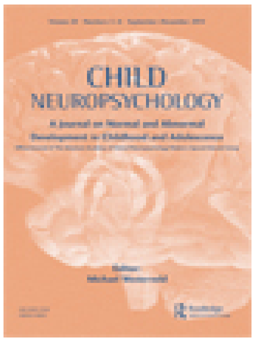

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**Child Neuropsychology**

A Journal on Normal and Abnormal Development in Childhood and Adolescence

ISSN: 0929-7049 (Print) 1744-4136 (Online) Journal homepage: https://www.tandfonline.com/loi/ncny20

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**To cite this article:** Jenny Retzler, Samantha Johnson, Madeleine Groom, Chris Hollis, Helen Budge & Lucy Cragg (2018): Cognitive predictors of parent-rated inattention in very preterm children: The role of working memory and processing speed, Child Neuropsychology, DOI: 10.1080/09297049.2018.1510908

**To link to this article:** https://doi.org/10.1080/09297049.2018.1510908

CHILD NEUROPSYCHOLOGY
https://doi.org/10.1080/09297049.2018.1510908



# Cognitive predictors of parent-rated inattention in very preterm children: The role of working memory and processing speed

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## ABSTRACT

Inattention is one of the most common neurobehavioral problems following very preterm birth. Attention problems can persist into adulthood and are associated with negative socio-emotional and educational outcomes. This study aimed to determine whether the cognitive processes associated with inattention differ between term-born and very preterm children. Sixty-five children born very preterm (<33+0 weeks' gestation) aged 8–11 years were recruited alongside 48 term-born controls (?37 20 +0 weeks' gestation). Both groups included children with a wide spectrum of parent-rated inattention (above average attention to severe inattention) measured as a continuous dimension using the Strengths and Weaknesses of ADHD and Normal-Behavior (SWAN) scale. The children completed tests to assess basic cognitive processes and executive function. A hierarchical multiple regression analysis was implemented to assess which neurocognitive processes explained variance in parent-rated inattention and whether these differed between preterm and term-born children. In both groups, poorer verbal and visuospatial short-term memory and poorer visuospatial working memory independently explained variance in parent-rated inattention. Slower motor processing speed explained variance in inattention among very preterm children only. The cognitive mechanisms associated with parent-rated inattention were predominantly overlapping between groups, but relationships between motor processing speed and inattention were unique to very preterm children. These associations may reflect risk factors for inattention in term and very preterm children. Future research should assess the efficacy of these cognitive processes as potential targets for intervention

**ARTICLE HISTORY**
Received 11 January 2018
Accepted 4 August 2018

**KEYWORDS**
Preterm; attention; executive function; processing speed; working memory

Very preterm (VP; <32$^{+0}$ weeks' gestation) birth is a risk factor for the development of neurobehavioral psychopathology, with inattentive behavior being the most common

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Supplemental data for this article can be accessed here.

adverse outcome (Aarnoudse-Moens, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2009). Risk of attention-deficit/hyperactivity disorder (ADHD) diagnosis is two–three times greater in VP children compared with children born at term, and mean symptom scores are significantly elevated even where children do not meet the threshold for diagnosis (Jaekel, Wolke, & Bartmann, 2013; Johnson & Marlow, 2011; Johnson et al., 2016). Notably, developmentally inappropriate inattentive behavior is more often elevated than hyperactivity/impulsivity among children born VP (Brogan et al., 2014; Johnson et al., 2016), and inattention is a stronger predictor of academic underachievement than hyperactivity/impulsivity in both VP (Jaekel et al., 2013) and general population samples (Sayal, Washbrook, & Propper, 2015). Moreover, inattentive behavior in the VP population persists into adulthood and has greater stability in VP than term-born individuals (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2016). Taken together, these findings suggest that inattention is a core, lifelong impairment following VP birth. Early detection of inattention and appropriate interventions may improve long-term outcomes for VP individuals.

Although rates of inattentive behavior are increased in VP children, it is unclear whether the underlying mechanisms are the same as those in the general population. While ADHD symptoms in the general population are considered to be of primarily genetic origin (Cornish et al., 2005; Faraone et al., 2005; Li, Sham, Owen, & He, 2006), increased risk for inattentive behavior in VP children may result from the combined impact of brain injury and neurodevelopmental disruption that is conferred following VP birth (Volpe, 2009). Indeed, a study of mothers who had given birth to term as well as preterm children indicated that genetic factors could not explain the relationship between preterm birth and ADHD (Lindström, Lindblad, & Hjern, 2011). Similarly, unlike in ADHD populations, studies have failed to find a relationship between psychiatric symptoms and socioeconomic status (SES) in preterm children (Loe, Lee, Luna, & Feldman, 2011). Moreover, evidence of a "gestational gradient," whereby the risk of psychiatric disorders increases as gestational age at birth decreases (Aarnoudse-Moens et al., 2009; Johnson, 2007), reinforces the idea that the increased ADHD prevalence in preterm populations is directly linked to preterm birth and/or perinatal medical factors, rather than to genetics or later environmental factors during development.

Different initial causal factors may lead to similar developmental trajectories with equivalent cognitive and neural mechanisms that result in similar phenotypic presentation. Alternatively, different causal factors may lead to separable trajectories that affect different cognitive mechanisms but still lead to similar phenotypic presentations. Whether the underlying mechanisms for inattentive behavior differ for those born VP from those born around term gestation is an important theoretical question with significant clinical implications. For instance, if the mechanisms underpinning inattentive behavior are equivalent to those in the term-born population, new and existing interventions that are efficacious in treating inattentive symptoms of ADHD may be appropriate. Conversely, if inattentive behavior arises from different mechanisms in those born preterm, alternative interventions with proven efficacy in the VP population specifically may be needed.

