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Research Article

Episodic and prospective memory difficulties in 13-year-old children born very preterm

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Abstract

Objectives: Children born very preterm (VP) are susceptible to a range of cognitive impairments, yet the effects of VP birth on long-term, episodic, and prospective memory remains unclear. This study examined episodic and prospective memory functioning in children born VP compared with their term-born counterparts at 13 years. **Method:** VP ($n = 81$: born <30 weeks' gestation) and term ($n = 26$) groups were aged between 12 and 14 years. Children completed: (i) standardized verbal and visuospatial episodic memory tests; and (ii) an experimental time- and event-based prospective memory test that included short-term (within assessment session) and long-term (up to 1-week post-session) tasks. Parents completed a questionnaire assessing memory functions in everyday life. **Results:** The VP group performed worse on all measures of verbal and visuospatial episodic memory than the term group. While there were no group differences in event-based or long-term prospective memory, the VP group performed worse on time-based and short-term prospective memory tasks than term-born counterparts. Parents of children born VP reported more everyday memory difficulties than parents of children born at term, with parent-ratings indicating significantly elevated rates of everyday memory challenges in children born VP. **Conclusions:** Children born VP warrant long-term surveillance, as challenges associated with VP birth include memory difficulties at 13 years. This study highlights the need for greater research and clinical attention into childhood functional memory outcomes.

Keywords: very preterm; very low birth weight; episodic memory; prospective memory; learning; cognition

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Susceptibility of children born very preterm (VP; <32 weeks' gestation) to a range of cognitive deficits (Anderson, 2014) and neuro-anatomical alterations in frontal, hippocampal, and subcortical regions places them at risk for impaired memory functioning (Nam et al., 2015; Omizzolo et al., 2014; Thompson et al., 2013; Vollmer et al., 2017), including in episodic memory (memory for past experiences; Tulving, 2002) and prospective memory (memory for future intended actions; Einstein & McDaniel, 1990). Despite their apparent propensity for vulnerability in these domains, there is lack of consensus regarding episodic memory in children born VP compared with their term-born peers (≥ 37 weeks' gestation), and little research has focused on prospective memory. Further investigation of episodic and prospective memory in children born VP is warranted, especially given the functional importance of these skills and potential adverse consequences of deficits in these areas for daily life.

Episodic memory, defined as learning and recall of newly learned information (Marsh & Roediger, 2012), is important for

knowledge acquisition (Greenberg & Verfaellie, 2010), academic achievement (Hassevoort et al., 2018) and identity development (Allebone et al., 2015). Prospective memory is required to remember to perform future-intended actions, such as remembering to attend football practice at 4:00 pm (time-based), or to hand in an assignment when the school bell rings (event-based) (Einstein & McDaniel, 1990).

Episodic and prospective memory have protracted developmental trajectories, and deficits in these domains may become more apparent in later childhood when increasing demands are placed on these skills as children progress through school (Wehrle et al., 2016). Episodic memory is underpinned by the medial temporal, prefrontal, and parietal lobes (Hebscher & Voss, 2020; Preston & Wagner, 2007) and basal ganglia (Gershman & Uchida, 2019) and improves throughout childhood (Gascoigne et al., 2013; Gott & Lah, 2014), coinciding with maturation of these underlying frontal-hippocampal networks (Ghetti & Bunge, 2012; Lebel et al., 2008). Effective prospective

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memory relies on adequate episodic memory functioning (Groot *et al.*, 2002; Kliegel *et al.*, 2002), and is governed by many of the same neural networks (Cona *et al.*, 2015), but with greater recruitment of executive functions (Kliegel *et al.*, 2002; Mahy *et al.*, 2014).

Studies using direct assessment of episodic memory have shown higher rates of episodic memory impairments in children born VP compared with term-born children (Luu *et al.*, 2011; Omizzolo *et al.*, 2014). Omizzolo *et al.* (2014) found that 7-year-olds born VP had significantly poorer delayed recall, but not immediate recall, of verbal associative information, as well as impaired memory for spatial information across all stages of learning and memory (i.e., from encoding to retrieval). Luu *et al.* (2011) found that adolescents born VP performed significantly worse than term-born children at all stages of memory for both verbal associative learning and episodic memory for more complex geometric figures. Conversely, others failed to report associations between gestational age and episodic memory performance (e.g., de Amorim *et al.*, 2013; Nassar *et al.*, 2019; Rushe *et al.*, 2001), owing to methodological variability, such as different assessment measures, inclusion of relatively high functioning target groups, or lack of subgroup analyses restricted to the most vulnerable children, born VP. More studies of episodic memory are needed in representative samples of children born VP, as this population is prone to altered development of brain structures considered to play a central role in episodic memory functioning, including the hippocampus (Thompson *et al.*, 2013), basal ganglia, and thalamus (Omizzolo, *et al.*, 2014).

