**Day-to day executive function in preschool children with congenital heart disease and controls: the role of a cognitively stimulating home environment.**

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Conflicts of Interest

The authors declare no conflicts of interest

**Abstract**

Objectives:

To assess the relationship between (1) environmental and demographic factors and executive function (EF) in preschool children with congenital heart disease (CHD) and controls and (2) clinical and surgical risk factors and EF in preschool children with CHD.

Study Design:

At 4-6 years of age, parents of children with CHD (n=51) and controls (n=124) completed the BRIEF-P questionnaire and the Cognitively Stimulating Parenting Scale (CSPS). Multivariate general linear modelling assessed the relationship between BRIEF-P composite scores (Inhibitory Self-Control Index (ISCI), Flexibility Index (FI), and Emergent Metacognition Index (EMI)) and group (CHD/control), sex, age at assessment, gestational age (GA), index of multiple deprivation (IMD) and CSPS scores. The relationship between CHD type, surgical factors and brain MRI injury rating (BIR) and ISCI, FI and EMI scores was assessed.

Results:

Presence of CHD, age at assessment, sex and IMD were not associated with EF scores. Lower GA was associated with higher ISCI and FI scores and age at assessment was associated with lower FI scores. Group significantly moderated the relationship between CSPS and EF, such that CSPS significantly predicted EF in children with CHD (ISCI: p=0.0004; FI: p=0.0015; EMI: p=0.0004) but not controls (ISCI: p=0.2727; FI: p=0.6185; EMI: p=0.3332). There were no significant relationships between EF scores and surgical factors, CHD type or BIR.

Conclusions:

Supporting parents to provide a cognitively stimulating home environment may improve EF in children with CHD. The home and parenting environment should be considered when designing intervention studies aimed at improving EF in this patient group.

**List of Abbreviations**

BIR = brain MRI injury rating; CHD = congenital heart disease; CSPS = cognitively stimulating parenting scale; EF = executive function; EMI - Emergent Metacognition ; FI = Flexibility Index; GEC = Global Executive Composite; HLHS = hypoplastic left heart syndrome ; IMD = Index of Multiple Deprivation; ISCI = Inhibitory Self-Control Index; MRI = magnetic resonance imaging; TGA = transposition of great arteries; TOF = tetralogy of Fallot; UVH = univentricular heart; WM = working memory; WMI = white matter injury

**INTRODUCTION**

Congenital heart disease (CHD) affects almost 1% of UK births and is the most common congenital malformation. Improvements in antenatal diagnosis, cardiac surgery, and perioperative care mean that most infants born with CHD now survive [1]. However, children and adults with CHD are at increased risk of adverse neurodevelopmental sequalae including impaired motor, language and cognitive development [2,3]. One important higher order cognitive function is executive function (EF). EF could be regarded as an umbrella term for a range of cognitive processes including: attention, working memory, planning, inhibition, self-monitoring, self-regulation, and initiation [4,5]. EF components have been related to early mathematics and reading abilities and children with higher EF are better prepared for schooling [6-8].

Previous studies have suggested that school aged children, adolescents and adults with CHD have an increased prevalence of EF difficulties [9-12]. In addition, perinatal, clinical [13-16] and family environmental factors [17] reportedly influence neurodevelopmental outcomes in individuals with CHD. We have shown previously that a more stimulating home environment is associated with better cognitive function in toddlers with CHD [18].

To date, there have been few studies assessing EF in preschool children with CHD and, to our knowledge, no studies have assessed the relationship between a cognitively stimulating home environment and EF in this at-risk group of children. The aims of this study were to (1) to assess the relationship between environmental and demographic factors and EF in preschool children with CHD and controls (a “heart healthy” community sample) and (2) to assess the relationship between surgical risk factors (days to surgery, time on bypass, days on intensive care) and EF in preschool children with CHD. We hypothesised (i) EF scores would be lower in children with CHD compared to the community sample, (ii) higher socioeconomic status and a more cognitively stimulating environment would be associated with higher EF scores in both groups and (iii) increased exposure to peri-surgical risk factors would be associated with lower EF in the CHD sample.

