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DOI: 10.3389/fpsyt.2020.00064

Document Version Peer reviewed version

Link to publication record in King's Research Portal

Citation for published version (APA):

Kinnaird, E., Stewart, C., & Tchanturia, K. (2020). Interoception in Anorexia Nervosa: exploring associations with alexithymia and autistic traits. *Frontiers in Psychiatry*, *11*, Article 64. https://doi.org/10.3389/fpsyt.2020.00064

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- Interoception in Anorexia Nervosa: exploring associations with alexithymia and autistic
   traits
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10 Keywords: anorexia nervosa, eating disorders, autism, alexithymia, interoception

- 11 Abstract
- 12 **Background:** Previous research on whether interoception is altered in anorexia nervosa (AN)
- using the heartbeat tracking task has yielded inconsistent results. However, no previous
- 14 research has examined whether interoception is associated with alexithymia and autistic traits
- in AN, conditions which are more prevalent in this population and thought to be related to
- 16 performance in this task. The aim of this study was to explore whether altered interoception
- 17 in AN is associated with alexithymia and autistic traits.
- 18 **Methods:** We assessed interoceptive accuracy using the heartbeat tracking task in n=37
- 19 people with AN, and n=37 age and gender matched healthy controls (HC), and explored
- 20 within the AN group if interoceptive accuracy was related to self-rated alexithymia or autistic
- traits. We also assessed self-reported interoceptive ability, and the relationship between
- subjective and actual performance.
- 23 **Results:** Heartbeat tracking task performance was not found to be altered in the AN group
- compared to the HC group. However, confidence ratings in task performance in the AN
- 25 group were lower compared to the HC group. Unlike the HC group, confidence ratings in the
- AN group did not correlate with task performance. Within the AN group there was no
- 27 relationship between interoceptive accuracy, alexithymia, and autistic traits, after controlling
- for the potential confounders of anxiety and depression. There was a relationship between
- 29 confidence ratings and illness severity in the AN group.
- 30 **Conclusion:** The results found no differences between heartbeat tracking task performance in
- 31 people with AN compared to HC. There was no association between task performance,
- 32 alexithymia and autistic traits in AN. Results do suggest that people with AN exhibit lowered
- confidence in their task performance, and that they may lack insight into this performance
- 34 compared to HC. The findings are discussed in the context of potential significant limitations
- of the heartbeat tracking task, with recommendations for future research into interoception in
- 36 AN.
- 37

38

# 1. Introduction

Anorexia nervosa (AN) is an eating disorder (ED) characterised by the restriction of energy
intake resulting in low body weight, a resistance to weight gain, and altered body image
(American Psychiatric Association, 2013). Early research on AN suggested that this food

- 42 restriction, and associated symptoms such as altered body image and problems identifying
- 43 emotions, may be driven by a difficulty detecting internal bodily sensations (Bruch, 1962).

44 This concept of sensitivity to bodily stimuli has come to be understood under the wider term

- of interoception, or "the sense of the physiological condition of the entire body" (Craig,
- 46 2002). Interoception encompasses how the brain identifies, interprets and integrates internal
- 47 stimuli. Altered interoception is associated with a number of processes thought to be related
- to the development and maintenance of AN, including appetite regulation, emotion
  regulation, self-awareness, and motivation (Craig, 2002; Critchley & Garfinkel, 2017; Kaye,
- Wagner, Fudge, & Paulus, 2011; Paulus & Stein, 2006). Research into interoception has
- 50 wagner, Fudge, & Faulus, 2011, Faulus & Stern, 2000). Research into interoception has 51 encompassed various definitions of key terms, including similar terms being used by different
- 52 studies to describe different concepts (Khalsa, Adolphs, et al., 2018). Recently, Garfinkel and
- 53 co-authors (2015) have defined interoceptive accuracy (objective ability to detect internal
- 54 stimuli), interoceptive sensibility (self-perceived ability to detect internal stimuli), and an
- 55 individual's metacognitive insight into their objective ability. The current study will use these
- 56 definitions when discussing different aspects of interoception, including when referring to
- 57 previous research which used different terms.
- 58 Studies on whether interoceptive accuracy is altered in AN have yielded mixed findings.
- 59 Although earlier research often focused on hunger and satiety detection, more recent studies
- on interoceptive accuracy in AN have most commonly used measures of cardiac
- 61 interoception, specifically the heartbeat tracking task (Schandry, 1981). Using the heartbeat
- 62 tracking task, two initial studies found that people with AN had lower interoceptive accuracy
- 63 (Pollatos et al., 2016; Pollatos et al., 2008). By contrast, three more recent studies using the
- same measure found no significant differences between people with AN and healthy controls
- 65 (HC) (Ambrosecchia et al., 2017; Lutz et al., 2019; Richard et al., 2019). One previous study
- has used a heartbeat discrimination task, finding no differences between people with AN and
   HC (Eshkevari, Rieger, Musiat, & Treasure, 2014). By contrast, research on interoceptive
- HC (Eshkevari, Rieger, Musiat, & Treasure, 2014). By contrast, research on interoceptive
  sensibility in AN consistently suggests that people with AN self-report a lack of confidence
- 69 in their ability to detect their internal stimuli compared to HC (Jenkinson, Taylor, & Laws,
- 70 2018). It should be noted that these previous interoceptive sensibility studies have primarily
- used the interoceptive subscale of the Eating Disorder Inventory (EDI) (Garner, Olmstead, &
- 72 Polivy, 1983). This subscale has been criticised for potentially measuring emotional, rather
- than somatic awareness (Eshkevari et al., 2014), and for not distinguishing between a lack of
- 74 acceptance of emotional arousal, and a lack of clarity surrounding internal stimuli (Merwin,
- 75 Zucker, Lacy, & Elliott, 2010). The subscale also primarily focuses on the sensations of
- <sup>76</sup> hunger and satiety, rather than including a range of different body sensations (Lutz et al.,
- 77 2019).

