitative clinical research during a pandemic

The following section represents a reflective piece of work, exploring the experience of conducting clinical research in an inpatient setting during the COVID-19 pandemic.

1 Introduction

Psychiatric inpatient settings have the potential to be highly stressful working environments (Totman et al., 2011). In February 2020, I began conducting a quantitative research project on the joint mechanisms of emotion regulation in new parents with severe mental illness and their infants. After a year of interrupted hospital access due to the COVID-19 pandemic, I was presented with data collection demands that challenged me personally and professionally.

Though I was motivated about and committed to my clinical research role, in late 2020 I began to consider the multiple factors exerting a pressure on my project and, in tandem, me. I examined the evidence base on clinical workforces during the pandemic, speculating that my experience might overlap with this. As suspected, I found literature showing that others faced challenges that were not dissimilar. In the UK National Health Service (NHS), there has been a clear accounting of pressures associated with working during the pandemic. These include increased risk of personal strain (Liberati et al., 2021), and - in perinatal services - concerns regarding safeguarding, and the impact of mask-wearing on infant development (Wilson et al., 2021). I also wondered whether my experience would be shared by researchers working with clinical populations during the pandemic, which was partially confirmed by a smaller literature (Aksoy et al., 2021; Dhont et al., 2020); these studies identified links between perceived reduction in productivity and guilt, as well as uneasiness over fear of contracting and spreading COVID-19.

In light of this, I consulted with UK based qualitative researchers about the potential value of documenting my own experience.[21] This suggestion was met with strong interest. Subsequently I felt encouraged to 'tell my story,' which is one of a publicly funded, quantitative investigator conducting research with patients with severe mental illness during a pandemic. I highlight the methodological and financial dimensions to my role, as I believe these factors influenced how I experienced issues during the research process.

I recognise that the health risk posed by the pandemic affected all individuals in the UK during 2020, and particularly those working in physical health and care home settings. Within this chapter, I do not wish to suggest that researchers working with severe mental illness are in any sense more at risk than

[21]Thanks to Jamie Enoch and Jessica Eastland-Underwood for several useful discussions, with special thanks to Jamie for reading over this piece of writing a number of times.

others, but rather that there are some particular aspects of research within inpatient psychiatric settings during national crisis that give rise to specific personal and professional challenges.

In order to express my experiences in a way that might be both personally edifying and externally informative, I judged that an auto-ethnographic methodology would be appropriate. Auto-ethnography is a qualitative research process used for relating one's own personal experience to a broader social or cultural context. Its goal is 'to bring cultural interpretation to the autobiographical data of researchers' (Chang, 2008, p. 56). In this case, my personal situation reflects broader themes of (1) ambivalence and (2) research waste, both of which are connected to internal conflicts of interest within the investigator during research practice.

In this chapter, I will document these experiences according to auto-ethnographic principles. This will culminate in some practical recommendations related to research ethics and early career development, which I will suggest are practices that may improve the way we conduct publicly funded quantitative clinical research.

2 Method

Auto-ethnography is part autobiography and part ethnography. Ethnography is a research approach assuming observation of participants is the key to understanding culture - that is, the ideas, customs and behaviours of a particular group (Hammersley, 2018; Jupp, 2006). Autobiography is a self-written report of a person's life experiences (Wagner-Egelhaaf, 2019). Hence, auto-ethnography is a research practice that analyses personal experience to elucidate aspects of culture. Put plainly: in conducting an auto-ethnography, the researcher uses their own experience as a source of data, and then conducts qualitative analysis of that data.

2.1 Epistemology

In terms of its history and epistemology, auto-ethnography stands in contrast to positivism. Some of the key tenets of positivist philosophy are that: (1) objective truth may be identified via verifying and replicating observable results, and (2) an objective reality exists that is independent of the investigator (though various positivist schools exist, see: Clark, 1998). This line of inquiry broadly underlies much quantitative research in the scientific community. Auto-ethnography, however, relates to postmodernist perspectives. These suggest that the findings generated by scientists are fundamentally interlinked with aspects of the scientists themselves (including, for example, their vocabularies and their cultural backgrounds; Carré, 2019; Rorty, 1982). Postmodernists are less concerned with universal facts, and more oriented towards individual narratives, the meaning of which can be interpreted and understood in a multitude of ways (Barthes, 1977; Sim, 2011).[22] In addition,

[22]Postmodernists are not without concern for facts though, particularly given the emergence of a 'post-truth' society (see: Kien, 2021).

postmodernists resist the impulse to enact colonial research practices ('authoritatively entering a culture, exploiting cultural members, and then leaving to write about the culture while disregarding relational ties to cultural members'; Ellis et al., 2011, p. 2). Auto-ethnographers are therefore postmodern in their efforts to produce research that is accessible, unconcerned with statistical generalisation, and likely to shed light on issues of identity politics and ethics.