In the present study, we measured relationships between cognitive processes and parent-rated inattention in children born VP and at term. Cognitive processes may reflect an intermediate point on the pathway from translation of underlying neurobiological risk factors to the observed clinical or behavioral phenotype. They can therefore provide insights into the neurological mechanisms underlying complex behavioral phenotypes such as inattention. To reduce the range of cognitive processes evaluated in this study, we selected measures of executive function (EF) that have previously been mechanistically linked with inattentive behavior in studies of children with ADHD and/or those born preterm. These include working memory (storage of information with concurrent processing of additional information, also referred to as an "executive attention" process), inhibitory/interference control (suppression of prepotent responses/distracting information), and shifting (flexibly directing attention between tasks).

Poor working memory has been related to teacher-rated inattentive behavior in community (Gathercole et al., 2008), VP (Mulder, Pitchford, & Marlow, 2011) and ADHD samples (Castellanos & Tannock, 2002; Diamond, 2005; Kasper, Alderson, & Hudec, 2012, Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005), with larger effect sizes for visuospatial working memory (visuospatial-WM) than verbal working memory (verbal-WM) in VP children (de Kieviet, van Elburg, Lafeber, & Oosterlaan, 2012) and those with ADHD (Martinussen et al., 2005). In addition, poor inhibitory control predicted inattentive symptoms in children with ADHD (combined and inattentive subtypes; Chhabildas, Pennington, & Willcutt, 2001), although evidence in VP children is mixed (Aarnoudse-Moens, Weisglas-Kuperus, Duivenvoorden, van Goudoever, & Oosterlaan, 2013; Mulder et al., 2011; Scott et al., 2012; Shum, Neulinger, Ocallaghan, & Mohay, 2008). Finally, shifting is impaired in children with ADHD (Cepeda, Cepeda, & Kramer, 2000) and has been implicated as a risk factor for the ADHD inattentive subtype in extremely preterm (<28 weeks gestation) children aged 5–6 years (Scott et al., 2012). Thus, EFs, particularly visuospatial-WM and shifting, are associated with ADHD and inattentive behavior in term-born and VP children, but few studies have directly compared the relative contribution of EFs to inattentive behavior in these populations. It therefore remains unclear whether the cognitive mechanisms underlying inattentive behavior are equivalent in preterm and term-born children.

In addition to the assessment of EF processes, we included measures of visuospatial and verbal short-term memory (visuospatial-STM; verbal-STM), processing speed, and visuospatial processing in the current study. These more basic cognitive processes are known to be impaired in VP children (Mulder et al., 2011; Shum et al., 2008; Simms et al., 2015). In spite of evidence that visuospatial-STM predicts parent-rated inattention (Shum et al., 2008), it is often absent from studies investigating cognitive mechanisms of preterm inattentive behavior, including those investigating working memory. Similar evidence of importance for inattention has not yet been established for other basic processes, but visuospatial processing has been shown to impact upon the mathematics abilities of children born preterm (Simms et al., 2015), and each of the basic processes may contribute nonspecifically to the EFs measured in this study. Accordingly, we felt it important to model each of these basic processes as predictors of inattentive behavior and to control for their influence when measuring associations between EFs and parent-rated inattention.

The role of processing speed was of particular interest. Multiple studies have shown that children born VP are at increased risk of slow processing speed compared with term-born peers (Aarnoudse-Moens, Duivenvoorden, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2012; Foulder-Hughes & Cooke, 2003; Luciana, Lindeke, Georgieff, Mills, & Nelson, 1999; Mulder et al., 2011; but see Aarnoudse-Moens et al., 2013; de Kieviet et al., 2012). Processing speed has also been implicated in term-born inattention more generally (Diamond, 2005). Importantly, however, in a direct comparison, the association between slow processing speed and parent-rated inattention previously observed in VP children using both verbal and motor processing speed tasks was not evident in term-born children (Mulder et al., 2011). Studies have linked the increased risk of poor processing speed to atypical white matter growth following preterm birth (Soria-Pastor et al., 2008), and it has been proposed that this could lead to a cascade of impairments resulting in both inattention (Mulder et al., 2011) and poor academic attainment (Rose, Feldman, & Jankowski, 2011). On the basis of a clear preterm-specific developmental pathway that slow processing speed results from aberrant white matter growth conferred by preterm birth, further exploration of whether or not the impact of processing speed is indeed preterm-specific, as indicated by emerging evidence (Mulder et al., 2011), is warranted.

Processing speed is a difficult concept to define, with a wide variety of measures across different sensory modalities (e.g., audio or visual targets) and response domains (e.g., motor, verbal). These different measures are assumed to tap into the same underlying concept; however, they may, in fact, lead to contradictory results. Most measures comprise multiple mental processes (e.g., stimulus detection, stimulus evaluation, response initiation) and may well favor the particular domain of evaluation or response, any of which may be impaired. For instance, the tasks used in Mulder et al. (2011) favored verbal and motor domains (part one of the Same Worlds task from the TEA-Ch, in which children read out a string of ones and twos as quickly as possible, and the Sky Search task from the TEA-Ch, in which children circle targets in a large display as quickly as possible). Computer-based response time measures of processing speed used in the previous studies of inattention that had lengthy tasks (Aarnoudse-Moens et al., 2013; de Kieviet et al., 2012) may also have been susceptible to interference from lapses in attention. As such, the task in this study (a short finger-tapping task which did not require detection of a stimulus in order for the response to be made) was selected to measure processing speed while minimizing the number of “processes” required and domains involved, and reducing the opportunity for contamination from attentional lapses.