**METHODS**

The study was approved by the National Research Ethics Committee (19/LO/0451). In accordance with the declaration of Helsinki, informed written parental consent was obtained before questionnaire data were collected. (Please see Appendix for further details of the parental consent process).

**Participants**

Inclusion criteria for the CHD sample were children with critical or serious CHD who underwent neonatal brain magnetic resonance imaging (MRI) as part of the Congenital Heart Imaging Project (CHiP) (REC: 07/H0707/105) between September 2014 and May 2018 and who had surgery or intervention by cardiac catheterization within the first year of life. Critical CHD was defined as hypoplastic left heart syndrome (HLHS), transposition of the great arteries (TGA), pulmonary atresia with intact ventricular septum, interruption of the aortic arch, and all infants requiring surgery within the first 28 days of life with the following conditions: coarctation of the aorta (COA), aortic valve stenosis, pulmonary valve stenosis; tetralogy of Fallot (TOF), pulmonary atresia with ventricular septal defect, and total anomalous pulmonary venous connection. Serious CHD was defined as any cardiac lesion not defined as critical, which requires cardiac catheterization or surgery before one year of age [19,20].

Inclusion criteria for the control sample were children who participated in the Developing Human Connectome Project (dHCP, https://www.developingconnectome.org/, REC: 14/LO/1169) and whose parents had consented to be approached for further research studies. We approached parents of dHCP participants who were the same age (projected age at assessment) as participants with CHD. Exclusion criteria for both groups were children born before 31 weeks gestational age (GA).

**Executive Function Assessment**

EF was assessed using the Behaviour Rating Inventory of Executive Function, Preschool Version (BRIEF-P) [21] which is a 63-item parent completed questionnaire. The BRIEF-P has been validated and is widely used in research follow-up [22,23], in various communities [24,25] and in different clinical settings [26,27] to assess the presence and severity of executive dysfunction in day-to-day situations. It contains five clinical scales that denote different aspects of executive functioning: Inhibit, Shift, Emotional Control, Working Memory, and Plan/Organize. (Further details of the BRIEF-P scales can be found in the Appendix).

Three indexes can be derived from the BRIEF-P: Inhibitory Self-Control (ISCI), Flexibility (FI), and Emergent Metacognition (EMI). This study utilises raw scores to determine ISCI (derived from inhibition and emotional control raw scores), FI (derived from the shift and emotional control raw scores) and EMI (derived from the working memory and plan/organise raw scores) as summary measures of EF. The ISCI represents a child’s ability to modulate responses, actions, emotions, and behaviour via appropriate inhibitory control. The FI represents a child’s ability to switch flexibly between actions, responses, emotions and behaviour. The EMI represents a child’s ability to initiate, plan, organise, execute and sustain future-oriented problem solving [21]. The raw scores of all three indexes were used for analysis in order to account for the full range of variation in these scales. Higher scores represent poorer EF.

**Cognitively Stimulating Parenting Scale**

The Cognitively Stimulating Parenting Scale (CSPS) [18,28,29] completed by parents is a 28-item questionnaire adaptation of the Home Observation for Measurement of the Environment (HOME) Inventory [30]. The CSPS assesses the availability and variety of experiences that promote cognitive stimulation at home and in the family. This includes availability of educational toys, parental interactions such as teaching words or reading stories, and cognitively stimulating activities such as family excursions or trips [18].

**Index of Multiple Deprivation**

Index of multiple deprivation (IMD) was derived from the residence postcode when follow-up questionnaires were posted to parents. IMD is a composite measure of socioeconomic status in England, combining information from seven domains to produce an overall relative measure of deprivation. Residential postcode was used to calculate IMD from the 2015 data release and reported as quintiles and percentile ranks. (<http://imd-by-postcode.opendatacommunities.org/> ; Accessed 13 December 2022).

**Clinical Data**

The number of days from birth to corrective or final palliative surgery, time on bypass during surgery, and number of days on the intensive care unit (ICU) post-surgery, were obtained from the hospital records. In children who underwent more than one surgery, days on ICU and time on bypass were summed across procedures.

