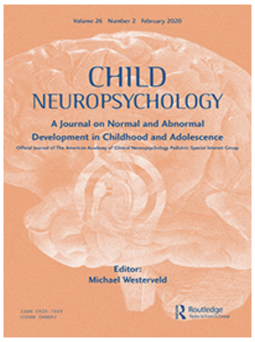

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Neurocognitive processes underlying academic difficulties in very preterm born adolescents

E. Sabrina Twilhaar[a], Jorrit F. De Kieviet[a], Ruurd M. Van Elburg[b,c] and Jaap Oosterlaan[a,d]

[a]Clinical Neuropsychology Section, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands; [b]Early Life Nutrition, Danone Nutricia Research, Utrecht, The Netherlands; [c]Department of Pediatrics, Amsterdam Gastroenterology & Metabolism and Amsterdam Reproduction & Development, Amsterdam UMC, University of Amsterdam, Emma Children's Hospital, Amsterdam, The Netherlands; [d]Department of Pediatrics, Amsterdam Reproduction & Development, Emma Neuroscience Group, Amsterdam UMC, University of Amsterdam and Vrije Universiteit Amsterdam, Emma Children's Hospital, Amsterdam, The Netherlands

ABSTRACT

Very preterm birth is associated with academic difficulties, but the underlying neurocognitive mechanisms of these difficulties remain largely unclear. The present study aimed to assess the role of working memory (WM), attentional processes, and processing speed in academic difficulties of very preterm born adolescents at 13 years. Participants included 55 very preterm and 61 full-term adolescents. Academic performance, visuospatial WM, alerting, orienting, executive attention, sustained attention, and processing speed (simple and choice reaction time [RT]) were compared between groups. Mediation analyses with multiple, parallel mediators were performed to examine whether these functions mediate the relation between very preterm birth and academic performance. Very preterm born adolescents showed poorer reading comprehension, arithmetic, visuospatial WM, alerting, sustained attention, and choice RT than full-term controls. The relationship between very preterm birth and arithmetic was mediated by visuospatial WM, sustained attention, and choice RT. The relationship between very preterm birth and reading comprehension was mediated by visuospatial WM and choice RT. The findings indicate that very preterm birth affects arithmetic and reading comprehension through its negative effect on visuospatial WM, sustained attention, and processing speed. These neurocognitive processes may identify very preterm born children at risk for academic difficulties and could serve as targets for interventions.

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KEYWORDS
Very preterm birth; academic performance; working memory; attention; processing speed

Despite advances in neonatal care, very preterm birth (<32 weeks gestation) has a long-lasting impact on a child's development. Academic performance is a domain of particular interest for long-term follow-up studies as it is related to life chances, health, and life expectancy (Cutler & Lleras-Muney, 2010; McMahon & Oketch, 2013). A recent meta-analysis showed that preterm born children scored three-

CONTACT E. Sabrina Twilhaar e.s.twilhaar@vu.nl Clinical Neuropsychology section, Vrije Universiteit Amsterdam, Van der Boechorststraat 7, Amsterdam, BT 1081, The Netherlands

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quarter of a standard deviation lower on arithmetic and about half a standard deviation lower on reading and spelling than their full-term born peers (Twilhaar, de Kieviet, Aarnoudse-Moens, van Elburg, & Oosterlaan, 2018). The prevalence of learning disability, either with or without comorbid intellectual disability, is significantly higher among children born extremely preterm (38%) compared to full-term born children (3%) (Johnson et al., 2016). Moreover, preterm born children are more likely to receive special educational assistance (Twilhaar et al., 2018). Despite this, we recently observed that academic impairments in very preterm born children remained stable during primary school (Twilhaar, de Kieviet, van Elburg, & Oosterlaan, 2019).

In order to improve academic outcomes in very preterm children, mechanisms underlying academic difficulties need to be clarified. Here we focus on three core neurocognitive processes: working memory (WM), attention, and processing speed. WM is a system that enables to keep information in mind while performing complex cognitive tasks and its capacity is positively related to academic performance (Alloway & Alloway, 2010; Gathercole, Pickering, Knight, & Stegmann, 2004). Attention is a multifaceted construct. One fundamental ability closely linked to WM and academic performance is attentional control (Checa, Rodríguez-Bailón, & Rueda, 2008; McVay & Kane, 2012; Rueda, Checa, & Rothbart, 2010). Attentional control includes the ability to actively maintain task-relevant information and inhibit task-irrelevant information or prepotent responses (Engle & Kane, 2003). Finally, processing speed has been found to provide a unique contribution to academic performance next to WM (Christopher et al., 2012; Swanson & Beebe-Frankenberger, 2004).