Therefore, previous research suggests that while people with AN self-report a lowered ability 78 79 to detect internal stimuli, it is unclear whether this equates to objectively lowered interoceptive accuracy. One potential reason for this variability in previous findings is the 80 methodology. The majority of studies on interoceptive accuracy in AN have used the 81 heartbeat tracking task, but this method has come under increasing scrutiny. Heartbeat 82 tracking can be influenced by a number of factors, including BMI (Rouse, Jones, & Jones, 83 1988), cardiac variables (Knapp-Kline & Kline, 2005), and prior knowledge about typical 84 85 heart rates (Murphy et al., 2018). It has also been suggested that heartbeat tracking scores reflect participant beliefs about heart rate, rather than actual counted heartbeat sensations 86 (Brener & Ring, 2016; Desmedt, Luminet & Corneille, 2018). In addition, the test has low 87 test-retest reliability, and does not relate to other measures of cardiac interoception (Ring & 88 89 Brener, 2018; Wittkamp et al., 2018). An additional difficulty in using this test to measure interoceptive accuracy in AN is the potential influence of related clinical variables. For 90 example, previous research has considered the role of depression and anxiety when exploring 91 this area, variables known to be associated with altered interoceptive accuracy 92

- 93 (Ambrosecchia et al., 2017; Dunn et al., 2007; Eley et al., 2004; Pollatos et al., 2008).
- 94 However, to date, no research has explored whether there is an association between
- alexithymia, autistic traits and interoception in AN (Westwood et al., 2016; Westwood, Kerr-
- 96 Gaffney, Stahl, & Tchanturia, 2017).