The primary goal of the present study was to determine whether the cognitive mechanisms underlying parent-rated inattention differ between VP and term-born children with similar levels of inattention. Previous studies addressing this question have used term-born control groups who score in the normal range for inattentive behavior and compared them with preterm groups with high inattentive behavior scores (e.g., Aarnoudse-Moens et al., 2013; de Kieviet et al., 2012; Mulder et al., 2011). By not including term-born children who display the full range of inattentive behavior, these studies may have failed to accurately capture associations between cognition and (in)attention that are present in their term-born control groups. In the present study, we, therefore, recruited VP children and a term-born comparison group with varying levels of inattentive behavior, as rated by their parents, ranging from above average attention to severe inattention, in order to identify and compare underlying cognitive predictors of inattention in term-born and VP children. Importantly, this design facilitated direct comparison of cognitive predictors of inattentive behavior in VP and term-born children with an equivalent range of scores. Moreover, previous studies investigating inattentive behavior in VP children have used scales designed to detect clinically significant inattention (e.g., Mulder et al., 2011; Shum et al., 2008). These scales can be insensitive to the full range of attention scores in nonclinical samples and often include only a small number of items that assess inattention specifically, which may not capture the full range of these traits observed in children born VP. We therefore selected a dimensional measure of inattentive behavior appropriate for use in nonclinical samples, the Strengths and Weaknesses of ADHD and Normal-Behavior (SWAN; Polderman et al., 2007; Swanson et al., 2006, 2012) scale, which is designed for teachers or parents to complete.

The aims of the current study were to establish whether parent-rated inattention is associated with impairment in basic cognitive processing (visuospatial processing, processing speed, visuospatial-STM, verbal-STM) and/or in EF (shifting, interference control, visuospatial-WM, verbal-WM) when basic cognitive processes are accounted for, and whether these associations differed between VP and term-born children. It was hypothesized that (1) working memory would predict parent-rated inattention in both groups; (2) visuospatial-WM would explain more variance in parent-rated inattention than verbal-WM in both groups; (3) processing speed would predict parent-rated inattention only in VP children; and (4) variation in performance on EF tasks would explain parent-rated inattention beyond that explained by basic cognitive processing.

## Materials and methods

### *Ethical standards*

Ethical approval was granted by a UK NHS Research Ethics Committee (Coventry and Warwickshire; Ref: 13/WM/0203), and informed parental consent was obtained for all the children.

### *Participants*

#### *VP children*

All babies born ≤32 weeks' gestation from January 1 2003 to March 31 2006 admitted for neonatal intensive care in Nottingham University Hospitals NHS Trust were identified from hospital records and traced to determine their vital status. Of 407 traced, one child was deceased leaving a total of 406 eligible births. A further 8 children resided outside the study area (>1 hour travel). The parents of the first 296 (72.9%) eligible children for whom contact details were available were contacted to invite their child to participate in the study, of which 94 (23.2% of eligible births) were recruited. The parents of the remaining 102 VP children were not contacted because it was not feasible to test more children within the time constraints of the study. Of the recruited children, 8 parents withdrew consent prior to assessment, and testing could not be scheduled for a further 21 children, resulting in a final study sample of 65 VP children (16% of eligible births). Exclusion criteria were (1) neurological or sensory impairment precluding participation in testing and (2) nonfluency in English of the parent or child. No children were excluded.

The final VP sample had a mean gestational age of $29^{+6}$ weeks ($SD$ = $1^{+6}$ weeks); mean birth weight 1.48 kg ($SD$ = 0.42 kg); 36 male (55.4%). These children did not differ significantly with respect to gestational age ($p$ = .89), birth weight ($p$ = .59), or sex ($p$ = .81) from the VP children not recruited ($n$ = 406). However, the recruited children were of significantly higher SES ($p$ = .006), as measured using the English Indices of Multiple Deprivation (McLennan et al., 2011). No VP children in the sample were on stimulant medication for ADHD.

### Term-born children

Recruitment of term-born children was conducted in two stages. In Stage 1, the study was advertised to parents of children aged 8–11 years in the local community via emails to families on the University of Nottingham volunteer database, letters sent via local schools, a press release, flyers, and posters distributed in the local community. Parents of 124 children completed an online survey to establish demographic information, screen for exclusion criteria (outside age-range, diagnosis of neurological or sensory disorder, nonfluency in English of parent or child, gestation of $<37^{+0}$ weeks or $\geq 42^{+0}$ weeks), and obtain scores on the SWAN scale. No children met the exclusion criteria. Once parents had completed the survey, children were selected and invited for the second stage based on their scores on the parent-rated SWAN scale. Specifically, we recruited children so that seven points on the SWAN scoring scale were represented, reflecting a range of attentional abilities (far below average, below average, slightly below average, average, slightly above average, above average, and far above average). Of 124 term-born children initially screened, a total of 96 children were selected and invited for Stage 2. Of those selected, 43 did not respond to invitations to participate or could not attend and 5 more withdrew. Parents of the remaining 28 children were not contacted because their children's SWAN scores were already well represented within the recruited test sample. Consequently, 48 term-born children entered the study and undertook the study assessments. No term-born children were on stimulant medication for ADHD.

## Materials and procedure

Children undertook a battery of tasks measuring basic cognitive processing and EF, and parents completed questionnaire measures of clinical symptoms.

### Participant characteristics and clinical symptoms

An age-standardized estimate of full scale IQ (FSIQ-2) was calculated from the Wechsler Abbreviated Scale for Intelligence (Wechsler, 1999) using the vocabulary and matrices subtests. Inattentive and hyperactive-impulsive behavior were measured using the SWAN. To characterize the sample more fully, measures of risk of ADHD, ASD, and anxiety disorder were assessed using the Conners 3-P (Conners, 2008), parent-rated Social Communication Questionnaire Lifetime version (SCQ; Rutter, Bailey, & Lord, 2003), and Multidimensional Anxiety Scale for Children-2 Parent (MASC-2P; March, Parker, Sullivan, Stallings, & Conners, 1997), respectively, with higher scores indicating greater symptoms. Children with scores above the predefined clinical cutoff were classified as "at risk" of diagnosis on these measures.