2.2 Materials and analysis

Practically, auto-ethnography uses two analytical approaches. The first of these is a 'microscopic' approach, in which details and small segments of data are evaluated and probed; the second is a 'macroscopic' approach, where data is compared with other people's cases as well as social science constructs, ideas and theories (Chang, 2008). The source material for the data analysed in this study is a journal I wrote during the period of my clinical research. This included reflective entries about my day-to-day experience on the ward, separate from the formal data collection of the clinical research. This journal data may be limited in that I was inherently 'involved' at the time of writing, making it more difficult to detach and consider my experiences more contextually. However, an advantage of this source material is that the data is less likely to be influenced by long-term memory, which may obscure the details of past events.

2.3 Cultural themes

As auto-ethnography is concerned with relating microscopic details of one's personal situation with macroscopic features of the wider context, I have chosen to organise the analyses below around two broad themes. In qualitative research, a 'theme' can be understood as a concept that links numerous portions of a set of transcripts together (Morse & Field, 1995). These are often expressed as assertions (e.g., 'eye disease in old age as a loss of independence') and include ideas that people generally believe, find acceptable and understand at face value; they usually, though not necessarily, have a high degree of generality (DeSantis & Ugarriza, 2000; Spradley, 1979). The concepts used in this study to contextualise aspects of my research practice are those of ambivalence and waste. Ambivalence is 'an attitude towards the future consisting of both a positive (optimistic) outlook and a negative (pessimistic) one' and a feeling of being 'in between' (Jovanović, 2016, p. 3). Waste is an umbrella term referring to the disposal of unused resources. It can be understood in both symbolic and material terms, and has historically been understood in popular discourse as a moral problem (given links between disposability, convenience, and laziness; Glucksberg, 2013). Anthropological studies of waste commonly lead to questions over what is valuable to some and expendable to others (Hawkins & Muecke, 2002).

2.4 Ethics

This chapter includes no reference to individual patients, and the names of any supervisory figures have been pseudonymised. Though names have been changed, the transcript excerpts included here

may refer to teams or team members that are recognisable through association. Full consent was therefore obtained from those overseeing my work. This chapter was also permitted as part of the clinical research study approved by the local Health Research Authority (London Queen Square Research Ethics Committee; IRAS 263692). Privacy, confidentiality and data security of all participants has been ensured.

2.5 Autobiographical context

Benoot and Bilsen (2016) suggest that auto-ethnographies require a degree of autobiographical information, including some about the author and their present occupation. As such, I provide the following brief outline. I am a working age woman from the UK, with a master's degree in psychology and some prior experience of working in the caring profession. I began my PhD at the end of 2018, on the subject of parental mental health and early childhood development. One part of the PhD was intended to be a clinical research project involving parents who had moderate to severe mental illness, as well as their infants, under the care of the NHS. The first participant's data was collected in February 2020, following which the COVID-19 pandemic necessitated national lockdowns. This led to a complete lack of access to clinical sites, followed by a period of partial but restricted access between August and December 2020. In December of that year, vaccinations were yet to be rolled out, meanwhile the coronavirus variant known as the alpha strain became widespread in the UK. At this time my household included a vulnerable person. During this period, I also became aware of some of my ambivalent attitudes towards the research project, as well as my concerns over research waste. Subsequently I have decided to structure the remainder of this chapter according to the following themes: ambivalence linked with individual responsibility; ambivalence linked with investigator identity; and research waste as a problem of production.

3.1 Ambivalence linked with individual responsibility

> 'There are so many difficulties for the researcher role at the [ward] during the pandemic. Not having a physical space to work/base myself due to maximum room occupancies; participants forgetting they have met me due to masks/high staff turnover … the lack of easy/quick transport to and from the hospital; the stress of working around staff or patients who have or have recently had coronavirus… Social distancing is impossible with families. I often speak and build rapport with mothers in the communal nursery area, where it is common to be asked to hold a baby while mothers are temporarily engaged elsewhere. One of the easiest ways to connect with mothers is also to play with or hold the baby to help soothe them. I have learned a huge amount about working on the ward in the past few months but I am reluctant to increase my days due to the lack of workable office space and potential coronavirus exposure. The ward has just had an outbreak of coronavirus so working in the hospital feels risky, even with mask wearing and everything.'