97 Autism is a neurodevelopmental disorder associated with differences in social

- 98 communication, and restricted behaviours and interests (American Psychiatric Association,
- 2013). People with AN exhibit heightened levels of autistic traits compared to HC
- 100 (Westwood et al., 2016), and qualitative research suggest that altered interoception could
- 101 contribute to disordered eating in autistic adults (Kinnaird, Norton, Pimblett, Stewart, &
- 102 Tchanturia, 2019; Kinnaird, Norton, Stewart, & Tchanturia, 2019). Research suggests that
- 103 interoceptive accuracy may be lowered in autism (Garfinkel et al., 2016; Palser, Fotopoulou,
- Pellicano, & Kilner, 2018), although other studies have found no differences in autism
- 105 compared to HC (Nicholson, Williams, Carpenter, & Kallitsounaki, 2019; Nicholson et al., 2019; Schwadar, Mach. Present & Carrier 2015)
- 106 2018; Schauder, Mash, Bryant, & Cascio, 2015).
- 107 It has been suggested that apparent differences in interoceptive accuracy in autism could in 108 fact be related to the higher levels of alexithymia seen in autistic populations (Brewer, Happe,
- 109 Cook, & Bird, 2015; Kinnaird, Stewart, & Tchanturia, 2019; Livingston & Livingston, 2016;
- 110 Mul, Stagg, Herbelin, & Aspell, 2018; Shah, Hall, Catmur, & Bird, 2016). Alexithymia is
- associated with lower interoceptive accuracy, to the extent that it has been hypothesised to be
- the product of impaired interoception (Brewer, Cook, & Bird, 2016; Herbert, Herbert, &
- Pollatos, 2011; Murphy, Catmur, & Bird, 2018). Furthermore, this relationship may be
- specific to clinical populations: a recent meta-analysis found no relationship between
- interoception in control populations, but found that lowered interoception was related to
- heightened alexithymia in EDs and autism (Trevisan et al., 2019). However, this study used a
- broad definition of interoception, described as "interoceptive awareness", including attention,
  detection, magnitude, discrimination, accuracy, insight, sensibility, and self-report abilities
- surrounding bodily cues (Khalsa et al., 2018). Therefore, the findings related to a broadly
- defined construct of interoception, incorporating a number of different measurement
- approaches. Moreover, the meta-analysis considered EDs as a single category rather than
- distinguishing between AN, bulimia nervosa (BN) and binge eating. No previous study has
- specifically investigated the relationship between interoceptive accuracy as measured using
- 124 the heartbeat tracking task and alexithymia in AN.
- 125 Therefore, any attempt to investigate the associations between autistic traits and interoception 126 in AN would also require a consideration of the role of alexithymia, with research suggesting
- 127 alexithymia is heightened in people with AN (Westwood, Kerr-Gaffney, Stahl, & Tchanturia,
- 128 2017). However, to date the associations between different facets of interoception,
- 129 alexithymia, and autism in AN have not been explored. The aim of this exploratory study was
- to address this gap in the literature by investigating the following hypotheses using theheartbeat tracking task:
- 132 1) People with AN would exhibit lowered interoceptive accuracy compared to HC.
- 133 2) People with AN would self-report lowered interoceptive accuracy compared to HC.
- 134 3) People with AN would exhibit poorer metacognitive insight into their task performance compared to HC.
- 1364) There would be an association between interoceptive accuracy, alexithymia and autism within the AN group.

- In the context of a lack of previous research in this area, the current study only examined 138
- associations between interoceptive accuracy, alexithymia, and autistic traits in AN. It does 139
- not present hypotheses surrounding the expected relationships. 140

#### 2. Methods 141

#### **2.1 Participants** 142

- Participants with AN (n=37) were recruited from a specialist ED treatment service. 143
- Additional participants were recruited by advertising online with a UK based ED charity. All 144
- participants met DSM-V criteria for AN as assessed using the Structured Clinical Interview 145
- for DSM (SCID-5) (First, Williams, Karg, & Spitzer, 2015). Participants were excluded if 146
- they reported a neurological condition or serious medical condition. Participants with AN 147
- were included if they had a previous diagnosis of autism. 148
- Age and gender matched HC (n=37) were recruited through the local university and through 149
- advertising online. Exclusion criteria for HC included any history of EDs or mental health 150
- conditions, neurological or serious medical conditions, or a prior diagnosis of autism. These 151
- were confirmed through screening using the SCID-5 and the Autism Spectrum Quotient 152
- (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). Participants received £20 153
- for taking part in the study. 154

#### **2.2 Measures and Procedure** 155

#### 156 2.2.1 Interoceptive Accuracy.

Interoceptive accuracy was assessed using a heartbeat tracking task, which requires 157

participants to detect their own heartbeats (Schandry, 1981). Participants were asked to 158

silently count their heartbeats during four randomised time windows (25, 35, 45, and 100 159

- 160 seconds), and then at the end of each window to report the number of counted heartbeats to
- 161 the researcher. Participants were verbally cued to begin counting by the researcher, and then
- cued to stop counting when a timer alarm sounded. Participants then verbally reported the 162 number of heartbeats counted. Actual number of heartbeats were measured using a pulse
- 163 oximeter with the sensor attached to their index finger. An interoceptive accuracy score was 164
- calculated for each time trial for each participant using the formula 1 (|nbeatsreal nbeatsreal nbeatsread nbeat165
- nbeatsreported)/((nbeatsreal + nbeatsreported)/2), with resulting scores averaged across the 166
- four trials to give an overall score for each participant (Garfinkel, Seth, Barrett, Suzuki, & 167
- Critchley, 2015). 168
- Although the efficacy of the heartbeat tracking task as a measure of interoceptive accuracy 169
- has recently come under scrutiny, this task was chosen as it has been used in the vast majority 170
- of previous research on interoceptive accuracy in AN, alexithymia and autism (Brener & 171
- Ring, 2016; Murphy, Brewer, Hobson, Catmur, & Bird, 2018). As the aim of this study was 172 to explore whether heartbeat tracking task performance could be related to alexithymia and
- 173 autistic traits in AN, the current study has continued to use this method.
- 174