**Neonatal neuroimaging**

Brain MRI was obtained prior to surgery in children with CHD and in the neonatal period for control children. MRI pulse sequence parameters are described in [20]. Images were reported by a perinatal neuroradiologist. Lesions were classified as focal arterial ischemic stroke, white matter injury (WMI), cerebellar hemorrhage, or intraventricular hemorrhage as we have reported previously [20]. WMI was classified into normal, mild, moderate or severe [31]. Overall each baby was categorized into one of four brain injury groups: normal, mild (intraventricular hemorrhage, and/or cerebellar hemorrhage ≤2 mm, and/or mild WMI), moderate (cerebellar hemorrhage >2 mm and/or moderate WMI), and severe brain injury (focal arterial ischemic stroke and/or severe WMI) as described previously [20].

**Statistical analyses**

All data were analysed in SPSS v28. Data were assessed for normality using histograms, Shapiro-Wilks tests, skewness and kurtosis values. ISCI, FI and EMI scores, CSPS, GA at birth and age at assessment were not compatible with a normal distribution.

**Assessing the relationship between EF scores and demographic and environmental factors**

Multivariate general linear modelling was undertaken to assess the relationship between ISCI, FI and EMI scores, group (CHD or control) sex, age of assessment, GA at birth, IMD and CSPS scores. Results were corrected for multiple tests using FDR correction [32] and p<0.05 after correction was considered significant. In a post-hoc analysis, moderated multiple regression analyses were conducted to examine the role of group (CHD or control) in the relationship between CSPS and EF outcome measures, controlling for age, sex, GA, IMD and BIR using the PROCESS 4.2 macro [33].

**Assessing the relationship between peri-surgical clinical factors and EF scores in the CHD group**

The relationship between CHD type (1) Abnormal mixing [i.e. TGA, truncus arteriosus], (2) Left sided lesions [i.e. COA], and (3) Right sided lesions [i.e. TOF, pulmonary atresia or stenosis, tricuspid atresia], surgical factors and BIR (moderate and severe BIR were combined) and ISCI, FI and EMI scores were assessed. Age at assessment, sex, GA at birth, IMD and CSPS scores, were included as covariates in the analysis. Kruskal-Wallis tests were used for categorical data. Associations between continuous variables and ISCI, FI and EMI scores were tested using non-parametric partial correlations accounting for the covariates. Results were corrected for multiple tests (3 EF measures) using FDR correction [32] and p<0.05 after correction was considered significant.

**Secondary analyses**

All analyses were repeated after removing children with CHD who had a confirmed or suspected genetic disorder.

**RESULTS**

**Participants**

Eighty parents of children with CHD agreed to receive questionnaires and 61 were returned (76% return rate). Five children were excluded as they were born at less than 31 weeks GA and 5 children did not have cardiac surgery. Data from 51 children with CHD were included in the analysis. Five children in the CHD sample had confirmed or suspected genetic abnormality (2 children had CHARGE syndrome, 2 had 22q11 deletion and 1 child had a suspected but not confirmed genetic abnormality). The relationship between cognitive outcome and CSPS scores at 2 years in 43 of these children was described previously [18] .

188 parents of control children agreed to receive questionnaires and 130 were returned (69% return rate). Six children were born at less than 31 weeks GA. The final control sample size was 124 children. 16 control children did not complete neonatal neuroimaging. Figure 1 (available at [www.jpeds.com](https://www.jpeds.com/)) shows details of participant recruitment.

**Primary cardiac diagnoses and clinical data of CHD cohort**

The primary cardiac diagnoses and clinical characteristics of the children with CHD are summarised in Table 1.

**Demographic, Environmental and brain MRI scores in children with CHD and controls.** Table 2 (available at [www.jpeds.com](https://www.jpeds.com/)) shows the demographic, environmental and brain MRI ratings for the children. Children with CHD were born at a younger GA (p<0.001) and had lower CSPS scores (p=0.003). There was no difference between CHD and controls in sex distribution (p = 0.573), IMD (p=0.856), BIR (p=0.149) or age at assessment (p=0.773).