There is good reason to believe that children born VP are also at risk of deficits in prospective memory. Prospective memory relies on episodic memory, which may be an area of vulnerability in this population, as discussed previously. Effective prospective memory also relies on executive functioning, in which children and adolescents born VP have high rates of impairment (Anderson, 2014), associated with white matter pathology and dysmaturation (Nam *et al.*, 2015; Vollmer *et al.*, 2017). Yet, research on prospective memory in children born VP is scarce. Only two studies to date have examined prospective memory in this population, and both showed that children born VP had poorer prospective memory than their term-born peers at 7–9 years (Ford *et al.*, 2016) and 13 years of age (Isaacs *et al.*, 2003). However, both studies focused on short-term event-based tasks (response to an external cue within an assessment session). To date, time-based and long-term tasks (completed beyond an assessment session) have not been examined, despite these tasks being more sensitive to prospective memory deficits (Bedard *et al.*, 2018; de Mendonça *et al.*, 2018). Comprehensive assessment of prospective memory is needed to clarify the nature of prospective memory functioning in children born VP and to inform targets for development of effective interventions.

This study aimed to examine functional memory in children born VP by examining episodic and prospective memory in VP and term-born groups of children at 13 years of age. Based on preliminary evidence to date, it was hypothesized that children born VP would demonstrate poorer episodic and prospective memory than term-born children.

Methods

Study participants and procedure

Participants were children born <30 weeks' gestational age who enrolled in the VIBeS Plus study, a randomized controlled trial of a preventative care program designed to improve infant development, behavioral regulation, parent–child interactions and

parent mental health (Spittle *et al.*, 2009). A cohort of 120 eligible infants born VP were recruited at term-equivalent age from the Royal Women's Hospital and Royal Children's Hospital in Melbourne between January 2005 and January 2007. This included infants without congenital anomalies likely to affect neurodevelopment and for the purpose of the intervention, who were discharged from hospital by 4 weeks of age corrected for prematurity, lived within 100 km of the hospital and were born to English-speaking families. Participants were randomized to the intervention or standard follow-up conditions. No significant cognitive benefits of the intervention were observed at 2 (Spittle *et al.*, 2010), 4 (Spencer-Smith *et al.*, 2012), or 7–8-year follow-ups (Spittle *et al.*, 2016). Therefore, the children born VP from the intervention and standard follow-up groups were combined in the current study.

A comparison group of children born at term (born ≥ 37 weeks' gestation) was recruited from metropolitan Melbourne kindergartens at 4 years of age. Eligible participants were from English-speaking families and without history of significant congenital abnormalities or developmental difficulties.

The current study used data from the VIBeS Plus 13-year follow-up, which was approved by the Royal Children's Hospital Human Research Ethics Committee and was completed in accordance with the Helsinki Declaration. Participants were assessed between September 2018 and March 2020. All children underwent a neuropsychological assessment at 13 years, corrected for prematurity to minimize bias in cognitive test scores in those born preterm (Wilson-Ching *et al.*, 2014). Assessors were blind to perinatal history and previous assessment performances. At the 13-year follow-up, 81 of 118 (69%) surviving children born VP were assessed, while 26 of 41 (63%) children in the term group were assessed (see Figure 1). Data collection was terminated prematurely due to COVID-19 restrictions.

Measures

Episodic memory

The Children's Memory Scales (CMS; Cohen, 1997) Dot Locations and Word Pairs subtests, validated for use in children aged 5–16 years, were used to measure spatial and verbal episodic memory, respectively. Dot Locations involves learning the spatial location of an array of eight dots on a four-by-four grid across three learning trials with a 5-s exposure. A distractor trial is followed by a fourth recall trial and a delayed recall trial 20–30 min later. The Word Pairs subtest requires participants to immediately recall the second word from 14 abstract word pairs, heard over three learning trials, with feedback for errors. Delayed recall and recognition trials are administered 20–30 min later. Both subtests yield Learning, Immediate Recall and Delayed Recall scores, as well as a Recognition score for the Word Pairs subtest. Scores were converted to age-standardized scaled scores ($M = 10$, $SD = 3$).

Test-retest reliability coefficients range from .70 to .81 and .73 to .94 for Dot Locations and Word Pairs scores, respectively, in children aged 13–14 years (Cohen, 1997), indicating acceptable-to-excellent reliability (Groth-Marnat & Wright, 2016). Patterns of intercorrelations of CMS subtests provide evidence of adequate convergent and divergent validity and the CMS has demonstrated clinical sensitivity in detecting mild-to-moderate memory difficulties in children with neurodevelopmental disorders (Cohen, 1997).