Very preterm birth is associated with an increased risk for deficits in WM (Hutchinson, De Luca, Doyle, Roberts, & Anderson, 2013; Luu, Ment, Allan, Schneider, & Vohr, 2011), several aspects of attention (Mulder, Pitchford, Hagger, & Marlow, 2009; Van de Weijer-Bergsma, Wijnroks, & Jongmans, 2008; Wilson-Ching et al., 2013), and processing speed (Hutchinson et al., 2013; Mulder, Pitchford, & Marlow, 2011). Only a small number of studies have examined the role of these neurocognitive deficits in academic difficulties of very preterm born children. Based on the assumption that processing speed is a core function underlying other neurocognitive functions (Kail & Salthouse, 1994), Rose, Feldman, and Jankowski (2011) and Mulder, Pitchford, and Marlow (2010) showed that academic difficulties after (very) preterm birth were accounted for by slower processing speed and, in addition, by WM deficits in preterm compared to full-term born children. However, others state that WM and processing speed independently contribute to higher-order cognitive functioning (Redick, Unsworth, Kelly, & Engle, 2012), or presume that attentional control forms the foundation for other neurocognitive functions, such as WM and processing speed (Anderson, 2002). In addition, the role of different aspects of attention for academic difficulties in very preterm born children remains largely unknown. The present study therefore aims to examine WM, various aspects of attention, and processing speed in very preterm born children compared to full-term peers and to clarify the contribution of these processes, without assuming a certain hierarchy, to academic difficulties in this population.

Methods

Participants

This study included 55 adolescents born very preterm (<32 weeks of gestation) and/or with very low birth weight (<1500 g). These adolescents were recruited from a Dutch cohort of 102 very preterm infants born between 2001–2003 who were enrolled in a randomized placebo-controlled trial on the effects of enteral glutamine supplementation in the first month of life (Van Den Berg, Van Elburg, Twisk, & Fetter, 2004). From these 102 infants, 13 died in the neonatal period, one was excluded because of a chromosomal translocation, 11 refused to participate, 15 could not be traced, and one had severe disabilities that prevented participation. As a result, 61 adolescents participated in this 13-year follow-up, of which 55 adolescents completed all questionnaires and tests. Academic performance data were unavailable for three of these 55 adolescents. We previously reported no differences between very preterm born adolescents in the glutamine-supplemented and placebo group on neurodevelopmental outcomes at 13 years (Twilhaar, de Kieviet, Oosterlaan, & van Elburg, 2017). Therefore, very preterm born adolescents were considered as one sample. Controls were classmates of the very preterm participants or recruited from schools located in proximity to Amsterdam and were born at term (≥37 weeks of gestation). Moreover, parents of full-term born adolescents were systematically asked whether their child was ever diagnosed with a developmental, behavioral, learning, or neurological disorder, which was an exclusion criterion for participation. A total of 61 full-term born adolescents participated. Academic performance data were not available for one adolescent and two parents gave no permission to obtain data from the school.

Materials

Academic performance

Reading comprehension, spelling, and arithmetic performance were assessed using standardized tests (Janssen, Verhelst, Engelen, & Scheltens, 2010; Mols & Kamphuis, 2010; Weekers, Groenen, Kleintjes, & Feenstra, 2011) developed by the Dutch National Institute for Educational Measurement (Gillijns & Verhoeven, 1992). These tests are part of a pupil monitoring system that assesses children's academic performance in grade one to grade six in 90% of the primary school in the Netherlands. For this study, the most recent test scores were used (i.e., grade six test scores for most participants). The tests were developed based on item response theory. Standardized test scores for each academic domain were transformed into z-scores to facilitate interpretation.

Visuospatial working memory

An adapted version of the spatial span task developed by Nutley, Söderqvist, Bryde, Humphreys, and Klingberg (2009) was used to assess visuospatial WM. Stimuli (yellow dots) appeared in a 4 × 4 grid on a touch screen in a sequence of increasing length. Participants were asked to reproduce the sequences in reversed order by tapping on the screen. Sequence length, path crossing, and distance between stimuli determined trial difficulty. Each difficulty level consisted of two trials. The task was terminated if both trials of the same difficulty were erroneously reproduced. The highest completed difficulty level multiplied by the number of correct trials was used as a measure of WM (Nutley et al., 2009).