#### 2.2.2 Interoceptive Sensibility. 175

- In the context of previous criticism of the EDI interoceptive subscale (Eshkevari et al., 2014; 176
- 177 Lutz et al., 2019; Merwin et al., 2010), interoceptive sensibility was assessed using total
- scores on the awareness sub-scale of the Porges Body Perception Questionnaire (BPQ) 178
- (Porges, 1993). The subscale uses 45 questions to assess self-reported awareness of bodily 179
- 180 symptoms, with participants answering on a Likert Scale from "never" to "always". A higher
- score indicates higher interoceptive sensibility. The subscale has previously been used in 181

interoception research, including in autistic populations, but has not previously been used in
people with AN (Garfinkel et al., 2015; Garfinkel et al., 2016). A recent meta-analysis found
that the BPQ was significantly positively associated with alexithymia (Trevisan et al., 2019).

Interoceptive sensibility was additionally assessed using task confidence ratings: immediately
following the heartbeat tracking task, participants were asked to rate how confident they were
in their task performance on a scale from 1 (least confident) to 100 (most confident).

#### 188 **2.2.3 Metacognitive insight.**

189 Metacognitive insight into performance was operationalised as the correspondence between

190 interoceptive accuracy (heartbeat tracking task) and interoceptive sensibility (BPQ and

191 confidence ratings) (Murphy, Catmur & Bird, 2019; Khalsa et al., 2018). In the present study

this was measured as group correlations between heartbeat tracking scores, and BPQ and

193 confidence ratings.

### 194 **2.2.4 Clinical variables.**

195 Alexithymia was measured using the Toronto Alexithymia Scale (TAS-20) (Bagby, Parker,

196& Taylor, 1994). The TAS-20 is a self-report measure of alexithymia (the inability to label

197 and describe emotions in the self) with good internal consistency and test-retest reliability. A

198 higher score indicates higher levels of alexithymia. The TAS-20 is widely used in research in

both autistic and ED populations (Kinnaird, Stewart, et al., 2019; Westwood et al., 2017).

200 Autistic traits were measured using the Autism Spectrum Quotient (AQ) (Baron-Cohen et al.,

201 2001). The AQ is a continuous measure of autistic traits, with higher scores indicating higher

202 levels of autistic traits. The AQ has previously been used in AN populations, with people

with AN typically scoring higher compared to HC (Westwood et al., 2016). Whilst the AQ

does include a cut-off score, with scores above 32 indicating potentially clinically significant
 levels of autistic traits, recent research has questioned the ability of the AO to distinguish

levels of autistic traits, recent research has questioned the ability of the AQ to distinguish
"true" autism cases in populations with high levels of autistic traits (Ashwood et al., 2016;

206 True autism cases in populations with high levels of autistic traffs (Ashwood et al., 2016; 207 Conner, Cramer, & McGonigle, 2019; Sizoo et al., 2015). Consequently, beyond screening

HC for high autistic traits at the beginning of the study, the AQ was only used in the analysis

209 as a continuous measure.

210 Previous research has suggested that the relationship between alexithymia, autism and

211 interoceptive accuracy cannot be successfully measured without accounting for the role of

anxiety and depression (Murphy et al., 2018). Therefore, anxiety and depression were

213 measured using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith,

1983). The HADS is a widely used 14-item self-rating instrument for anxiety and depression.

The clinical threshold is 10 for each scale.

# 216 **2.3 Procedure.**

217 The study received ethical approval from North East - Newcastle & North Tyneside 2

218 Research Ethics Committee (18/NE/0193). All subjects gave written informed consent in

accordance with the Declaration of Helsinki. All testing took place during a single study visit.

220 Following informed consent, participants completed questionnaires and self-reported

221 demographic information. Height and weight were measured on the day of testing to assess

BMI scores. If a participant with AN was currently in treatment, their BMI was taken from

their most recent measurements in clinical notes. Participants with AN additionally self-

reported their illness duration. Participants then completed the heartbeat tracking task, and

rated their confidence in their task performance. A small number of participants did not

complete all questionnaires but did complete all screening measures and experimental tasks:

any difference in group numbers across each self-report measure has been highlighted in theresults.