### Basic cognitive processing

The finger-tapping subtest from the Developmental Neuropsychology Test II (NEPSY-II; Korkman, Kirk, & Kemp, 2007) was used to measure motor processing speed. A composite score was calculated by averaging the seconds taken for 20 finger-tapping repetitions on the dominant and nondominant hand. Higher scores represent slower processing speed.

The total raw score from the NEPSY-II arrows subtest (Korkman et al., 2007) was used to assess visuospatial processing. On each trial the child was presented with a target surrounded by arrows on a page and was required to indicate which arrows were pointing to the center of the target. Higher scores represent better visuospatial processing.

Short-term memory was assessed using computer-based verbal and visuospatial immediate serial recall tasks programed using PsychoPy (Peirce, 2007). The verbal task involved recalling single-syllable words, while the visuospatial task involved recalling locations on a four-by-four grid. The task began with only two items to remember, and increased in one-item increments up to a maximum of 8 items. To proceed to the next span level, two of the three trials in that span level had to be recalled correctly. The total number of items recalled in the correct serial position was calculated. Higher scores represent better short-term memory.

### Executive functions

The tasks used to measure working memory were identical to the short-term memory tasks described above with the addition of a 5000 ms retention interval between the list presentation and recall. During this interval, the children completed a concurrent processing task. To achieve comparable concurrent processing during both the verbal- and visuospatial-WM tasks, the same task was used. Children were presented with a series of pictures of two faces. They were asked to judge whether the pictures were of the same person or two different people and to respond out loud by saying "same" or "different." This task does not involve auditory stimuli, and previous research suggests that it is not related to visual short-term memory ($r = 0.05$; Burton, White, & McNeill, 2010), therefore it was considered relatively domain-neutral and likely to result in comparable cognitive load in both verbal- and visuospatial-WM tasks. Scoring was conducted as for the short-term memory tasks above, with higher scores indicating better working memory.

Switching and interference control were measured using a modified version of the Switching, Inhibition, and Flexibility task (FitzGibbon, Cragg, & Carroll, 2014), a computerized shape and color-matching task programed using PsychoPy (Peirce, 2007). Children were required to match a target stimulus presented in a box in the top center of the screen to one of two response stimuli presented below, on the basis of a verbal instruction stating whether they should match the stimuli based on either color or shape (*Figure S1*). On congruent trials, the correct response stimulus was identical to the target. On incongruent trials, the correct response stimulus matched the target on the relevant dimension (color or shape) and the incorrect response stimulus matched the target on the irrelevant dimension, creating conflict. Cronbach's alpha indicated good internal reliability of this task (congruent switch trials = 0.89; congruent non-switch trials = 0.79; incongruent switch trials = 0.75; incongruent non-switch trials = 0.89). A measure of interference control was calculated by subtracting median response time on correct congruent trials from that on correct incongruent trials to produce a cost score. Higher cost scores represent poorer interference control. Trials also differed in the level of switching. In pure blocks, all trials were matched on the same dimension (e.g., color). Within mixed blocks, on non-switch trials the matching dimension in the current trial was the same as in the previous trial (e.g., a color trial followed by a color trial), while on switch trials the matching dimension was different to the previous trial (e.g., a color trial followed by a shape trial). Local switch costs were calculated by subtracting the median response time on correct non-switch trials from correct switch trials. Global switch costs were calculated by subtracting the median response time on correct trials in the pure blocks from those in the mixed blocks. Higher cost scores represent slower switching.

### *Analysis*

Analyses were conducted using IBM SPSS (Version 22.0). Term and VP groups were first compared on participant characteristics, demographic information, and clinical symptoms using independent samples *t*-tests for continuous data and chi-square tests for categorical data. As children in both groups presented with similar levels of parent-rated inattention, group differences in cognitive performance were not necessarily expected but were analyzed to provide context. To test the group differences across cognitive measures, a multivariate analysis of covariance was conducted on all of the cognitive measures with group as a between-subjects factor and age as a covariate to account for the older age of the VP children. Significant multivariate effects were followed up with appropriate univariate ANOVAs and *post hoc* tests.

A hierarchical multivariable linear regression was then conducted to assess cognitive predictors of parent-rated inattention. Variables entered into the models were selected based on partial correlations controlling for age. These correlations were initially collapsed across both groups to maximize the power to detect associations that were consistent across groups, and then repeated separately by group. Where a correlation was significant only in one group, Fischer's *r*-to-*z* was applied to assess the statistical significance of the between-group difference in the size of the correlations. Variables that were significantly correlated with parent-rated inattention ($p < .05$) in one or both groups were then entered into the regression model. All predictor variables were grand-mean centered to minimize the effects of multicollinearity on model interpretation that can result from the introduction of interaction terms (Jaccard, Wan, & Turrisi, 1990). Group and age were entered into the first step. In the second step, the basic cognitive processing measures of motor processing speed, verbal-STM, and visuospatial-STM were entered. In the third step, the EF measures of visuospatial-WM and verbal-WM and interference control were added. In the final step, group interaction terms were added to investigate any between-group differences in cognitive predictors of parent-rated inattention. In the third and fourth steps, a data-driven forward-entry selection technique was used so that only those variables that added significant variance above that accounted for in the preceding steps were entered to better separate out effects amongst variables that are related to one another (Aarnoudse-Moens et al., 2013; see *Tables S1 and S2* for the full correlation matrix).