Prospective memory

The PM Test was adapted for use with children from existing, behavioral prospective memory tests validated in adults (e.g., Royal

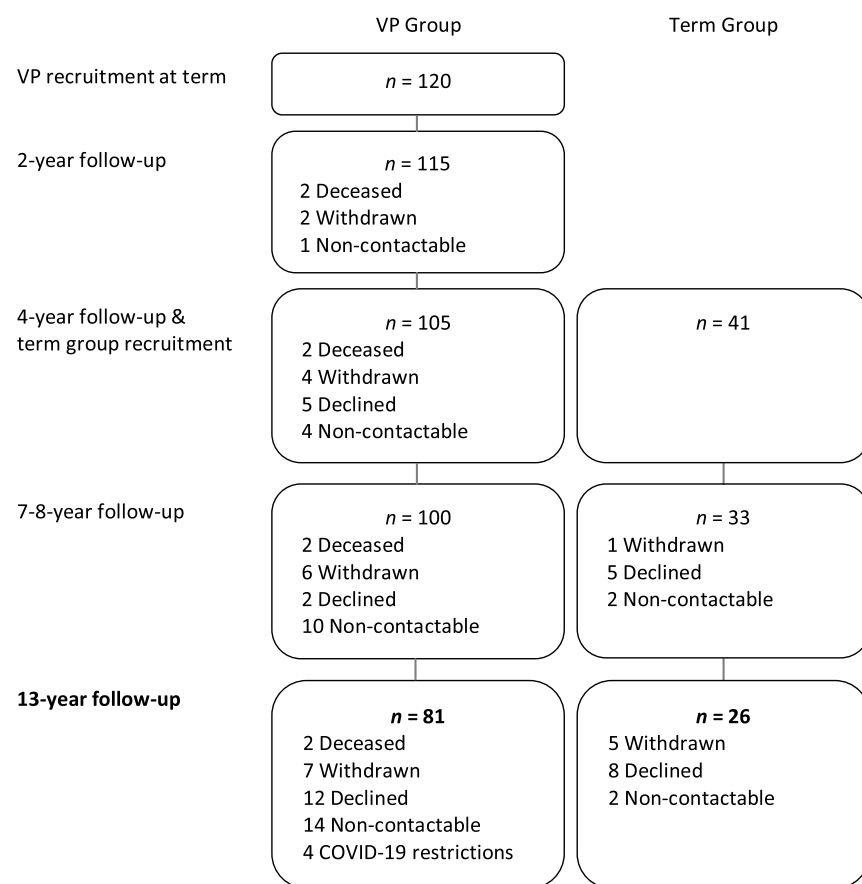


Figure 1. Flow diagram illustrating participant recruitment and allocation. *Note.* Number of participants lost to follow-up by reason for nonparticipation at each timepoint are cumulative from initial recruitment until 13 years (i.e., there were only two deaths overall).

Prince Alfred Prospective Memory Test [RPA-ProMem], Rivermead Behavioral Memory Test [RBMT] – 3rd edition, Memory for Intentions Screening Test [MIST]; Radford et al., 2011; Wilson et al., 2008; Woods et al., 2008). The MIST has been previously adapted for use with children (Mills et al., 2021; Robey et al., 2014). We adopted a similar approach, with a broader range of time delays across short-term (within assessment session) items, and inclusion of long-term (up to 1-week post-session) items, similar to the design of the RPA-ProMem.

The PM Test comprised eight items, with an equal weighting of time- and event-based items across six short-term items and two long-term items, respectively (see Supplementary Table 1 for full list of items). Thus, each item formed part of two scales (e.g., time-based and short-term). Items were designed to mimic everyday prospective memory tasks that may be encountered in the age range of participants in this study. For example, item 5 (Supplementary Table 1) requires the participant to remember to get a pen when they return to their desk from a standing activity. This item mimics real-world examples of prospective memory tasks, such as teachers asking students to prepare certain materials for an activity in a classroom environment, or instructions that parents might give their children when they transition between activities.

Short-term items were administered at set times throughout a 4-hr neuropsychological assessment and long-term items required participants to respond up to 1-week following the assessment. Event-based items required participants to respond to environmental cues (e.g., timer sound, when instructed to sit at the table), whilst time-based items required participants to monitor the time on their preferred device (personal watch, mobile phone, or

surroundings) and respond at set times. Items were scored 0 (no response or incorrect response at incorrect time), 1 (partial correct response) or 2 (correct response at correct time). Scores were summed to yield a Total score (ranging from 0 to 16) as well as Time-based (0–8), Event-Based (0–8), Short-Term (0–12), and Long-Term (0–4) scores.