### 229 **2.4 Analysis.**

- 230 Statistical analyses were performed using Stata (version 15.0) software. Interoceptive
- accuracy scores were calculated for each of the time intervals, and averaged to give an overall
- score. Mean heart rate (MHR) was assessed by calculating the participant's heart rate across
- each time trial, and then averaging the data to give an overall MHR estimate.
- The variables age and interoceptive sensibility (BPQ scores) were found to be non-normally
- distributed and were transformed. The following variables were found to be non-normally
- distributed and could not be transformed: BMI, EDE Global scores, HADS depression,
- 237 interoceptive accuracy scores, and confidence in task performance scores. In addition to the
- 238 non-normal distribution, interoceptive accuracy scores were found to be highly skewed
- 239 (skewness= -1.39, kurtosis= 5.32). Therefore, non-normally distributed variables were
- analysed using non-parametric tests, and are summarised in the results using median and
- interquartile range (IQR) values instead of means and standard deviations (SD).
- Group differences on each variable were calculated using t-tests, or Mann-Whitney U tests
- for non-parametric variables that could not be transformed. Correlations were performed
- within each group to establish relationships between the heartbeat tracking task, and the BPO
- and confidence ratings.
- 246 Within the AN group only, a multiple linear regression analysis was performed with
- 247 interoceptive accuracy (overall mean score) as the dependent variable to explore the relative
- 248 contributions of autistic traits and alexithymia, whilst also controlling for the role of anxiety
- and depression as recommended by previous research (Murphy et al., 2018). Correlational
- analyses were performed to assess relationships between confidence scores and clinical
- 251 variables in the AN group.

#### 252 **3. Results**

#### 253 **3.1 Clinical and Demographic Characteristics**

- In the AN group (n=37), 31 participants had restrictive AN (83.78%), whilst 6 participants
- had binge/purge AN (16.22%). Mean illness duration was 9.41 years (*SD* 7.72). 29
- 256 participants were receiving treatment for their AN at the time of study participation (78.38%),
- and 8 participants were not receiving treatment (21.62%). Of the participants receiving
- treatment, the majority (*n*=23, 62.16%) were receiving outpatient treatment, and a minority
- (n=6, 16.22%) were in inpatient treatment. 24 participants with AN (64.86\%) were taking
- 260 psychotropic medication. 3 participants with AN reported a prior diagnosis of autism. In
- addition, the majority (n= 24, 64.86%) of participants in the AN group reported at least one
- 262 comorbid clinical diagnosis. The most common clinical diagnoses were depression (n=15)
- and anxiety (n=10), and n=5 participants reported a diagnosis of borderline personality
- disorder. Diagnoses reported by only one participant were bipolar disorder, obsessive-
- compulsive disorder, and post-traumatic stress disorder.
- 266 Group differences are summarised in Table 1. Participants were matched on age and gender,
- and exhibited no differences in MHR. As expected, participants with AN had lower mean
- 268 BMIs compared to the HC group, and scored higher on measures of alexithymia, ED
- symptomatology, autistic traits, depression and anxiety.

#### 270 **3.2 Interoceptive Accuracy**

- 271 Heartbeat tracking scores are summarised in Table 2. There were no significant differences
- between groups on the overall heartbeat tracking score, or at any time point, with small effectsizes.

### 274 **3.3 Interoceptive Sensibility**

- 275 There were no significant differences between groups in interoceptive sensibility as measured
- by the BPQ (HC mean= 117.61 (n= 36, SD= 43.00), AN mean= 115.43 (n= 37, SD= 24.49),
- 277 t(71) = 0.21, p = 0.833, d = 0.05). The AN group did score significantly lower on their
- confidence rating in their interoceptive accuracy task performance, with a medium effect size (HC median= 50, IQR= 43.00, AN median= 40, IQR= 38), U= 477.5, p= 0.025, d= 0.54).

### 280 **3.4 Metacognitive Insight**

- In the HC group, there was no relationship between the heartbeat tracking task and BPQ
- scores (r=0.09, p=0.605). There was a significant positive correlation between heartbeat
- tracking scores and confidence ratings (r=0.60, p < 0.001). By contrast, in the AN group
- there was no correlation between the heartbeat tracking task and the BPQ (r=0.17, p=0.322),
- or the confidence ratings (r=0.26, p=0.117).