Additional analyses were performed to examine the role of IQ. Specifically, significant interactions with the Group factor (identified in the fourth step of the regression analysis) were further analyzed to check for the influence of IQ on the relationship between Group and a specific cognitive measure (presented in *Supplementary information*). This approach was chosen rather than including IQ as a covariate in all steps of the regression analysis for the following reasons. The measurements used in the IQ test are likely to rely on some of the same cognitive skills measured in the study, and thus IQ adjustment may mask variance of interest (Taylor, 2006). In addition, cognitive deficits associated with VP birth are better described as selective deficits than global cognitive impairment (Johnson, 2007) and it is, therefore, more informative to investigate the independent contribution of specific cognitive processes to inattention in VP children, without controlling for global cognitive impairments by covarying IQ. Finally, arguments fully described in Dennis et al. (2009) detail the ways in which IQ does not meet the logical, statistical, nor theoretical requirements for a covariate in neurodevelopmental analyses. Specifically, covarying IQ results in a comparison of groups at a value of IQ that is unrepresentative of the populations of interest and can, therefore, lead to unrealistic interpretation of results. The findings relating to IQ are reported in *Supplementary information* and provide reassurance that the main findings reported below are not attributable to group differences in IQ.

## Results

### *Treatment of data*

A total of 19 items (0.001% of all Conners data) were missing across the full sample, and two MASC-2P questionnaires had one item missing each. These values were replaced with the subscale mean for each individual. SCQ questionnaires for a further five children contained >15% missing data, MASC-2P questionnaires for three children contained 50% missing data, SWAN questionnaires were missing for six VP children, and FSIQ-2 scores were missing for one child. Therefore, these children were excluded from analyses of group characteristics.

Little's test indicated that missing data for variables involved in subsequent analyses were missing completely at random ($\chi^2(109) = 99.965$, $p = .720$), thus missing data points (5.4%) were replaced using the expectation maximization procedure implemented in SPSS. No multivariate outliers were detected. Assumptions for each statistical analysis were checked, and where appropriate, corrections of violations were applied and are reported. As the correlations guided the selection of variables for the regression analysis, Bonferroni correction was deemed too conservative and was, therefore, not applied to the correlational analyses. Elsewhere, Bonferroni-corrected alpha levels were applied and are reported.

### *Participant characteristics*

Table 1 shows the demographic information, participant characteristics, and scores on clinical symptom questionnaires for the term-born and VP children. By design, the groups did not differ significantly on SWAN-inattention scores. There were also no significant differences on the SWAN-hyperactivity/impulsivity subscale and the Conners subscales or in the proportion of children who scored “at risk” for ADHD. Further, VP and term-born children did not differ significantly on sex, ethnicity, SES, anxiety disorder symptoms, or ASD symptoms. As the term-born group was significantly younger than the VP group (based on chronological age), age was covaried in subsequent analyses. Similarly, VP children had significantly lower IQ than term-born children, and the impact of this was assessed in *Supplementary information*.

There was a significant multivariate group effect on task performance when controlling for age ($V$ = 0.244, $F$(9,102) = 3.3663, $p$ = .001) and a significant main effect of age ($V$ = 0.235, $F$(9,102) = 3.475, $p$ < .001).

Univariate statistics revealed significantly faster motor processing speed in VP compared with term-born children (Table 2), while term-born children had significantly better visuospatial-STM than those born VP. Between-group differences were not observed in performance on other tasks.

### *Cognitive predictors of parent-rated inattention*

Partial correlations between cognitive performance and parent-rated inattention (as measured using the SWAN) controlling for age (*Tables S1 and S2*) indicated that motor processing speed, visuospatial-STM, verbal-STM, visuospatial-WM, verbal-WM, and interference control were significantly correlated with parent-rated inattention in one or both groups. These variables were entered into a hierarchical multiple regression with parent-rated inattention as the dependent variable (Table 3).

In Model 1, age and group did not explain significant variance in parent-rated inattention ($F$(2,110) = 1.994, $p$ = .141). With the addition of basic cognitive processing variables, Model 2 explained 22.9% of the variance ($F$(5,107) = 6.350, $p$ < .001), with both visuospatial-STM and verbal-STM, but not motor processing speed, explaining significant unique variance.

Of the EF predictors, only visuospatial-WM contributed enough unique variance to be entered into Model 3. The model was significantly improved ($\Delta R^2$ = 0.043*) and explained 27.3% of the variance in parent-rated inattention ($F$(6,106) = 6.608, $p$ < .001). Age, verbal-STM, and visuospatial-WM each explained unique variance.

In the final step, with the introduction of interaction terms, only the group×processing speed interaction contributed enough unique variance to be entered into Model 4. This model significantly improved upon Model 3 ($\Delta R^2$ = 0.031*) and explained 30.4% of the variance in parent-rated inattention (Model 4; $F$(7,105) = 6.538, $p$ < .001). In this model, verbal-STM and visuospatial-STM, visuospatial-WM, and the interaction between group and motor processing speed each explained unique variance (Figure 1).

From these planned analyses it was not possible to determine whether the group by processing speed interaction was driven by children with lower SWAN scores (reflecting better than average attention) or by those with higher SWAN scores (reflecting poorer than average attention). It was also considered possible that the presence of a relationship between parent-rated inattention and motor processing speed only in children born VP may have been affected by lower IQ in the preterm children. In order to clarify these issues, two *post hoc* analyses (*Supplementary information.*) were performed.