Attention

The Attention Network Task (ANT) was used to assess alerting, orienting, and executive attention. These networks are involved in, respectively, the achievement and maintenance of an alert state, selection of information from sensory input, and resolving conflict (Posner & Petersen, 1990). The target stimulus was an arrow pointing leftward or rightward that was flanked by four arrows pointing in the same (congruent trials) or opposite (incongruent trials) direction as the target. Stimulus presentation was preceded by either a central cue in the middle of the screen, a spatial cue indicating the location of the upcoming target, or no cue. Difference in reaction time (RT) and accuracy between no cue and central cue trials, central cue and spatial cue trials, and congruent and incongruent trials reflect alerting, orienting, and executive attention, respectively. Trials were presented in four blocks of 48 trials.

The Sustained Attention to Response Task (SART; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) measures sustained attention. The digits 1–9 were alternately presented in sequential order. Participants had to respond to frequent go-trials (all digits, except 3) and to withhold their response to infrequent no-go-trials (digit 3). The task consisted of three test blocks of 225 trials each. The number of commission errors (i.e., erroneous responses to digit 3) served as a measure of lapses of sustained attention (McVay & Kane, 2012; Smallwood et al., 2004).

Information processing speed

Simple RT was assessed by a task that required participants to respond as quickly as possible to a stimulus (a smiley) appearing at the center of the screen. Adolescents used the index finger of their dominant hand to press the response button. The task consisted of one block of 60 trials.

Choice RT was assessed using a four-choice RT task, the Alternating Serial Reaction Time task (Howard & Howard, 1997). Stimuli consisted of a row of four squares corresponding to four response buttons. If one of the squares turned yellow, adolescents were required to press the corresponding button as fast as possible. Uneven trials belonged to a fixed sequence (3124) that was repeatedly presented and alternated with random trials. Only random trials that occurred with a low frequency (see Howard & Howard, 1997) were used to measure choice RT. Trials were presented in 15 blocks of 85 trials each.

Procedure

The study was conducted according to the principles of the Declaration of Helsinki (World Medical Association, 2013) and approved by the local research ethics committee. Both parents and adolescents signed informed consent. Tests were individually administered in a quiet room by trained testers using standardized instructions. Academic performance data were requested from schools with written consent of both parents and adolescents.

Statistical analyses

Groups were compared on demographic variables using independent samples *t*-test and chi-square test. Group differences on measures of academic performance, WM, attention, and processing speed were analyzed using univariate analyses of variance. ANT data were analyzed with repeated-measures analysis of variance with cue and target condition as within-subject factor and group as between-subjects factor. Cohen's *d* was used to quantify effect sizes, with .20, .50, and .80 representing small, medium, and large effects (Cohen, 1992). Mediation analyses were performed to test whether the relation between very preterm birth and academic performance was mediated by those neurocognitive measures that significantly differentiated between very preterm and full-term adolescents. A parallel multiple mediator model (Figure 1) was tested according to methods described by Preacher and Hayes (2008) with the PROCESS macro for SPSS version 3.0 (Hayes, 2017). The parallel multiple mediator model assumes possible correlation, but no causal relation between mediators. The bootstrap confidence intervals of 95% for indirect effects were produced using the percentile method based on 5000 resamples (Preacher & Hayes, 2008). Effect sizes of the indirect effects are described by the partially standardized effect size (MacKinnon, 2012), which indicates the size of the effect in terms of standard deviation units in academic performance.

Results

Very preterm born adolescents participating in the current study showed higher birth weight and a lower rate of mild intraventricular hemorrhage than those who were lost to follow-up (eTable 1). Characteristics of the very preterm and full-term samples are shown in Table 1. Groups did not differ on age, sex, and parental education level.