In this entry, numerous barriers to research practice arising from COVID-19 mitigations are described: building capacity, social distancing, and masks. Though there is an indication that aspects of the work are manageable and enriching, this is overshadowed with multiple concerns about health and safety, sustaining relationships with patients, as well as travelling to and being able to work effectively at the hospital. This can be understood as an ambivalent presentation as my disposition is doubtful, and characterised by equivocation ('I have learned a huge amount but…'; 'working in the hospital feels risky, even with…').

The above uncertainty reflects the way in which members of society, nationally and internationally, have had to balance their motivation to continue working in high-risk settings with genuine concerns of contracting coronavirus and spreading it to others (Menon & Padhy, 2020). These concerns are common among perinatal staff in Mother and Baby Units in the UK (Wilson et al., 2021), and similar ethical dilemmas have been explored amongst other frontline health and social care workers (Maraqa et al., 2021; Nyashanu et al., 2020). Given healthcare workers often initially sign up to their professions without the expectation that they will be exposed to extensive personal danger, bioethicists suggest that healthcare workers be explicitly supported with their 'role-related conflicts' during infectious disease outbreaks; for example, with strategies such as education, disclosure, psychological support, and harm minimisation (Lipworth, 2020). I balanced my motivation to continue my research with concerns for my household's health by using reflexive exercises (e.g., problem-solving and worry postponement interventions; Versluis et al., 2016) as well as practical mitigation strategies (e.g., walking rather than taking public transport to commute to the hospital).

As I questioned how or whether to continue working in a high-risk setting during the pandemic, I was also reminded of the ways in which some political ideologies position individuals – rather than the collective - as responsible for the health and wellbeing of society (Greene, 2008). These 'individualisation ideologies' arguably have poor outcomes for public health; they can increase health inequalities by benefitting those with higher socio-economic status (those who have the educational and social capital necessary to 'exercise responsibility' and avoid high-risk settings) while failing to provide protections for marginalised groups who may not be able to adopt health promoting behaviours (Cardona, 2020). The fact that I had a monthly student stipend afforded me the privilege of eventually suspending my work on the ward; a choice that would not have been available to others without this financial guarantee.

3.2 Ambivalence linked with investigator identity

A further challenge I encountered while working as a researcher on the ward during the pandemic centred on the presentation of professional identity. Having not previously worked as a researcher in a clinical setting before, this would likely have been a learning experience irrespective of the public health context. Ward environments are busy and often involve a large number of staff working on

different days; formal introductions are therefore not always practicable or memorable. The COVID-19 pandemic meant that there were often staff-shortages and additional temporary staff due to illness and isolation, so my 'learning experience' was amplified:

> 'In supervision today I discussed with Miriam how to position myself as a ward staff member. I have been having difficulty explaining who I am when first meeting new patients. Even though I say that I am conducting research, I find that people usually assume I am a nurse. I try to behave confidently and calmly on the ward, with a professional air, but I am concerned sometimes that people over-assume my ability to de-escalate or contain patients in crisis, especially during times when the unit is low on staff.
>
> I wonder that the ambiguous presentation of my role to patients is due to a lack of confidence. I think this (and my concern over inadvertently causing any patient distress) plays into my unwillingness to [assess] participants spontaneously.'

In this example, the ambivalent sensation of feeling 'in between' is apparent in the lack of clarity over how I should introduce myself to others. On the one hand, there is a will to present an image of a confident professional, while on the other hand there is unease about having the level of my training overestimated. This was thrown into relief during times when extra support was needed on the ward floor, and I would be asked to assist with practical infant care and supervision. This represents, in part, a common feature of the pandemic; short-staffing created by illness and self-isolation led to the need to 'pitch in' on an equal basis regardless of role (Kerins et al., 2021; Spanier et al., 2021; Willan et al., 2020). As a clinical researcher, this was a further 'role-related conflict' that I had to manage. This likely would have been a consideration even pre-pandemic, given the high rate of vacancies in the NHS mental health workforce (Addicott et al., 2015); but the pandemic amplified it.