**Relationship between BRIEF-P scores and demographic and environmental factors in children with CHD and controls.**

Table 3 shows BRIEF-P raw scores and T-scores in children with CHD and controls. Multivariate general linear modelling identified no significant relationships between presence of CHD, age at assessment, sex, IMD, and EF scores. GA at birth was significantly negatively correlated with ISCI and FI scores and age at assessment was significantly negatively associated with FI. CSPS was significantly negatively correlated with ISCI, FI and EMI scores (Table 4). When Brain MRI injury rating was added to the multivariate analysis (n=108 controls), the relationships between all 3 EF scores and CSPS remained significant. ISCI and FI remained significantly negatively correlated with GA at birth and age at assessment remained significantly negatively correlated with FI (Table 5, available at www.jpeds.com).

**The moderating effect of group on the relationship between a cognitively stimulating home environment, GA, and executive function scores.**

There was a significant interaction of group (CHD, control) and CSPS scores in predicting all three EF outcomes (ISCI: p=0.045; FI: p=0.034; EMI: p=0.038) in childhood such that CSPS scores significantly predicted all three EF outcomes in children with CHD (ISCI: p=0.0004; FI: p=0.0015; EMI: p=0.0004) but did not in controls (ISCI: p=0.2727; FI: p=0.6185; EMI: p=0.3332) (Figure 2 A-C). There was no significant interaction of group (CHD, control) and GA in predicting any of the 3 EF outcomes (ISCI: p=0.2866; FI: p=0.1118; EMI, p=0.4579).

**Relationship between CHD type, surgical factors or brain MRI injury ratings on EF in the CHD group**

There were no significant relationships between BRIEF-P scores and surgical factors, CHD type or brain MRI injury rating (Table 6, available at [www.jpeds.com](https://www.jpeds.com/)).

**Secondary analyses excluding children with confirmed or suspected genetic disorders.**

The results were largely unchanged when the 5 children with confirmed or suspected genetic disorders were excluded. See Appendix for further details.

**DISCUSSION**

This study investigated the influence of demographic, environmental and clinical factors on 3 indexes of EF (ISCI, FI, EMI) measured using the BRIEF-P Questionnaire in children with CHD who underwent surgery within the first year of life and controls at 4 to 6 years of age. While there have been several studies assessing EF in individuals with CHD, to our knowledge, this is the first to describe the relationships between EF and demographic, surgical, environmental factors and brain MRI injury ratings in preschool children with CHD and controls.

Our results did not demonstrate any significant differences in day-to-day EF scores between children with CHD and controls when controlling for relevant demographic and environmental factors. In addition, when assessing only the children with CHD, we did not identify any significant relationships between EF and peri-surgical clinical factors, CHD type or brain MRI injury rating. However, we identified a significant interaction between group (CHD, controls) and a cognitively stimulating home environment for various aspects of EF: ISCI, FI and EMI. CSPS scores significantly predicted all three EF outcomes in the CHD group but did not in controls.

This study provides further evidence of the role of a cognitively stimulating home environment in cognitive performance and executive function in at-risk groups of children. We have shown previously that a more cognitively stimulating home environment is associated with higher cognitive scores on the Bayley Scales of Infant and Toddler Development-3rd edition at 22 months in toddlers with CHD [18] and this study highlights that the benefits of a cognitively stimulating home environment persist until preschool age. In preterm children at 4-7 years, cognitively stimulating parenting was associated with decreased developmental psychopathology and executive dysfunction [29] and, in both term and preterm born children, cognitively stimulating parenting supported academic resilience in middle childhood [28]. There is a great deal of interest in understanding how enriched environments affect outcome in children at risk of neurodevelopmental disorders [34,35] but, to date, there are very few studies which include controls [36]. Although the mechanisms are not clear, our findings suggest a cognitively stimulating environment increases child resilience leading to improved neurodevelopmental outcomes in at-risk groups of children.