In cases in which a single time-based or event-based item was not administered due to factors unrelated to the child's ability (e.g., administration error, written tasks unable to be completed due to neurosensory impairment, school/home assessments requiring protocol changes), a score was imputed using the median of the remaining scores of that scale (i.e., remaining time- or event-based scores). Subscale scores were recorded as missing if more than one item from the scale was not administered.

Parent-reported episodic and prospective memory

Parents rated their children's functional memory on the Observer Memory Questionnaire – Parent Form (OMQ-PF; Gonzalez et al., 2008), validated for use with children aged 5–16 years. The OMQ-PF comprises 27 items of memory function in everyday scenarios that demand utilization of episodic memory (e.g., “does your child recall details of previous conversations?”) and prospective memory (e.g., “do you have to provide reminders for your child?”), as well as items of parents' perceptions about their child's memory function (e.g., “compared with other children of the same age, his/her memory ability is poor”). Items were scored on a 5-point Likert scale, with some reversed scored items, and summed to produce a total score ranging from 27 to 135, whereby higher scores reflect more optimal memory. The mean total score in a sample of 376 healthy Australian children who participated in a validation study

Table 1. Participant characteristics

	Very Preterm	Term
	(<i>n</i> = 81)	(<i>n</i> = 26)
Neonatal characteristics		
Gestational age (weeks), <i>M</i> (<i>SD</i>)	27.5 (1.5)	39.5 (1.3)
Birthweight (grams), <i>M</i> (<i>SD</i>)	1056.7 (125.9)	3528.2 (461.4)
Male sex, <i>n</i> (%)	41 (51)	12 (46)
Multiple birth, <i>n</i> (%)	27 (33)	–
Antenatal corticosteroids, <i>n</i> (%)	68 (84)	–
Postnatal corticosteroids, <i>n</i> (%)	3 (4)	–
BPD, <i>n</i> (%)	22 (27)	–
Proven/suspected NEC, <i>n</i> (%)	8 (10)	–
Moderate-severe WMI, <i>n</i> (%)	7 (10) ^a	–
IVH grade III/IV, <i>n</i> (%)	4 (5)	–
Cystic PVL, <i>n</i> (%)	2 (2)	–
CP diagnosis at 4 years, <i>n</i> (%)	5 (6)	0
Characteristics at 13 years		
Age (corrected for prematurity), <i>M</i> (<i>SD</i>)	13.4 (0.4)	13.2 (0.3)
FSIQ-2, <i>M</i> (<i>SD</i>)	104.2 (13.6)	114.3 (8.3)
FSIQ-2 < 70, <i>n</i> (%)	1 (1)	0
Higher social risk, <i>n</i> (%)	29 (37) ^b	4 (15)

Note. *n* = number; *M* = mean; *SD* = standard deviation; BPD = bronchopulmonary dysplasia; NEC = necrotizing enterocolitis; WMI = white matter injury; IVH = intraventricular hemorrhage; PVL = periventricular leukomalacia; CP = cerebral palsy; FSIQ-2 = estimate of intellectual ability based on two subtests.

^aMRI data available for *n* = 72.

^bQuestionnaires returned for *n* = 79.

Higher social risk refers to the presence of multiple sociodemographic factors known to affect development based on family structure, primary caregiver education, primary income earner employment status and occupation, language spoken at home, and maternal age at birth.

was 107.26 (*SD* = 13.00) (Gonzalez et al., 2008). Total scores were considered invalid if two or more items of the questionnaire were incomplete.

The OMQ-PF has demonstrated sound internal consistency, with item-total coefficients ranging from .36 to .79 and Cronbach's α of .92 (Gonzalez et al., 2008). In healthy children, the scale correlates primarily with measures of novel associative learning. The OMQ-PF is sensitive to memory impairment in children with temporal lobe epilepsy and has been shown to correlate more strongly with several memory measures in this population than in healthy controls.

Across all age-standardized measures (CMS subtests), scores greater than one standard deviation below the normative mean were classified as falling below age expectations; a cut-off that has been used to define impairment relative to typically developing children in this cohort previously (Spittle et al., 2016), other studies of children born VP (Pittet-Metrailler et al., 2019), and other pediatric populations (Azevedo et al., 2020; Perrin et al., 2019). A cut-off of one standard deviation acknowledges the potential functional implications of mild reductions from normative comparisons (Sohlberg & Mateer, 2001). A cut-off of greater than one standard deviation below the term group mean was used when age-standardized normative data were unavailable (PM test and OMQ-PF).

General intellectual ability

Two Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II; Wechsler & Zhou, 2011) subtests (Vocabulary and Matrix Reasoning) were used to obtain an estimate of full scale intellectual ability (FSIQ-2; *M* = 100, *SD* = 15). Participants with an estimated FSIQ-2 greater than two standard deviations below the test norm mean (i.e., <70) were categorized as having a general intellectual impairment.