### 286 3.5 Relationship with Clinical Variables

- 287 The relative contribution of autistic traits, alexithymia, anxiety and depression to
- interoceptive accuracy were calculated using a regression analysis within the AN group only.
- 289 There were no significant relationships between any of these clinical variables and
- 290 interoceptive accuracy.
- 291 Correlations between clinical variables and task confidence ratings were also explored within
- the AN group only. There were no significant relationships between confidence ratings and
- alexithymia, autistic traits, anxiety or depression in the AN group. However, there was a
- significant negative relationship between confidence ratings and ED severity as measured by
- 295 the EDE-Q Global score (r= -0.41, p= 0.012).

### 296 **4. Discussion**

297 The overall aim of this study was to explore whether interoceptive accuracy as measured by the heartbeat tracking task is associated with alexithymia and autistic traits in AN. Contrary 298 to the hypothesis that people with AN would exhibit lowered cardiac interoceptive accuracy 299 300 compared to HC, the study found no significant differences between groups in heartbeat tracking performance. This is in line with a number of recent studies, including two that were 301 published after the hypotheses for the current study were generated (Ambrosecchia et al., 302 2017; Lutz et al., 2019; Richard et al., 2019). The findings of the present study, and more 303 recent research, contrast with previous research using the heartbeat tracking task in AN which 304 found lowered accuracy in this population (Pollatos et al., 2016; Pollatos et al., 2008). One 305 potential explanation for this variation in findings are differences in the AN samples used in 306 each study, such as differences in BMI, age, comorbidities, illness duration, and treatment 307 status. For example, the participants with AN in this study were receiving a range of different 308 treatments (inpatient, outpatient, or no treatment), compared to participants receiving self-309 help only in the Pollatos et al (2008) study. The participants in the current study additionally 310 had lower BMIs, higher mean illness duration, and were slightly older compared to this initial 311 study. This reflects concerns that heartbeat tracking task performance is associated with state-312 dependent factors (Wittkamp et al., 2018). For example, Richard et al (2019) found that 313 interoceptive accuracy was associated with inpatient treatment progress, with higher accuracy 314 associated with higher BMIs and longer time in treatment. 315

The second hypothesis of this study was that people with AN would exhibit lowered 316 interoceptive sensibility (self-perceived interoceptive aptitude) compared to HC. Findings on 317 interoceptive sensibility were mixed: there were no differences between groups on the BPQ, a 318 measure of self-reported awareness of bodily symptoms, but people with AN did report lower 319 confidence in their interoceptive task performance. The third hypothesis of this study was that 320 people with AN would exhibit poorer metacognitive insight, operationalised as group 321 correlations between performance and BPO/confidence ratings. The finding that there was a 322 positive correlation between task performance and confidence ratings in the HC group, but 323 not the AN group, suggests that people with AN may lack insight into their interoceptive 324 325 abilities (Murphy, Catmur & Bird, 2019; Khalsa et al., 2018). Significantly, lower confidence ratings were correlated with higher ED symptomatology in the AN group, indicating that this 326 lack of insight may be related to ED severity. If individuals with AN have less confidence in 327 328 their ability to detect interoceptive sensations, this could result in a reliance on other cues, such as prior beliefs around likely interoceptive responses. The possibility that people with 329 AN rely on predicted sensations, as opposed to the detection of actual sensations, is supported 330 by research suggesting that people with AN find it difficult to detect actual interoceptive 331 332 responses from anticipated responses (Khalsa et al., 2015). Individuals with AN were more likely to falsely endorse changes in interoceptive sensation in the absence of stimulation, and 333 reported more intense cardiorespiratory sensations compared to HC, during pre-meal states. 334 335 This prediction error between actual and anticipated responses is also thought to be altered in other conditions with heightened prevalence in AN, including autism, anxiety and depression 336 (Garfinkel et al., 2016; Paulus & Stein, 2010). Future research should consider further 337 338 investigating the concept of metacognitive insight in interoception in AN, in particular the role that this might play in interoceptive prediction errors. 339

Alternatively, the lower confidence ratings found in this study may reflect the fact that low
self-esteem is very common in people with AN (Jacobi, Paul, de Zwaan, Nutzinger, &
Dahme, 2004). Therefore, the findings of this study could reflect a generalised lack of
confidence in ability, rather than a lack of confidence specific to interoceptive performance.
It should be noted that the current results contrast with the findings of Lutz et al (2019) who
found no difference between groups in task confidence ratings.