**Table 1.** Characteristics of term-born and very preterm children.

| | Very preterm ($n$ = 65[a]) | Term ($n$ = 48[a]) | $p$ |
|---|---|---|---|
| Participant characteristics | | | |
| Gestation (weeks) | | | |
| Mean (*SD*) | $29^{+6}$ ($1^{+6}$) | $40^{+0}$ ($1^{+1}$) | |
| Range | 26–32 | 37–42 | |
| Age (years) | | | |
| Mean (*SD*) | 10.1 (0.9) | 9.6 (1.0) | .006* |
| Range | 8.4–11.5 | 8.0–11.7 | |
| FSIQ-2[b] | | | <.001* |
| Mean (*SD*) | 101.1 (13.9) | 111.1 (9.9) | |
| Range | 67–131 | 83–127 | |
| Score <70 *n*(%) | 1 (1.5%) | 0 (0.0%) | .383 *ns* |
| Demographics, *n*(%) | | | |
| Female sex | 29 (44.6%) | 22 (45.8%) | .898 *ns* |
| Ethnicity | | | .855 *ns* |
| White | 47 (82.3%) | 42 (87.5%) | |
| Mixed | 7 (12.3%) | 4 (8.3%) | |
| Asian | 1 (1.8%) | 1 (2.1%) | |
| Black | 1 (1.8%) | 1 (2.1%) | |
| Chinese | 0 (0%) | 0 (0%) | |
| Other | 1 (1.8%) | 0 (0%) | |
| Socioeconomic Status (SES) | | | .074 *ns* |
| Low SES | 12 (18.5%) | 13 (27.1%) | |
| Middle SES | 25 (38.5%) | 9 (18.8%) | |
| High SES | 28 (43.1%) | 26 (54.2%) | |
| Conner's 3 ADHD symptom scores | | | |
| Conner's 3 *T*-scores, mean *(SD)* | | | |
| DSM ADHD/I | 62.11 (15.48) | 57.79 (13.51) | .136 *ns* |
| DSM ADHD/C | 61.63 (14.42) | 58.48 (14.08) | .399 *ns* |
| Inattention | 60.71 (15.64) | 57.13 (12.29) | .215 *ns* |
| Hyperactivity/Impulsivity | 62.15 (16.24) | 59.06 (14.47) | .297 *ns* |
| IA-HI correlation, *r* | 0.78 | 0.83 | .233 *ns* |
| Conner's 3 scores above clinical cutoffs, *n*(%) | | | |
| DSM ADHD/I | 22 (34.4%) | 12 (25.0%) | .286 *ns* |
| DSM ADHD/C | 21 (32.3%) | 13 (27.1%) | .549 *ns* |
| Inattention | 22 (33.8%) | 10 (20.8%) | .129 *ns* |
| Hyperactivity/Impulsivity | 22 (33.8%) | 15 (31.3%) | .771 *ns* |
| SWAN symptom scores[c] | | | |
| Inattention | | | |
| Mean (*SD*) | −.068 (10.89) | −4.67 (12.22) | .080 *ns* |
| Range | −26 to 26 | −27 to 20 | |
| Hyperactivity/Impulsivity | | | |
| Mean (*SD*) | −2.86 (11.130) | −6.71 (12.549) | .099 *ns* |
| Range | −27 to 25 | −27 to 27 | |
| MASC anxiety disorder total symptom scores[d] | | | |
| *T*-scores, mean*(SD)* | 55.87 (13.59) | 52.42 (10.50) | .147 *ns* |
| *T*-scores above clinical cutoffs, *n*(%) | 17 (27.0%) | 9 (18.8%) | .310 *ns* |
| SCQ autism spectrum symptom scores[e] | | | |
| Lifetime symptom scores, mean*(SD)* | 6.66 (7.67) | 5.53 (5.88) | .327 *ns* |
| Scores above clinical cutoffs, *n*(%) | 11 (17.7%) | 3 (6.5%) | .086 *ns* |

Age reflects chronological age for VP children. Continuous variables were compared using independent samples *t*-tests, rank variables were compared using Pearson's chi-square, and correlations were compared using Fischer's *r*-to-*z*. *SD* = standard deviation, FSIQ-2 = two-subtest full scale intelligence quotient calculated using the Wechsler Abbreviated Scale for Intelligence. IA-HI correlation = correlation between inattentive (IA) and hyperactive-impulsive (HI) symptoms as measured using the Conner's 3 subscale *T*-scores. *$p$ < .05, *ns* = not significant. [a]accurate unless otherwise indicated. [b]VP($n$) = 65, term($n$) = 47 due to missing data; [c]VP ($n$) = 57, term($n$) = 48 due to missing data; [d]VP ($n$) = 64, term($n$) = 48 due to missing data; [e]VP ($n$) = 62, term($n$) = 46 due to missing data.

**Table 2.** Age-adjusted marginal means and standard errors (SE) on cognitive measures in term-born and very preterm children.

| | Very preterm | | Term | | Between-group differences | | |
|---|---|---|---|---|---|---|---|
| Measure | Mean | SE | Mean | SE | *F* | *p* | $\eta_p^2$ |
| VS-P | 27.47 | 0.47 | 28.47 | 0.55 | 3.13 | .048 | 0.054 |
| MPS[a] | 6.51 | 0.13 | 7.19 | 0.15 | 5.89 | .004* | 0.097 |
| V-STM | 37.58 | 1.26 | 42.17 | 1.48 | 4.93 | .009 | 0.078 |
| V-WM | 21.18 | 1.25 | 26.72 | 1.47 | 4.40 | .014 | 0.072 |
| VS-STM | 34.32 | 1.47 | 40.86 | 1.72 | 11.38 | <.001* | 0.171 |
| VS-WM | 16.17 | 1.21 | 18.58 | 1.47 | 2.83 | .063 | 0.049 |
| Local switching[a] | 92.39 | 22.14 | 67.42 | 25.95 | 1.02 | .365 | 0.018 |
| Global switching[a] | 231.01 | 18.32 | 244.84 | 21.47 | 0.19 | .827 | 0.003 |
| Interference control[a] | 201.52 | 13.49 | 160.27 | 15.80 | 2.52 | .085 | 0.044 |

These results reflect the model corrected for age. [a]For these measures, higher scores reflect poorer performance. *$p$ < .005 (Bonferroni-corrected alpha). VP: very preterm; $\eta_p^2$: partial eta squared; VS-P: visuospatial processing; MPS: motor processing speed; V-STM: verbal short-term memory; V-WM: verbal working memory; VS-STM: visuospatial short-term memory; VS-WM: visuospatial working memory.