While our finding that group (CHD or control) did not influence EF scores is supported by a recent study in preschool children at 5 years with CHD which showed that parent rated EF scores did not differ from normative means [37], other studies have identified impaired EF at older ages in individuals with CHD. However recent meta-analyses have shown considerable between-study heterogeneity, including differences in study designs in EF assessments, and outcomes in this population [38,39].

In a mixed CHD case series of 8 to 16 year olds, BRIEF metacognition index was raised relative to test norms and above the 90th centile in 24% of cases [40]. At school age (9 years), a higher proportion of children with CHD who required surgery in the first year of life had elevated metacognition and behavior regulation scores compared to controls. In this study, aortic obstruction rather than UVH was associated with worse EF scores [9]. In adolescents, a case-control study found that rates of EF impairment, assessed using [Delis-Kaplan Executive Function System (D-KEFS)](https://www.pearsonclinical.co.uk/store/ukassessments/en/delis/Delis-Kaplan-Executive-Function-System/p/P100009078.html), were almost twice as high for the CHD sample compared to controls, and distinct EF profiles were observed between CHD types [10] . In another study in adolescents with TGA who underwent the arterial switch operation as infants, the Global Executive Composite (GEC) scores on the BRIEF-P and BRIEF-T questionnaires were significantly worse than the expected population mean [11]. Similarly, in adolescents with TOF, both parent- and teacher-reported GEC scores were higher than the expected population mean, with a higher number of scores being of clinical concern. It is worth noting that the adolescents self-reports were similar to normative values, suggesting the adolescents do not consider themselves to have EF impairments [41]. In adults, a large UK study showed individuals with CHD exhibited deficits in problem solving, attention, and verbal fluency compared to normative data [12]. However, a recent study in a heterogenous sample of adults with CHD showed that self-reported and informant-reported EF scores were similar to normative data and were similar between different CHD types [42].

To date, the number of studies comparing EF in preschool children with CHD to control children are limited. Using face-to-face assessments to measure cognitive inhibition and flexibility, behavioural inhibition and working memory in children with TGA and controls aged 4-6 years, Calderon and colleagues [43] demonstrated worse EF scores in almost all tests in the TGA group (n=45) compared to controls (n=45). However, demographic characteristics of the control group were not compared to the TGA sample, and so it is possible that, in addition to CHD, demographic and environmental factors may play a role in these differences. Prenatal diagnosis of TGA was significantly related to cognitive flexibility, controlling for family SES and parental education level [43]. Prenatal diagnosis enables planning for perinatal care, including appropriately trained staff and medication in the delivery room [44], and is associated with improved hemodynamic stability [45-47]. All but one child in our study was diagnosed antenatally and so this may, at least in part, contribute to our findings of no differences in EF between control and CHD groups.

In our sample of mixed CHD diagnoses, we did not observe any association between CHD type and EF. However, our sample did not include any children with HLHS, who are at greater risk of EF impairments in later childhood and adolescence [10]. Risk factors for neurodevelopmental impairments in children with CHD include lower GA at birth [48,49], longer times to surgery, time on cardiopulmonary bypass, length of hospital stay [13-16]. We did not observe a relationship between perinatal clinical or surgical factors and EF outcomes in our CHD group. However, despite excluding children born at less than 31 weeks, lower GA at birth was associated with worse ISCI and FI scores. Preterm birth is a recognised risk factor for poorer EF [50]. Previous studies have shown that preschool children born extremely low birth weight have poorer Inhibition and working memory, while those born late preterm also showed impaired working memory abilities [51]. Another study of very preterm children (assessed between 4 and 12 years) identified difficulties in Inhibition, working memory and planning when compared to term-born controls [52]. Even as young adults, those born very preterm continue to show impaired inhibition and mental flexibility when compared to controls [53]. Our findings could be studied in relation to timing of brain maturational changes occurring during the last trimester of gestation, when most preterm infants are born. Corticostriatal pathways, centrally implicated in the establishment of FI and ISCI [54] reach their maximal growth phase from 24 weeks GA to term [55]. Metacognition is predominantly anchored in prefrontal brain regions [56] which reach maximal growth in adolescence [57]. Such timing of prefrontal cortex maturation could possibly explain why we did not observe a relationship between GA and EM in this study.