Finally, the study hypothesised that there would be an association between interoceptive 346 accuracy, alexithymia and autism within the AN group. The findings of this study did not 347 support this hypothesis, with no relationships found. Consequently, it is possible that 348 interoceptive accuracy is not linked to alexithymia and autistic traits in AN, and is rather 349 associated with other drivers, such as treatment duration or BMI (Richard et al., 2019). 350 However, it should be noted that interoceptive accuracy, autism and alexithymia have not 351 consistently been linked in previous studies: two recent studies have found no associations 352 between autism and interoceptive accuracy in adults (Nicholson et al., 2019; Nicholson et al., 353 2018). Similarly, two additional studies have found no association between interoceptive 354 accuracy and alexithymia (Nicholson et al., 2018; Zamariola, Vlemincx, Corneille, & 355 Luminet, 2018). 356

It is likely that these mixed findings on the relationship between cardiac interoceptive accuracy, alexithymia and autism, and indeed for the inconsistent results surrounding interoceptive accuracy in AN, is related to the heartbeat tracking task itself. The heartbeat tracking task was chosen for the current study as it has been used in the majority of previous research on interoceptive accuracy in AN, alexithymia and autism. However, as previously outlined, heartbeat perception can be influenced by a number of factors beyond the control of the current study. For example, a recent study exploring alexithymia and interoceptive

accuracy in a sample of 287 participants initially found no relationship, and subsequently 364 only detected a relationship after accounting for 10 additional control variables (Murphy et 365 al., 2018). Some of these variables were accounted for in group comparisons in the present 366 study: for example, there were no significant differences between groups on age or mean 367 heart rate. However, groups in the current study significantly differed on other variables, 368 including anxiety, depression, BMI, and alexithymia. Although the present study is the one of 369 the largest studies on interoceptive accuracy in AN to date (n=74 compared to n=76 in 370 Richard et al. (2019)), it was not possible to account for the potential roles of all these 371 variables owing to the relatively small sample size limiting the ability to perform a large 372 multi-variable regression analysis. Additionally, the non-parametric distribution limited the 373 ability to control for variables in group comparisons using ANCOVAs. Finally, the current 374 study did not include a control task to account for the possible influence of participant beliefs 375 376 about heart rates, or the possibility that they were counting time rather than heartbeats. However, a strength of the current study was that it controlled for anxiety and depression 377 whilst exploring the relationship between interoceptive accuracy, alexithymia and autism in 378 people with AN (Murphy et al., 2018). 379

Therefore, the findings of this study should be understood in the context of the limitation that 380 there are a number of problems associated with using the heartbeat tracking task as a measure 381 of interoceptive accuracy. Future research in this area should consider adapting the heartbeat 382 task to control for potential covariates identified by Murphy et al. (2018), or by modifying the 383 task instructions to instruct participants to specifically count their felt heartbeats, rather than 384 reporting an estimate (Desmedt et al., 2018). Alternatively, studies on interoception in AN 385 could move away entirely from the heartbeat tracking task to a more robust measure of 386 interoceptive accuracy. For example, recent studies on cardiac interoception in AN have 387 instead used bolus intravenous infusions of isoproterenol to artificially raise heartbeat and 388 respiratory rate in a controlled manner, and then asked participants to rate their changing 389 390 sensations using a dial (Khalsa et al., 2015; Khalsa et al., 2018). Whilst this type of methodology is more invasive compared to the heartbeat tracking task, it does allow for a 391 more highly controlled approach. 392

Significantly, these studies similarly found no difference in interoceptive accuracy, but did 393 find prediction errors made specifically in the context of meal anticipation. This appeared to 394 be related to heightened anxiety, and atypical interoceptive representation of the heartbeat: 395 individuals with AN located sensations in the left side of their chest in the absence of actual 396 stimulation (Khalsa et al., 2018). Further research should consider exploring aspects of 397 interoception in AN other than accuracy, including the ability to discriminate between 398 sensations, or magnitude estimations. The finding in these studies that altered interoception is 399 potentially specific to meal anticipation also warrants further research. In the current study, 400 proximity of the task to meals was not considered. It is possible that task performance, 401 particularly for AN participants, could have been influenced by task timing in relation to 402 meal anticipation. Interestingly, in the current study people with AN did not self-report 403 generalised problems with detecting bodily symptoms, as measured by the BPQ. Taken 404 405 together with previous research suggesting elevated difficulties as measured using the EDI (Jenkinson et al., 2018), these findings support the possibility in AN are specifically 406 associated with hunger and satiety sensations, or sensations associated with emotion detection 407 only, rather than representing a generalised difficulty. Future research could consider 408 409 focusing on whether interoceptive differences in AN are associated with specific states, such as heightened emotional arousal, hunger and satiety, or meal anticipation. 410

- 411 In conclusion, the current findings indicate that there are no differences in heartbeat tracking
- 412 task performance in people with AN compared to HC, and that this performance is not
- 413 associated with alexithymia or autistic traits within AN populations. However, these findings
- are presented in the context of potentially significant limitations with the chosen
- methodology. The study did find that people with AN potentially exhibit lower metacognitive
- 416 insight. Recommendations are made for future research in this area.