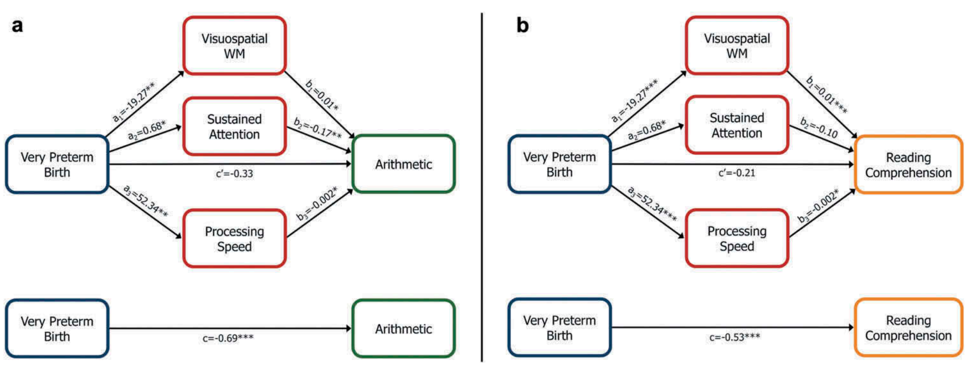

Figure 1. Estimated effects of the parallel multiple mediator model on the effect of very preterm birth on arithmetic performance (A) and reading comprehension (B) through visuospatial working memory (WM), sustained attention, and processing speed. The total effect of very preterm birth on arithmetic and reading comprehension is indicated by *c*. The direct effect of very preterm birth on arithmetic and reading comprehension, controlling for visuospatial WM, sustained attention, and processing speed is indicated by *c′*.

Table 1. Sample characteristics.

	Very preterm (n= 52)	Full-term (n= 58)	p-value
Sex, n (%) boys	26 (50)	24 (41)	.37
Age, years, M (SD)	13.32 (0.31)	13.27 (0.54)	.55
Parental education, n (%) ≥bachelor degree or equivalent	31 (60)	35 (60)	.94
IQ[a], M (SD)	99.25 (15.42)	110.07 (10.67)	<.001
Motor impairment[a,b], n (%)	16 (31)	4 (7)	.001
GA, weeks, M (SD)	29.36 (1.47)		
BW, grams M (SD)	1278.60 (354.67)		
SGA, n (%)	12 (23)		
Cesarean section, n (%)	29 (56)		
Multiple birth, n (%)	13 (25)		
BPD, n (%)	13 (25)		
IVH grade I/II, n (%)	7 (14)		
IVH grade III/IV, n (%)	1 (2)		
PVL, n (%)	2 (4)		
PDA, n (%)	7 (14)		
ROP, n (%)	4 (8)		
NEC, n (%)	0 (0)		
≥1 serious neonatal infection[c], n (%)	31 (60)		
Glutamine supplementation, n (%)	25 (49)		

M, mean; SD, standard deviation; IQ, intelligence quotient; GA, gestational age; BW, birth weight; SGA, small for gestational age; BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; NEC, necrotising enterocolitis.
[a]Data available for 51 very preterm and 61 full-term born children.
[b]Movement ABC total test score ≤5th percentile of the normative population.
[c]Sepsis, pneumonia, meningitis, pyelonephritis, or arthritis diagnosed based on a combination of clinical signs and positive culture.

Academic performance

Compared to full-term peers, very preterm born adolescents had lower scores for reading comprehension and arithmetic (Table 2). Effect sizes were moderate. No significant difference between groups was found for spelling.

WM, attention, and processing speed

Results for WM, attention, and processing speed are presented in Table 2. WM performance was poorer in very preterm born adolescents compared to controls. Repeated-measures analysis on data of the ANT revealed that the difference in RT between no cue and center cue trials (*alerting*) was significantly smaller in very preterm born adolescents compared to controls, indicating impaired alerting attention in very preterm born adolescents. Differences in RT between center cue and spatial cue trails (*orienting*) and between congruent and incongruent trials (*executive*) were not different between groups. Accuracy for alerting, orienting, and executive attention was not different between groups, but the overall accuracy rate was significantly lower in very preterm adolescents than controls. On the SART, very preterm born adolescents made more commission errors than full-term born adolescents, indicating impaired sustained attention. No differences between groups were found for simple RT, but choice RT was significantly increased in very preterm compared to full-term adolescents.

Table 2. Academic performance, working memory, attention, and processing speed of very preterm and full-term born adolescents.