**Table 3.** Regression model for cognitive predictors of parent-rated inattention.

| | Inattention | | | |
|---|---|---|---|---|
| | Model 1 $R^2$ = .035- | Model 2 $R^2$ = .229*** $\Delta R^2$ = .194*** | Model 3 $R^2$ = .272*** $\Delta R^2$ = .043* | Model 4 $R^2$ = .304*** $\Delta R^2$ = .031* |
| **Predictor** | | | | |
| Group | 0.180 | 0.111 | 0.092 | 0.107 |
| Age | 0.021 | 0.173 | 0.194* | 0.138 |
| MPS | | 0.171 | 0.119 | 0.160 |
| Visuospatial-STM | | −0.232* | −0.175 | −0.192* |
| Verbal-STM | | −0.290** | −0.233* | −0.204* |
| Visuospatial-WM | | | −0.239* | −0.221* |
| Verbal-WM | | | – | – |
| Interference control | | | – | – |
| Group×MPS | | | | 0.190* |
| Group×visuospatial-STM | | | | – |
| Group×verbal-STM | | | | – |
| Group×visuospatial-WM | | | | – |
| Group×verbal-WM | | | | – |
| Group×interference control | | | | – |

*$p$ < .05; ** $p$ < .01;*** $p$ < .001. –: did not meet criteria for forward entry model selection; MPS: motor processing speed; STM: short-term memory; WM: working memory.

## *Group differences in task performance*

First, the VP sample was divided into two subgroups based on parent-rated SWAN scores: better attenders (SWAN score of zero or below) or poorer attenders (SWAN score of one or above), where a score of "0" reflects average attention. Correlations between parent-rated inattention scores and motor processing speed in the VP group demonstrated that the association between motor processing speed and parent-rated inattention in children born VP was observed in poorer attenders only.

Second, IQ was included as a covariate in split-group partial correlations between motor processing speed and parent-rated inattention. The magnitude of partial correlations between motor processing speed controlling for the effect of IQ, along with age,

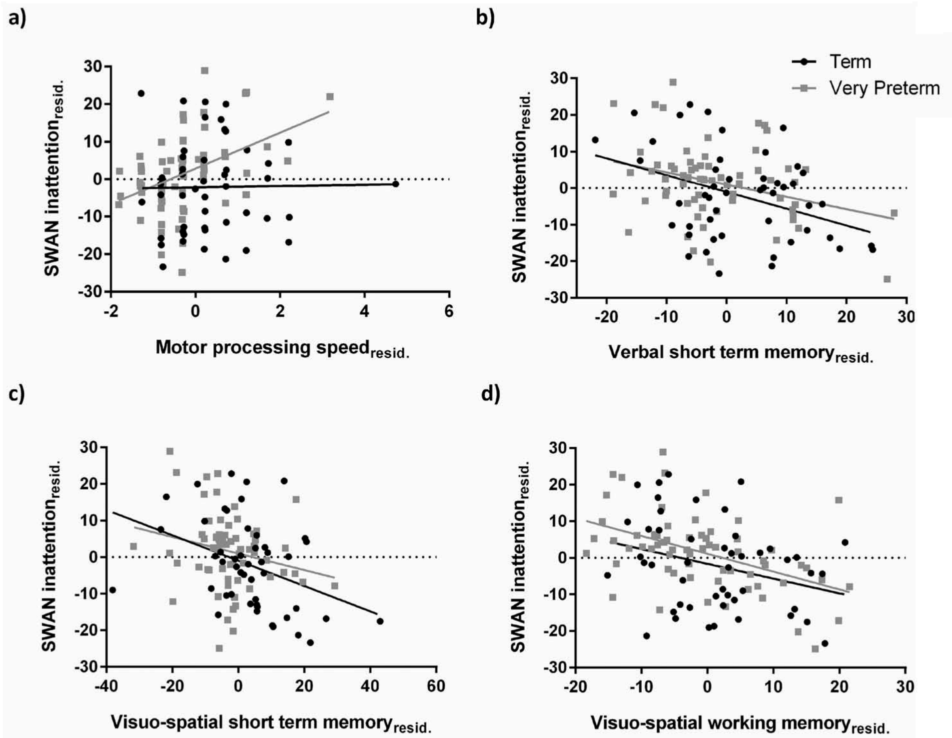


Figure 1. Scatter plots showing the association between parent-rated inattention and (a) motor processing speed, (b) verbal short-term memory, (c) visuospatial short-term memory, and (d) visuospatial working memory while controlling for age at assessment.

Note: Values plotted are unstandardized residuals (resid.: residual) from regressing each variable against age. The dotted line represents "average" attention, positive scores indicate more severe ratings of inattention, and negative scores indicate above average ratings of attention. Grey: very preterm children; Black: Term-born children.

was very similar to those observed without controlling for IQ. This indicated that group differences in IQ did not account for the group interaction with motor processing speed and parent-rated inattention.

## Discussion

This study aimed to determine whether the cognitive processes associated with parent-rated inattention differ between term-born and VP children. The groups were compared on the associations between specific aspects of EF (visuospatial-WM, verbal-WM, inhibition, interference control), basic cognitive processes (verbal-STM, visuospatial-STM, and motor processing speed), and parent-rated inattention. Visuospatial-WM was a significant predictor of parent-rated inattention in VP and term-born children after controlling for the variation explained by STM. In children born VP only, parent-rated inattention was also predicted by slower processing speed.

### *Executive function*

As hypothesized, visuospatial-WM predicted parent-rated inattention in both groups. This builds on previous evidence that working memory is a key factor underlying inattentive behavior in VP (Aarnoudse-Moens et al., 2013; Mulder et al., 2011) and term-born children (Gathercole et al., 2008) and further extends previous research by demonstrating that the effects of visuospatial-WM cannot be fully explained by variance in short-term memory, a more basic cognitive process. The results also suggest a larger role for visuospatial-WM than verbal-WM, consistent with previous findings in ADHD (Martinussen et al., 2005), VP (de Kieviet et al., 2012), and typically developing (Gathercole et al., 2008) children.