We also found that younger age of assessment was associated with higher FI scores. Cognitive flexibility begins developing after the age of 3, and there continues to be rapid advances between the ages of 4 to 6 in children [58]. On the other hand, we did not observe significant associations between age at assessment and the two other BRIEF-P indices, ISCI and EMI. We interpret these results in relation to timing of development of emerging metacognition and inhibitory self-control, as the age range of our study participants was relatively narrow. Although development of metacognition begins in early childhood [59], significant improvements in children’s capacity to reflect and efficiently evaluate their performance becomes established later, between 5.5 and 7.5 years [60]. Improvements in inhibitory control refine throughout childhood and adolescence [61] and are particularly pronounced later in childhood and the pre-adolescent years (age 8-11), in association to fronto-striatal brain maturation [62].

We found no effect of brain injury on EF scores. However, there were few infants with moderate to severe brain injury on MRI in our sample. The role of neonatal WMI and later EF is not clear as, to our knowledge, there have been no other studies assessing the role of neonatal brain injury on preschool EF in CHD. While moderate-severe neonatal WMI has been associated with reduced full scale IQ at 6 years [63], a meta-analysis reported that there was no consistent relationship between preoperative brain injury and neurodevelopmental outcome in this study group [64].

A major strength of our study is that, rather than comparing to reported normative values of the BRIEF-P, we included a control group recruited from a community sample of children who have a similar sociodemographic background to our CHD sample, as assessed by the IMD. It is important to note that the normative ranges of the BRIEF-P were created from data collected from a population of young children living in six USA states prior to 2003 [65]. While these normative ranges were determined from a population that reflects 1999 UK census estimates for population demographic data (<https://www.hogrefe.com/uk/shop/behaviour-rating-inventory-of-executive-function-preschool-version.html>), potential changes in preschoolers’ behaviour over the last two decades are not accounted for.

Our study has some limitations. Our CHD sample size is not large, although it is similar to other studies at this age. In addition, our CHD sample were born at a younger GA than controls. This is characteristic of CHD cohorts, particularly those with a prenatal diagnosis [66] and we controlled for GA at birth in our multivariate analysis. Intellectual impairment is associated with poorer EF [67,68], and we did not include any measure of intelligence in our study. Our data collection commenced in October 2020, when face-to-face assessments were not possible due to the COVID-19 pandemic, and so our study design focused on parental questionnaires which did not require face-to-face assessments. It is not possible, therefore, to determine whether our findings are specific to EF or are part of a global cognitive pattern. In addition, it should be noted that parent-rated assessments of EF may assess different constructs to performance-based measures. In addition, the IMD was used in our analyses as a measure of neighbourhood deprivation, and this is based on the participant’s residence postcode. This measure has limited sensitivity and specificity for identifying individuals who are income or employment deprived [69], hence the lack of access to a complementary measure reflecting socio-economic status may represent a further limitation of our study.

In summary, day-to-day EF scores did not differ between preschool children with CHD and controls. However, a cognitively stimulating home environment was associated with better EF scores in the CHD sample but not in controls. This study suggests that impaired EF in survivors of CHD may be mitigated by supporting parents to provide a cognitively stimulating home environment prior to school-age and the home and parenting environment should be considered when designing interventional studies aimed at improving EF in children with CHD.

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**FIGURE LEGENDS**

*Figure 1. Flow chart of participant recruitment for both CHD and control groups*

*Figure 2. Cognitively stimulating parenting scale scores significantly predicted A. ISCI scores in the CHD group (p = 0.0004, R2 = 0.148) but not in controls (p=0.273, R2=0.02) B. FI scores in the CHD group (p = 0.0015, R2=0.149) but not in controls (p=0.619, R2=0.003). EMI scores in the CHD group (p = 0.0004, R2 = 0.129) but not in controls (p=0.333; R2=0.021). All analyses were co-varied for age at assessment, GA at birth, sex, IMD and BIR.*