	Very preterm	Full-term		
	M (SD)	*M (SD)*	*F*	*d*
Academic performance				
Reading comprehension, *z-score*	−0.28 (1.02)	0.25 (0.92)	8.19**	0.54
Spelling, *z-score*	−0.17 (0.91)	0.13 (0.98)	2.85	0.32
Arithmetic, *z-score*	−0.37 (1.10)	0.33 (0.77)	15.47***	0.73
Visuospatial WM	50.66 (32.45)	72.04 (34.75)	11.54**	0.63
ANT[a]				
Alerting				
Δ RT,[b] *ms*	31.02 (33.14)	46.19 (26.39)	7.33**	0.51
Δ Accuracy,[c] *% correct*	0.15 (3.31)	−0.85 (3.35)	1.64	0.30
Orienting				
Δ RT,[d] *ms*	95.76 (41.32)	101.89 (29.39)	0.84	0.17
Δ Accuracy,[e] *% correct*	1.05 (3.39)	1.84 (2.89)	1.10	0.30
Executive				
Δ RT,[f] *ms*	111.70 (56.28)	95.74 (27.37)	3.84	0.37
Δ Accuracy,[g] *% correct*	3.97 (5.17)	2.73 (2.83)	2.86	0.30
SART				
Commission errors, *%*	2.82 (1.57)	2.02 (1.32)	8.81**	0.55
Processing speed				
Simple RT, *ms*	264.53 (41.58)	274.27 (57.92)	1.04	0.19
Four-choice RT, *ms*	508.50 (122.30)	459.47 (49.29)	8.24**	0.54

M, mean; *SD*, standard deviation; SWAN, Strengths and Weaknesses of ADHD Symptoms and Normal Behavior; ANT, Attention Network Test; RT, reaction time; SART, Sustained Attention to Response Task; WM, working memory.
[a]Mean (*SD*) are difference scores, but F-value is derived from repeated-measures analysis.
[b]No cue – central cue, with a larger difference in RT indicating increased benefit of the central cue, being interpreted as better alerting attention.
[c]Central cue – no cue, with a higher value indicating increased benefit of the central cue, being interpreted as better alerting attention.
[d]Central cue – spatial cue, with a larger difference in RT indicating increased benefit of the spatial cue relative to the central cue, being interpreted as better orienting attention.
[e]Spatial cue – central cue, with a higher value indicating increased benefit of the spatial cue relative to the central cue, being interpreted as better orienting attention.
[f]Incongruent – congruent trials, with a smaller difference in RT indicating less interference from incongruence and therefore better executive attention.
[g]Congruent – incongruent trials, with a smaller value indicating less interference from incongruence and therefore better executive attention.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Mediation analysis

Since very preterm and full-term born adolescents differed on arithmetic and reading comprehension, mediation analyses were performed for these academic domains. Alerting did not correlate with reading comprehension (r = 0.01) and arithmetic (r = 0.13; eTable 2) and was excluded for further mediation analysis. Table 3 shows the total, direct, and indirect effects of very preterm birth on reading comprehension and arithmetic. The total effect is the effect of very preterm birth on academic performance. The direct effect is the effect of very preterm birth on academic performance, taking into account the selected mediators. The specific indirect effects represent the effect of very preterm birth on academic performance through a certain mediator controlling for the other mediators.

A graphical representation of the findings is shown in Figure 1. Arithmetic and reading comprehension scores of very preterm born adolescents were 0.36 SD and 0.31 SD lower, respectively, than scores of full-term born adolescents due to the negative

Table 3. Results of the mediation analysis with statistics of the total effect, direct effect, and the significant indirect effects of very preterm birth on reading comprehension and arithmetic.

	Point estimate	*SE*	95% CI Lower	95% CI Upper	R^2
Arithmetic					
Total effect *(c)*	−0.69	0.18	−1.05	−0.33	12%
Direct effect *(c′)*	−0.33	0.17	−0.68	0.01	33%
Indirect effects					
Total	−0.36	0.12	−0.63	−0.14	
Visuospatial WM (a_1b_1)	−0.12	0.07	−0.28	−0.02	
SART commission errors (a_2b_2)	−0.12	0.07	−0.29	−0.01	
Choice RT (a_3b_3)	−0.12	0.07	−0.27	−0.002	
Reading comprehension					
Total effect *(c)*	−0.53	0.19	−0.90	−0.15	7%
Direct effect *(c′)*	−0.21	0.19	−0.58	0.15	23%
Indirect effects					
Total	−0.31	0.11	−0.54	−0.13	
Visuospatial WM (a_1b_1)	−0.15	0.08	−0.32	−0.02	
SART commission errors (a_2b_2)	−0.07	0.05	−0.20	0.01	
Choice RT (a_3b_3)	−0.09	0.06	−0.24	−0.001	

SE, standard error, SART, Sustained Attention to Response Task; WM, working memory; RT, reaction time.