Social risk

Social risk was assessed to describe the sociodemographic status of the sample using the Social Risk Index (SRI; Roberts et al., 2008), reported by parents in a questionnaire at 13 years. The SRI is based on six factors, scored 0 (lower risk), 1 or 2 (higher risk), respectively: family structure (two caregivers, separated parents, single caregiver), highest level of primary caregiver education (tertiary, 11–12 years, <11 years), primary income earner employment status (full time, part time, unemployed) and occupation (skilled, semi-skilled, unskilled), language spoken at home (English, some English, no English), and maternal age at birth (>21 years, 18–21 years, <18 years). Scores from each factor were summed and used to categorize families into lower (0 to 1) or higher (≥ 2) social risk around the median, as has been done in this cohort previously (Roberts et al., 2008; Spittle et al., 2017).

Statistical analyses

Data were analyzed using Stata 16.0 (StataCorp, 2019). Univariable linear and logistic regressions were used for continuous and categorical variables, respectively, to compare VP and term groups on important demographic characteristics, as well as those who participated and those lost to current follow-up. In cases where the frequency was ≤ 5 for categorical participant characteristic variables, Fisher's exact test was used.

Mean group differences in continuous memory outcome data were examined using linear regressions, adjusted for social risk due to observed between-group differences in social risk (see Results) and the known association between higher social risk and poorer long-term cognitive outcomes in children born VP (Doyle et al., 2015). Models adjusted for age at assessment for outcome measures that were not age-standardized (prospective memory and parent-reported memory measures). Group differences in rates of below age-expected performance (categorical memory data) were examined using logistic regressions, also adjusted for social risk for the same reason. All models were fitted with generalized estimation equations (GEEs) with an exchangeable correlation structure and robust standard errors to adjust for correlations between twins within the same family.

Sensitivity analyses excluded children with significant developmental delay (defined as FSIQ-2 of <70 and/or formal diagnosis of cerebral palsy) to examine the possible influence of a small proportion of impaired children on the results.

To account for multiple comparisons, all significance values were corrected using the Benjamini–Hochberg false discovery rate of .05 (Benjamini & Yekutieli, 2001). Interpretation of results considered the overall pattern and magnitude of between-group differences across outcome measures.

Results

Participant characteristics

Participant characteristics are summarized in Table 1. The VP and term groups were similar in terms of sex distribution, but the VP group had a lower mean IQ (mean difference = -10.1 ; 95% confidence intervals [CIs] -15.7 to -4.5). Children in the VP group were also more likely to be slightly older (0.2 years; $-.01$ to 0.4) and of higher family social risk ($p = .05$, Fisher's exact test) (Table 1).

Among term group participants, those assessed and those lost to follow-up did not differ on any important characteristics (Supplementary Table 2). Among the VP group, those assessed and those lost to follow-up were similar across most important

Table 2. Memory outcomes and rates of below age-expected performance^a in children born very preterm compared with term-born controls

	Memory outcomes				Rates of below age-expected performance ^a			
	VP (<i>n</i> = 81) ^b	Term (<i>n</i> = 26)	Adjusted mean group differences		VP (<i>n</i> = 81) ^b	Term (<i>n</i> = 26)	Adjusted odds ratio	
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	β (95% CI) ^c	<i>p</i>	<i>n</i> (%)	<i>n</i> (%)	OR (95% CI) ^c	<i>p</i>
Visuospatial episodic memory (CMS DL)								
Spatial learning	9.3 (3.4)	11.2 (2.4)	-1.7 (-2.9 to -0.6)	.003	17 (21)	1 (4)	6.0 (0.8 to 47.9)	.09
Spatial immediate recall	9.8 (3.1)	11.5 (1.8)	-1.5 (-2.5 to -0.6)	.001	20 (25)	1 (4)	7.2 (0.9 to 57.1)	.06
Spatial delayed recall	10.4 (3.0)	12.0 (2.3)	-1.4 (-2.4 to -0.3)	.01	10 (13)	1 (4)	2.2 (0.3 to 19.7)	.47
Verbal episodic memory (CMS WP)								
Verbal learning	8.4 (2.8)	9.9 (2.1)	-1.5 (-2.6 to -0.4)	.009	25 (31)	3 (12)	3.6 (0.9 to 14.3)	.06
Verbal immediate recall	10.0 (3.5)	11.7 (2.7)	-1.6 (-3.0 to -0.2)	.02	11 (14)	1 (4)	3.6 (0.4 to 31.8)	.25
Verbal delayed recall	10.6 (3.3)	12.6 (2.5)	-1.8 (-3.1 to -0.6)	.004	11 (14)	0 (0)	N/A ^d	N/A
Verbal delayed recognition	9.8 (2.9)	11.1 (0.5)	-1.2 (-1.9 to -0.6)	<.001	10 (13)	0 (0)	N/A ^d	N/A
Prospective memory								
Total score	12.1 (3.0)	13.5 (1.9)	-1.1 (-2.1 to -0.2)	.01	28 (35)	4 (15)	2.7 (0.8 to 9.1)	.10
Time-based	5.6 (1.7)	6.8 (1.3)	-1.0 (-1.6 to -0.4)	.002	34 (43)	5 (19)	2.8 (0.9 to 8.4)	.06
Event-based	6.5 (1.7)	6.7 (1.4)	-0.2 (-0.8 to 0.5)	.61	20 (25)	6 (23)	1.1 (0.4 to 3.2)	.91
Short-term	9.3 (2.3)	10.6 (1.5)	-1.1 (-1.8 to -0.4)	.004	38 (48)	6 (23)	3.0 (1.1 to 8.5)	.03
Long-term	2.7 (1.4)	2.9 (1.1)	-0.01 (-0.5 to 0.5)	.98	16 (20)	3 (12)	1.5 (0.4 to 5.9)	.57
Everyday memory (OMQ-PF)								
Total score	99.9 (17.8)	116.2 (12.2)	-16.2 (-23.1 to -9.3)	<.001	48 (61)	3 (12)	12.1 (3.3 to 45.1)	<.001