In this transcript excerpt, there is also a disconnection between who I say I am (someone 'conducting research') and how I am perceived ('a nurse'). This may be reinforced by my discomfort with presenting solely as a scientist given my prior work in the caring profession. Though I am not a medic myself, this experience is resonant of physician-investigators who have traditionally been asked to 'see themselves as scientists only and not as doctors' in order not to 'conflate clinical trials and therapy, as well as patients and subjects … unwittingly [becoming] double agents with conflicting loyalties' (Katz, 1993, p. 28). Over time, the concept of asking clinician-investigators to shed their therapeutic identity has been challenged as being neither achievable nor necessarily desirable (Miller, 1998). Rather, the focus should be on developing an understanding of the *moral* identity of the carer-scientist, which begins with explicitly acknowledging the ethical issues arising from the conflicts of interest between the twin roles of scientist and carer in clinical research. As Miller puts it (1998, p. 1452):

> 'Investigators must recognise and manage the moral tensions between the norms of patient care and the requirements of scientific investigation. The construction of such a conception of professional integrity is not a matter of creating a new identity but of bringing to light and cultivating the refined self-understanding and comportment of exemplary clinical researchers. A key element in accomplishing this task is to reflect on the relationship between the physician investigator and the patient volunteer.'

If I were practising greater self-awareness, as Miller suggests, I might consider more closely my dual need to present 'confidently' while also having 'concern over inadvertently causing any patient distress.' A more confident clinical researcher may be more authentic, and in turn have greater ease engaging with and supporting participants and patients. But equally, being more reticent during the data collection process may lead to a more ethical and judicious practice. This perhaps illustrates a broader principle: that the tentativeness, questioning and caution that can come with a more ambivalent identity at work has its advantages as well as its drawbacks.

3.3 Research waste as a problem of production

The final theme I identified from the transcripts pertained to issues of research waste. Due to the restrictions on research and hospital sites during 2020, many of the researchers in my field of developmental psychopathology were unable to adequately conduct their research projects during that year, if at all.[23] This was also true of my own experience at that time:

> 'It is rare for these methods to be carried out with mums and babies on psychiatric wards. This situation makes it so hard to do the research, let alone fulfil my funder's aims … All this time invested will have been wasted, and there will be nothing to show for it …'

Here the concept of waste is explicitly introduced through the example of lost time, which is expressed in catastrophic terms. The conception is that not being able to carry out this research project is a distinctly and exclusively negative outcome. The use of the idiom 'having nothing to show for it' suggests the rhetoric of production, pointing to the way in which I am accustomed to thinking about my work in terms of output. This mentality has been explored in anthropological explorations of scientists at work; publications are 'manufactured goods' and laboratories resemble firms that 'produce almost at a loss; they talk and publish, but no one operates [on their findings]' (Latour & Woolgar, 2013, p. 87).

This production-focused orientation in my practice specifically, and in research culture more broadly, has been called into question by the positivist-empirical community. In particular, by scientists concerned with the speed at which scientific output is churned out: 'more speed, more haste, more

[23]During the time that these journal entries were written, I did not have access to additional funds beyond my existing PhD studentship. Additional months of funding became available the following year; however, I was not able to make use of these due to a clash with an upcoming employment contract.

stress, more waste' (Frith, 2020). This seems to be an issue that pre-dates the pandemic. Approximately 85% of the US national biomedical research investment (equivalent to approximately $200 billion) has been wasted due to the ways in which the research industry operates; the way research is 'chosen, designed, done, analysed, regulated, managed, disseminated, and reported' (Macleod et al., 2014, p. 101). One particular mechanism underlying research waste may be the way that fast, über-productive approaches to science potentially exacerbate issues with reproducibility. For example, through researchers' decisions to cut corners by quickly moving onto new projects rather than combing through and focusing on making sense of recent null results (Frith, 2020). This behaviour is reinforced by reward systems that incentivise 'quantity more than quality, and novelty more than reliability' (Ioannidis et al., 2014, p. 2). These issues of fast science and irreproducibility are crucial in the field of clinical research, and not only for financial reasons; innumerable preclinical studies have been found to be irreproducible, generating false hope for families awaiting break-through treatments (Freedman et al., 2015).

However, it is worth distinguishing between mitigable and unmitigable research waste. There is a difference between waste arising from fast, irreproducible science, and waste arising from a pandemic, particularly in the context of a PhD programme with time and funding restrictions. In the former instance, the onus is on all members of the scientific community - including scientists, funders, and research coordinators – to change; to promote better practice, and model greater 'scientific citizenship.' In the latter instance, research waste is ultimately a product of circumstances. The loss of projects and potential publications, while disappointing for early career researchers on fixed term contracts, may also provide an opportunity for reflecting on the way scientists are trained. Specifically, the goal of PhD programmes could be reappraised; perhaps we could reframe PhDs as being more about research quality, and less about novel and publishable results. Though this might seem to present a false dichotomy, there is evidence to suggest that results-focused science is often associated with numerous questionable research practices (John et al., 2012; Nosek et al., 2012; Simmons et al., 2011). In contrast to this, innovative approaches to scientific training have been adopted in new curricula that focus on principles of critical thinking, methodological rigor and social responsibility, with the end goal of avoiding bad science, and improving reproducibility (Bosch, 2018).[24]

[24]Other means of improving reproducibility and methodological rigor have also been suggested: capping annual publications (Frith, 2020); mandatory trial reporting (Munafò et al., 2017); multi-site, international collaborations (Ioannidis et al., 2014), and publishing formats such as Registered Reports (Chambers & Tzavella, 2020).