effect of very preterm birth on visuospatial WM, sustained attention, and choice RT. The specific indirect effects indicate that the separate effects of very preterm birth on visuospatial WM, sustained attention, and choice RT are each associated with a decrease of 0.12 SD in arithmetic scores, controlling for the other mediators in the model. Reading comprehension scores of very preterm born adolescents were 0.15 SD lower compared to full-term born adolescents, due to the effect of very preterm birth on visuospatial WM and another 0.09 SD through its effect on choice RT, controlling for the other mediators in the model. There was no significant difference in the strength of these indirect effects (difference = −0.05, 95% CI −0.23, −0.14). The estimate of the indirect effect of very preterm birth on reading comprehension through sustained attention was not significantly different from zero. As indicated by the direct effects, very preterm birth did not significantly affect arithmetic and reading comprehension independent of visuospatial WM, sustained attention, and choice RT.

Discussion

The present study described the contribution of deficits in WM, attention, and processing speed in very preterm born adolescents to the academic difficulties in this population. Very preterm born adolescents showed significantly poorer performance in arithmetic and reading comprehension than full-term peers. The sizes of these differences were moderate. For spelling, the difference between very preterm and full-term born adolescents was small and non-significant. Furthermore, very preterm born adolescents showed moderate deficits in visuospatial WM, alerting attention, sustained attention, and choice RT. Impairments in visuospatial WM, sustained attention, and choice RT were found to play a key role in the poorer arithmetic and reading comprehension performance in very preterm born adolescents. Deficits in visuospatial WM, sustained attention, and choice RT equally accounted for the poorer arithmetic performance of very preterm born adolescents compared to full-term peers. Reading comprehension was affected by very preterm birth through its effect on visuospatial WM and choice RT, but not on sustained attention.

Based on meta-analytic findings (Twilhaar et al., 2018) and the overlap in neural substrates of reading and spelling (Rapp & Lipka, 2011), we would have expected that the effect size for spelling and reading comprehension were more similar. However, with respect to reading, most studies in the aforementioned meta-analysis assessed word decoding instead of reading comprehension. A meta-analysis by Kovachy, Adams, Tamaresis, and Feldman (2015) made a distinction between these two components of reading and found a small difference between very preterm and full-term born children for decoding (d = 0.42) and a moderate effect for reading comprehension (d = 0.57), which was similar to the effect size in the present study. This larger impact of preterm birth on reading comprehension may be explained by the increased involvement of higher order neurocognitive processes in reading comprehension, as confirmed by the present findings, in comparison to word decoding (Kovachy et al., 2015). The same may apply to spelling. Dysfunction of the central-executive component of WM has been found to be associated with reading, but not with spelling deficits (Brandenburg et al., 2015). Another explanation for the slight discrepancy between the effect sizes for reading comprehension and spelling in the present study may be provided by the fact that, unlike English (an opaque language), Dutch is a transparent language. In English, the spoken language in most available studies, there is a strong correlation between reading and spelling, while this correlation is only moderate in transparent languages (Patel, Snowling, & de Jong, 2004), which was also true for our study (r = 0.57).

The important role of visuospatial WM deficits for both arithmetic and reading comprehension difficulties in very preterm born adolescents is in accordance with previous findings (Mulder et al., 2010; Rose et al., 2011). Regarding attention, very preterm born adolescents showed poorer alerting and sustained attention, but only sustained attention played a role in the arithmetic, but not the reading comprehension difficulties of these adolescents. The alerting network describes the change in cortical activation state in response to external events, whereas sustained attention refers to the internal maintenance of attention over prolonged time periods (Manly, Robertson, Galloway, & Hawkins, 1999; Posner, 2008). The current findings indicate that the intrinsic state of arousal that fluctuates over time, rather than cortical activation by external events, is key for arithmetic performance. Previous studies established the importance of sustained attention, measured using the SART, for reading comprehension as well (Jackson & Balota, 2012; McVay & Kane, 2012). In the current study, sustained attention was indeed associated with reading comprehension in the total sample. However, when taking visuospatial WM and choice RT into account, sustained attention did not independently mediate the relation between very preterm birth and reading comprehension. In line with previous studies, very preterm children showed slower processing speed (Hutchinson et al., 2013; Mulder et al., 2011), that was underlying the academic difficulties in this population (Mulder et al., 2010; Rose et al., 2011). RTs of very preterm born adolescents were primarily increased in situations requiring a decision to be made (choice RT) in contrast to RTs in response to a single stimulus (simple RT). This is in accordance with findings of Rose and Feldman (1996).