Note. VP = very preterm; *n* = number; *M* = mean; *SD* = standard deviation; β = regression coefficient representing mean group differences; CI = confidence interval; OR = odds ratio; CMS = children's memory scale; DL = dot locations subtest; WP = word pairs subtest; OMQ-PF = observer memory questionnaire-parent form; N/A = not applicable.

^aBelow age-expected performance defined as more than 1 *SD* below normative mean for age-standardized measures (CMS subtests), or more than 1 *SD* below the term group mean for all remaining measures (prospective memory test, OMQ-PF).

^b*n* ranges from 79 to 81 due to missing outcome data.

^c*n* ranges from 103 to 105 due to missing outcome and social risk data.

^dOdds ratio unable to be computed due to cell size of zero in one group.

All models adjusted for social risk, while linear regression models comparing prospective and everyday memory also adjusted for corrected age at assessment.

characteristics, although VP non-participants were of higher neonatal medical risk, including lower mean birthweight (-140; -242 to -38) and higher rates of necrotizing enterocolitis (odds ratio [OR] = 2.9; CIs 1.0 to 8.4) (Supplementary Table 2).

Episodic memory (CMS word pairs and dot locations)

The VP group performed poorer than the term group on all measures of visuospatial and verbal episodic memory (see Table 2). While the rate of below age-expected performance was higher in the VP group than the term group on episodic measures (odds ratios [ORs] ranging from 2.2 to 7.2), these differences did not reach statistical significance.

Prospective memory

The VP and term groups performed similarly on measures of event-based and long-term prospective memory, but there was evidence that the VP group performed more poorly on measures of time-based and short-term prospective memory relative to the term group (Table 2). There was a higher proportion of children in the VP group performing more than 1 *SD* below the control group across time-based and short-term aspects of prospective memory (ORs of 2.5 and 3.0, respectively), but the evidence was weak.

Parent-reported everyday memory (OMQ-PF)

Parents of children born VP reported more everyday episodic and prospective memory difficulties in their children compared with parents of children born at term (Table 2). A significantly greater proportion of children born VP displayed elevated functional memory difficulties based on parent ratings, as the VP group

had almost 12 times the odds to exhibit everyday difficulties than the term group.

All results remained the same after sensitivity analyses excluding children with significant developmental delay (*n* = 6) (Supplementary Table 3), and after adjusting for multiple comparisons.

Discussion

Our study provides strong evidence of memory difficulties in children born VP at 13 years relative to their term-born peers. We found episodic memory difficulties, encompassing learning, immediate recall, delayed recall and recognition, of both verbal and visual material in this population compared with term-born peers. We also documented selective prospective memory difficulties in VP 13-year-olds, involving time-based but sparing event-based prospective memory. Moreover, in our assessment, children born VP were more challenged by prospective memory tasks at short delays (within the assessment session) but not at long delays (up to a week post assessment). Between-group differences ranged from around half to three quarters of a standard deviation across episodic and prospective measures, respectively, indicating a moderate-to-strong effect. These findings were supported by parents of children born VP who reported greater challenges in their children's ability to undertake everyday memory tasks compared with parents of term-controls, to the effect of just under one-and-a-half standard deviations.