#### 417 **5. Acknowledgements**

The authors would like to thank the UK eating disorder charity Beat for their support with recruitment for this project.

#### 420 **6. Author Contributions**

- 421 All authors contributed to the design of the study. EK carried out data collection, and wrote
- the first manuscript draft. KT and CS contributed to the final manuscript. All authors read
- 423 and approved the final manuscript.

#### 424 **7. Funding**

- 425 EK was supported by a Medical Research Council Doctoral Training Partnership studentship
- 426 (MR/N013700/1). KT would like to acknowledge support from MRC and MRF Child and
- 427 Young Adult Mental Health (MR/R004595/1) and support from the Health foundation, an
- 428 independent charity committed to bring better health care for people in the UK (Ref: AIMS
- 429 ID): 1115447.

### 430 8. Conflict of Interest

431 The authors have no conflicts of interests to declare.

### 432 9. Data Availability Statement

- 433 The datasets for this manuscript are not publicly available because the authors do not have
- 434 permission to share the participant data publicly. Requests to access the datasets should be
- directed to Kate Tchanturia, kate.tchanturia@kcl.ac.uk.

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# **11. Tables**

	HC mean	AN mean	Test statistic	р	Effect
	( <b>SD</b> )	( <i>SD</i> )			size (d)
	( <i>n</i> =37)	( <i>n</i> =37)			
Age (years)	26.05	26.08	t(72) = -0.36	0.720	0.08
	(7.13)	(8.05)			
Gender	<i>n</i> = 35	<i>n</i> = 35		1.00	
	female	female			
	(94.59%),	(94.59%),			
	n=2 male	n=2 male			
	(5.41%)	(5.41%)			
BMI*	22.8 (4.4)	15.8 (1.2)	U=0	< 0.001	3.37
Mean Heart	72.27	69.19	t(72) = 1.24	0.219	0.29
Rate (MHR;	(10.12)	(11.22)			
beats per					
minute)					
Alexithymia	41.76	61.43	t(72) = -6.37	< 0.001	1.48
(TAS)	(13.45)	(13.12)			
EDE-Q	0.61 (0.89)	4.22 (1.33)	<i>U</i> = 10	< 0.001	3.20
Global*					
AQ	12.57	23.30	t(72) = -5.27	< 0.001	1.22
	(6.80)	(10.36)			
HADS	2 (3)	9 (5)	134.5	< 0.001	1.89
<b>Depression</b> *		<i>n</i> = 36			
HADS Anxiety	6.08 (3.90)	13.17	t(71) = -7.46	< 0.001	1.75
		(4.21)			
		<i>n</i> = 36			
*Data non-normally distributed. Medians and interquartile ranges presented, and					
data analysed using non-parametric methods.					

Table 1: Clinical and demographic group characteristics.

Table 2: Group differences in interoceptive accuracy scores.

	HC mean (SD) (n=37)	AN mean (SD) (n=37)	Test statistic	р	Effect size ( <i>d</i> )
Interoceptive	0.67 (0.35)	0.74 (0.28)	<i>U</i> = 580.5	0.261	0.26
Accuracy*					
25	0.68 (0.45)	0.83 (0.35)	<i>U</i> = 507	0.055	0.46
seconds*					
35	0.71 (0.58)	0.75 (0.29)	<i>U</i> = 600	0.361	0.21
seconds*					
45	0.70 (0.34)	0.71 (0.38)	<i>U</i> = 667.5	0.854	0.04
seconds*					

100 0	0.68 (0.30)	0.77 (0.29)	<i>U</i> = 586.5	0.289	0.25	
seconds*						
*Data non-normally distributed. Medians and interquartile ranges presented.						

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Table 3: Relative contribution of clinical variables to interoceptive accuracy within the ANgroup only.

	В	t	р
Autistic traits (AQ)	0.00	0.02	0.987
Alexithymia (TAS)	0.05	0.20	0.846
Anxiety (HADS)	-0.21	-1.10	0.278
Depression (HADS)	-0.07	-0.34	0.736

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