4 Discussion

This chapter suggests that clinical researchers have to acknowledge that their work is characterised by ambiguity and complexity (Rosenblum et al., 2016). Managing 'role-related conflicts' is particularly necessary during public health crises like infectious disease outbreaks (Lipworth, 2020).

In addition, mitigable and unmitigable waste is a feature of clinical research (Freedman et al., 2015). These ideas challenge career norms, whereby researchers commonly define their success according to the number of publications and citations they can produce (so-called 'bean-counting'; Chambers, 2019). Recognising the scale of research waste presents an opportunity to redefine the goals of scientific training programmes.

Clinical researchers may therefore benefit from reflecting on the multi-faceted nature of their role, as well as the methodological rigor of their research projects. There are several advantages to this reflexive approach. Firstly, it promotes researcher development. This chapter has shown that experiencing ambivalence over one's role may be a common feature of clinical research, but – particularly in public health crises - it can also result in confusion, ethical dilemmas, undue pressure and potential health and safety concerns. Reflecting on the experience of clinical research has helped me to understand the challenges of an ambiguous, carer-scientist role. However, discussing the experience with others has helped me to see the potential benefits of an ambivalent identity; for example, it has helped me learn that oscillating between different professional stances (e.g., assertiveness versus reticence) could be a sign of strong ethical principles in a researcher.

The second advantage of this reflexive approach is that it has the potential to improve the quality of future research. Slowing down and reappraising what success looks like within research may lead to a greater engagement with the principles of reproducible science (Munafò et al., 2017). Rather than assimilating to a culture that is preoccupied with publishing positive results, we can become conscious of prevalent, spurious research practices (John et al., 2012) and develop greater methodological rigor, so that we can use this as a means for developing more robust and meaningful research. Experiencing and reflecting on 'research waste' – whether through conversation or written exercises - can provoke wider debates on what the goal of scientific training could and should be, especially for those who are in receipt of public funds. An expansion of the curricula may be in order; as Bosch (2018) suggests, 'researchers who are educated more broadly will do science more thoughtfully, with the result that other scientists, and society at large, will be able to rely on this work for a better, more rational world' (p. 277).

Practically implementing a more reflexive approach for early career clinical researchers in the scientific community may be more challenging than discussing ideas about it in the abstract. While I benefitted from peer discussions, journaling, and both clinical and academic supervision, these channels may not be available or as easily accessible to all researchers. Signposting to both formal

materials (e.g., on identity formation; Rosenblum et al., 2016) and more informal or narrative accounts (e.g., on questionable research practices; Krishna & Peter, 2018; Price, 2021) may be an alternative strategy to instigate and aid more reflexive discussions about clinical research.

5 Positionality statement

To finish, I offer some final thoughts on the process of completing this auto-ethnographic account, and on adopting a non-positivist stance in comparison to the rest of my PhD. I found the experience to be challenging in several ways. Firstly, I felt that the more qualitative approach involved a more speculative or opinionated perspective than I have been used to in my quantitative work. I also found it difficult to take a 'first-person', individual approach, as I am accustomed to working within a team. This led to me having some discomfort over claiming authority on various topics, though I was encouraged by the idea that 'there is no wrong way' to write up qualitative research, provided one has transparently outlined one's epistemological assumptions. Finally, I was concerned about expressing a critical perspective about scientific culture and training programmes, as this is not my usual remit, and I am conscious of my relatively junior and potentially naïve worldview on these issues. Nonetheless, I found it personally valuable to delve into some of these issues in more detail; both in terms of reflecting back on my own research practices as well as in terms of engaging with the empirical literature on reproducible science. It was also somewhat liberating to write in a more personalised, reflective way. Lastly, I would note that I found it valuable to be able to dedicate some thought and time to my work on the ward, in the form of this account, despite not being able to complete my quantitative project. Given how formative the experience was, my PhD would have felt incomplete without a report of this time.

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