Our study is novel given the comprehensive assessment of prospective memory, incorporating both event- and time-based measures, in children born VP. The study revealed poorer performance in time- but not event-based prospective memory in children born VP. This differential difficulty in prospective memory may be related to time-based tasks being cognitively more demanding than

event-based tasks (Einstein *et al.*, 1995; Mahy *et al.*, 2014), and particularly sensitive to neurological impairments (Bedard *et al.*, 2018; de Mendonça *et al.*, 2018). The difference in cognitive demand between time- and event-based tasks may be related to the presence or absence of external cues. Event-based tasks include external cues that likely trigger cued retrieval, while time-based tasks rely primarily on internal processes, executive functions and time-monitoring, and require self-initiated retrieval processes (Einstein *et al.*, 1995; Mahy *et al.*, 2014). In children born VP, time-based prospective memory difficulties might be related to poorer executive functioning (Anderson, 2014) associated with white matter pathology and dysmaturation (Nam *et al.*, 2015; Vollmer *et al.*, 2017). Poorer episodic memory may also contribute to the observed prospective memory difficulties (Kinsella, 2010; Kliegel *et al.*, 2002; Mahy *et al.*, 2014).

Unlike previous studies (Ford *et al.*, 2016; Isaacs *et al.*, 2003), we did not find evidence for event-based prospective memory difficulties in children born VP compared with their term-born peers. It is possible that the measure used in our study was not sufficiently challenging to detect subtle deficits in event-based prospective memory. For instance, half of the event-based items in our measure required children to respond to a timer sound (event-based cue), which might have been a too obvious trigger. In contrast, other studies have used more subtle cues, such as verbal cues in conversation (phrase: “Let’s try something different”; Ford *et al.*, 2016) or even less obvious environmental cues (remembering to find an object whilst retracing a route; Isaacs *et al.*, 2003).

Our finding that children born VP exhibit poorer performance in short-term (within assessment session) prospective memory is consistent with previous studies (Ford *et al.*, 2016; Isaacs *et al.*, 2003), but surprisingly there was no evidence of difficulties in long-term (up to 1-week post-session) prospective memory in this group. We expected to find deficits in long-term prospective memory, given the vulnerability in short-term prospective memory that has previously been reported and because long-term tasks are more sensitive in detecting prospective memory impairments than short-term tasks (Bedard *et al.*, 2018; de Mendonça *et al.*, 2018).

A lack of between-group differences in long-term prospective memory in this study might again be due to the design of the measure. Short-term items were administered in a controlled assessment environment, compared with long-term items that provided participants with additional time for rehearsal, greater opportunity for exposure to external cues (e.g., twins inadvertently prompting one another or reminders from parents), and enabled them to employ additional strategies (e.g., to-do note or electronic reminder). In terms of scoring, there was a limited range of scores; with a maximum total score of four for long-term prospective memory, compared with 12 for short-term tasks. Leeway was also provided in scoring an item that required children to mail a questionnaire to account for postal delays. This made it challenging to differentiate between children who mailed their questionnaire on time or slightly late. Future research may consider the use of electronic media, although this could disadvantage children from lower socioeconomic backgrounds who might not have access to technological devices.

With regards to episodic memory, our study provides further insight into episodic memory difficulties in children born VP. Omizzolo *et al.* (2014) found deficits in younger children born VP at all stages (i.e., from encoding to retrieval) of episodic memory for spatial information, but only in delayed recall for verbal information. Our study found below age-expected episodic

memory performance at all stages of memory for both verbal and visual information; a similar pattern that has been observed in VP 16-year-olds (Luu *et al.*, 2011). Episodic memory difficulties in children born VP may be related to disrupted frontotemporal and cortical–subcortical networks, which are particularly critical for episodic memory (Hebscher & Voss, 2020; Preston & Wagner, 2007). Cross-sectional studies in children born VP have reported a reduction in hippocampal volume compared with term controls that may increase with age: 3% reduction in hippocampal volume during infancy (Thompson *et al.*, 2014), 6% reduction at 7 years (Omizzolo *et al.*, 2013), and 12–15% at 15 years (Nosarti *et al.*, 2002), with this magnitude of reduction persisting into adulthood (Aanes *et al.*, 2015). Abnormalities in other brain regions relevant to episodic memory have also been identified in children born VP, including in the fornix (Kelly *et al.*, 2020), basal ganglia and thalamus (Omizzolo *et al.*, 2014). Based on these studies, we postulate that children born VP may grow into memory deficits, such that episodic memory difficulties do not resolve, but rather persist as the episodic memory system matures across childhood (Ghetti & Bunge, 2012). Longitudinal research is needed to elucidate whether children born VP grow into their memory deficits, in line with the altered maturational trajectory of the hippocampus.