Neither interference control nor shifting predicted parent-rated inattention. Moreover, there were no between-group differences in performance on either of these measures, consistent with a meta-analysis reporting small effect sizes for impaired inhibitory control and shifting in preterm children (Mulder, Pitchford, Hagger, & Marlow, 2009). The pattern of associations with parent-rated inattention observed in the current study bolster evidence that specific EFs, such as visuospatial-WM, drive inattentive behavior, rather than global executive dysfunction.

### *Basic cognitive processing*

Both verbal-STM and visuospatial-STM were significant predictors of parent-rated inattention, with no evidence of differences in the strength of the relationship between groups. This adds to previous evidence showing associations between short-term memory and inattentive behavior in both VP and typically developing children (e.g., Shum et al., 2008; Tillman, Eninger, Forssman, & Bohlin, 2011), emphasizing the importance of controlling for short-term memory skills when assessing working memory.

Consistent with our hypotheses and with Mulder et al. (2011), motor processing speed predicted parent-rated inattention in VP but not term-born children, reflected in a significant group by processing speed interaction term, which could not be explained by group differences in IQ. *Post hoc* analyses indicated that the association between parent-rated inattention and motor processing speed in the VP group was specific to children with poorer than average parent-rated inattention. This suggests that slow motor processing speed is a risk factor for inattentive behavior in VP children rather than acting as a protective factor against inattentive behavior. While attempts were made to select a processing speed task that minimized confounders, the task was still domain-specific and performance differences may reflect general motor difficulties rather than processing speed per se. Further research is needed using measures that are more sensitive to covert neural transmission processes to clarify the role and specificity of processing speed in inattentive behavior among VP children.

### *Strengths and limitations*

The analyses reported here benefit from (1) a term-born comparison group with a similar parent-rated inattention range to the VP group, (2) a group of VP children representative of the population from which it was drawn in terms of birth weight, gestational age, and sex, (3) inclusion of basic cognitive processing measures in analyses assessing the influence of executive functioning, (4) a moderately large sample size, and (5) a dimensional approach to assessing inattention.

However, the study was limited by a number of factors. First, the study provides only correlational cross-sectional data, and although we propose that impaired cognitive processing underlies inattentive behavior, it is possible that the inattentive behavior itself caused poor performance on specific neuropsychological tests. Second, an apparent recruitment bias was evident in that the preterm sample assessed was of higher SES than the eligible VP cohort not studied. Although this limits the generalizability of the findings, in fact, the VP group were representative of the broader VP population in terms of birth weight, gestational age, and sex. Third, studies have shown that associations between cognition and inattentive behavior can differ between parent and teacher ratings (e.g., Aarnoudse-Moens 2013; Mulder et al., 2011), and inattentive behavior here was measured only using parent ratings. Nevertheless, parental ratings are an important source of information, indicative of how a child behaves in a range of environments. Finally, while VP and term-born groups were well matched for most characteristics, the term-born children were younger than the children born VP. The difference in age may be a consequence of the selection of a term-born group of children with higher parent-rated inattention. Accordingly, all analyses were adjusted for age. Of note, the amount of variance in parent-rated inattention explained by these cognitive predictors remains modest at 30.4%, suggesting that other cognitive processes may underpin inattentive behavior in addition to those identified here.

### *Implications*

VP children with no identified special educational needs often show high levels of inattentive behavior (Brogan et al., 2014). These difficulties may be overlooked in the classroom as VP children often do not cause class disruption, suggesting that more efforts need to be made to identify children who may benefit from intervention. These results build on existing research to identify cognitive processes that may underpin inattentive symptoms. The cognitive predictors identified may be useful both as candidates for intervention and to identify children who may be at risk.

Although the analyses reported here are cross-sectional, longitudinal studies have shown that cognitive performance in 2-year old children born VP can reliably predict cognitive ability throughout childhood and into adulthood (Breeman et al., 2016; Linsell, Johnson, & O'Reilly et al., 2018). Therefore, if weaknesses in particular cognitive domains or neural processes underpin later-emerging inattentive behavior, early identification of such risk factors may be possible. Identification of children who may benefit from intervention would allow for targeted support that could facilitate cognitive development to improve behavioral and academic outcomes, either by directly reducing symptoms or by providing compensatory support that indirectly reduces the risk of the consequences associated with inattention.

It is important to note that while the study design has drawn on the ADHD literature on the premise that inattention is one of the two core symptom domains of ADHD, the specificity of inattention to ADHD is not clear, and this study did not include independent diagnosis of participants. A key avenue for future research would be to investigate the influence of the predictors of inattention observed here in samples of term and preterm children with clinically diagnosed ADHD.

## *Conclusion*

The findings of this study indicate equivalent cognitive mechanisms for parent-rated inattention in term and VP children, but with an additional effect of processing speed among the VP group only. In both VP and term-born children, parent-rated inattention was associated with specific areas of weakness rather than difficulties in all areas of cognition. Visuospatial- and verbal-STM memory and visuospatial-WM were identified as predictors of parent-rated inattention in both VP and term-born children, while motor processing speed appeared to be a mechanism linked to parent-rated inattention in VP children only. Moreover, the findings demonstrated that the well-documented relationship between visuospatial-WM and parent-rated inattention was not accounted for by basic cognitive processing. These results present cognitive processes that may be potential targets for interventions.

## Acknowledgments

We would like to thank the families who participated, without whom this would not have been possible, and Valerie Astle for her help in identifying eligible VP patients.

## Disclosure statement

The authors declare that they have no conflict of interest.

## Funding

This work was supported by the Economic and Social Research Council [grant number 1230421].

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