Central to WM, sustained attention, and choice RT and important for higher-order cognitive abilities such as academic performance is the ability to control attention (McVay & Kane, 2012; Rueda et al., 2010). Important work by Engle and Kane (2003) showed that the relation between WM and higher-order cognitive abilities was driven by attentional control. Moreover, WM capacity and attentional control were related to lapses of sustained attention, which subsequently affected academic performance (Unsworth, McMillan, Brewer, & Spillers, 2012). In contrast to simple RT tasks, choice RT tasks tap into attentional control processes (Cepeda, Blackwell, & Munakata, 2013). Lapses in attention were found to affect the slowest RTs and these were correlated with general cognitive abilities (Schmiedek, Oberauer, Wilhelm, Süß, & Wittmann, 2007; Unsworth, Redick, Spillers, & Brewer, 2012). Very preterm born children were previously found to show increased proportions of extremely slow responses rather than an inability to make fast responses per se (De Kieviet, Van Elburg, Lafeber, & Oosterlaan, 2012). The increased demands on attentional control may thus explain the deficits in choice but not simple RT in very preterm born adolescents. Findings of the current study add to the vast amount of research showing that very preterm birth is associated with deficits in processes that are associated with attentional control or similar control systems (Aarnoudse-Moens, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2009; Anderson & Doyle, 2004; Burnett, Scratch, & Anderson, 2013; Mulder et al., 2009), such as Baddeley's (1996) central executive, Stuss et al.'s (1995) supervisory system, and Anderson's (2002) executive control system. However, the present study is one of the first to show that these deficits accounted for an important part for the poorer arithmetic and reading comprehension performance in very preterm born adolescents.

Early monitoring and intervention is key for the identification of children at risk for poor outcomes and prevention of academic failure. The current and previous findings by Rose et al. (2011) and Mulder et al. (2010) emphasize the assessment of WM, sustained attention, and processing speed in very preterm children as specific neuro-cognitive processes that are involved in higher-order cognitive functioning, such as academic performance (McVay & Kane, 2012; Mulder et al., 2010; Rose et al., 2011; Rueda et al., 2010). Academic difficulties in very preterm children are apparent from the first grade onwards and persist at least during primary school ages (Twilhaar et al., 2019). Previous studies have demonstrated that measures of WM and attentional control in preschool were predictive of academic performance in elementary school and beyond (Alloway & Alloway, 2010; Bull, Espy, & Wiebe, 2008; Gathercole et al., 2004; Sjöwall, Bohlin, Rydell, & Thorell, 2017). In a sample of extremely preterm born children, neurocognitive abilities at age six were related to academic performance at age 11 (Johnson, Wolke, Hennessy, & Marlow, 2011). Assessment of these specific neuro-cognitive processes before school entry may therefore be useful for identification of very preterm children at risk for academic difficulties. Early identification of these children would facilitate a proactive rather than reactive approach to provide timely support.

The very preterm cohort in this study was relatively small, recruited from a single-center NICU, and parental education level was high. This sample is therefore less representative for very preterm adolescents in the population and reported deficits may be underestimated. Indeed, while meta-analysis showed spelling difficulties in very preterm children (Twilhaar et al., 2018), this was not found in the current study.

However, effect sizes for reading comprehension and arithmetic were comparable to those obtained by meta-analysis (Twilhaar et al., 2018). Another limitation is that the neurocognitive processes, such as WM, have multiple aspects that may not be optimally captured using single tests.

In conclusion, very preterm birth affected arithmetic performance through its adverse effect on visuospatial WM, sustained attention, and choice RT. Reading comprehension was affected by very preterm birth through adverse effects on visuospatial WM and choice RT. This study contributes to the small number of studies that examined the relationship between neurocognitive functions and academic performance in very preterm born children. The findings provide important information about the underlying mechanisms of academic problems in this population, that is highly valuable for the identification of children at risk for poor academic outcomes and the development of interventions to improve these outcomes after very preterm birth. The independent contribution but interrelatedness of neurocognitive processes emphasizes the importance of studying these processes in concert rather than in isolation. This should also be acknowledged in the development of interventions to improve the academic outcomes of children born very preterm.

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ORCID

E. Sabrina Twilhaar http://orcid.org/0000-0001-7912-9883

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