Our study highlights that alongside episodic and prospective memory difficulties on testing, children born VP experience significant difficulties with memory in everyday life. The odds of below age-expected ability in everyday tasks that require episodic and prospective memory were twelve times higher in children born VP compared with term-born children, indicating that poor memory performance on direct assessment may be manifesting functionally in everyday situations. Of note, the greater magnitude of between-group differences based on parent-report compared with smaller group differences evident on direct memory assessment illustrates the potential benefit of a structured, one-to-one assessment setting with few distractions. The memory difficulties we identified in children born VP in an ideal assessment setting are likely to be more pronounced in everyday settings, such as classrooms. Consequences may be far-reaching, as episodic memory is important for learning new concepts (Greenberg & Verfaellie, 2010), academic progress (Hassevoort *et al.*, 2018), and development of self-identity (Allebone *et al.*, 2015). Prospective memory difficulties may have similar consequences, such as challenges with following through with classroom instructions and development of independence that is increasingly required as children progress through school (Henry *et al.*, 2014).

The wide-ranging memory difficulties we identified in children born VP highlight the need for intervention. Although few studies have evaluated memory interventions in children, some efficacy has been shown for compensatory strategies (e.g., electronic memory aids; Mahan *et al.*, 2017; Wilson *et al.*, 2009), instructional learning strategies (e.g., errorless learning; Haslam *et al.*, 2011; Haslam *et al.*, 2017), and programmatic approaches that combine training of metacognition, attention, and strategy use (Catroppa *et al.*, 2015). Broader memory rehabilitation literature suggests that interventions have most benefit when they combine approaches (e.g., internal and external strategies), target everyday memory complaints, and employ methods with clear functional relevance for everyday life (Parker *et al.*, 2017). For example, training children with everyday memory difficulties following acquired brain injury in both self-instruction and diary use has been found to significantly improve everyday functional outcomes, including frequency of diary use and ability to perform daily routines that require recall of information and events (Ho *et al.*, 2011). Our

results suggest comprehensive interventions that foster memory skills and promote generalizability of these skills to everyday life are warranted for children born VP.

The use of a comprehensive measure of prospective memory in this study was novel and a major strength, enabling us to explore more functional aspects of memory as they may manifest for children born VP in everyday contexts. However, we acknowledge some methodological limitations. The lack of validated measures of prospective memory in children resulted in the use of an experimental measure, the sensitivity, and validity of which are yet to be established. The nature of the prospective memory measure also limited the degree of environmental control that could be used to reduce the influence of external factors on participant performance. For example, participants were free to employ additional strategies and may have been exposed to additional prompting beyond the assessment setting for long-term items. There was sample size imbalance across groups, with a smaller control group, which can affect statistical power and increase the Type II error rate. Unfortunately, recruitment ceased early in line with government regulations limiting face-to-face assessment during the COVID-19 pandemic.

It is also important to note two considerations in the interpretation of our data. Firstly, our findings are based on scores corrected for prematurity, given that use of chronological age underestimates true cognitive ability in children born preterm throughout childhood and adolescence, particularly at lower gestational ages (Wilson-Ching et al., 2014). Age correction is uncommon in clinical practice, and group differences would likely be even greater without this correction. Secondly, measures with US norms can result in inflated scores in Australian samples, as has been observed across various measures for example, the Bayley-III (Spencer-Smith et al., 2015), original WASI (Beauchamp et al., 2013; Cheong et al., 2013), and WISC-IV (Hutchinson et al., 2013). This is the likely explanation for higher-than-expected IQ scores for the VP and control groups in our study.

We propose several directions for further research. Given development of executive functioning beyond 13 years (Anderson et al., 2001), further research is needed to understand the developmental trajectories of functional memory systems that interact with executive functions. More broadly, our findings and emerging evidence of prospective memory difficulties in other pediatric populations (e.g., traumatic brain injury; Phillips et al., 2018) highlight that research regarding functional memory in children is lacking and warrants further attention, which relies on further development and validation of pediatric prospective memory measures. Most importantly, intervention approaches are needed to support children with functional memory difficulties. These interventions may be informed by better understanding the mechanisms for poorer prospective memory in children born VP. To this end, examining the relationship between prospective memory functioning, episodic memory, and executive functions thought to underly effective prospective memory (i.e., working memory, planning, cognitive flexibility, inhibition, self-monitoring) may be an important starting point (Kliegel et al., 2002; Mahy et al., 2014). Finally, further research is required to understand whether the memory difficulties identified in children born VP are indicative of a specific vulnerability and primary memory deficit, or secondary to more generalized cognitive impairment.

This study emphasizes that the challenges associated with VP birth also often include functional memory difficulties, such as verbal and visuospatial episodic memory, time-based prospective memory, and everyday memory tasks. The continuation of

functional memory difficulties beyond early childhood also indicates the importance for more long-term surveillance of cognitive and functional outcomes in children born VP, and underscores the importance for clinicians to consider prospective memory in pediatric neuropsychological assessment.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S1355617722000170>

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Conflicts of interest. None.

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