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Risk factors for executive function difficulties in preschool and early school-age preterm children

Sari O'Meagher^{1,2}, Nenagh Kemp², Kimberley Norris², Peter Anderson^{3, 4}, Clive Skilbeck²

- 1. Department of Psychology, Royal Hobart Hospital, Hobart, Australia
- 2. School of Medicine (Psychology), University of Tasmania, Hobart, Australia
- 3. Monash Institute of Cognitive and Clinical Neurosciences, Monash University, Melbourne, Australia
- 4. Clinical Sciences, Murdoch Children's Research Institute, Melbourne, Australia

Corresponding author: Sari O'Meagher, University of Tasmania, School of Medicine (Psychology),

Private Bag 30, Hobart TAS 7001, Australia

Tel: +61 (0)3 6226 2237 Fax: +61 (0)3 6226 2883

Email: sari.omeagher@utas.edu.au

Short running title: Executive functions of young preterm children

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ABSTRACT

O'Meagher SH, Kemp NM, Norris K, Anderson PJ, Skilbeck CE.

Risk factors for executive function difficulties in preschool and early school-age preterm children.

Aim: To investigate the relationship between executive functioning and social and perinatal risk factors in four- to five-year-old preterm children.

Methods: 141 children born preterm (< 33 weeks of gestation) and 77 term comparison children were assessed using standardized measures of general intelligence and performance-based executive function tests prior to starting kindergarten. Parental and teacher reports of executive functioning were completed when the children commenced kindergarten. The preterm and the term comparison groups were compared on measures of intelligence and executive functions using independent groups *t*-tests, and multivariate regression analyses were performed to identify factors predictive of intelligence and executive functioning in the preterm group.

Results: The preterm group performed significantly more poorly than the comparison group on all intelligence and executive function tests. The parental reports of the preterm and term comparison children's executive function did not differ significantly, but the teachers reported elevated executive function difficulties for the preterm group. Higher social risk, in particular lower educational level of the main caregiver, was the strongest predictor for the preterm children's intelligence and executive function results.

Conclusion: Social risk factors are strongly associated with impaired early executive function outcomes in preterm children.

Keywords

Executive functions, preschool, preterm, risk factors, social risk

Key Notes

- Preterm children are at a higher risk of developing executive function difficulties than their fullterm peers.
- Social risk, and especially main carer education level, are key predictors for cognitive and executive function difficulties at school entry for preterm children.

Further studies investigating preventive and remedial strategies to address differences in

cognitive outcomes between preterm and full-term children are warranted.

Background

Preterm birth is defined as birth occurring before 37 weeks' gestation (1). It is known that school-age children born preterm are at increased risk of cognitive problems compared to their full-term peers, including executive function (EF) difficulties (2, 3). Executive functions, such as working memory, self-control, cognitive flexibility and organisational skills, form an important basis of successful entry to school. In fact, it has been reported that executive functions are more strongly associated with school readiness than is general intelligence (IQ) (4). Nevertheless, many preterm children are not routinely monitored in terms of their development, and when it does occur, surveillance is often limited to the first couple of years of preterm children's lives. This is largely due to lack of resources, but also a limited understanding of the persistence of higher order cognitive difficulties, which can occur despite acceptable developmental progress in infancy.

Given the importance of executive functions for the transition to school in preterm children, the early detection of children at high-risk of EF difficulties has implications for surveillance and early intervention. There are numerous early medical and demographic factors that may help identify high-risk children, including gestational age, male sex, higher social risk, and neonatal complications associated with longer hospital stays (e.g., brain injury, and infections). While previous research has demonstrated that these factors predict school-age cognitive outcomes (5-8), it is less clear whether they are predictive of preschool general intelligence and executive functioning. Some researchers have found associations between medical/demographic factors and EF in preschool populations (e.g., 9,10), but these studies have often used less well known tasks, rather than standardized assessment tools. It is important to gain a better understanding how we can utilize both the knowledge of medical and demographic risk factors and clinical assessment results to identify children most at risk. Early identification of children at risk of EF and cognitive deficits allows for intervention and remediation prior to school-entry, thereby potentially reducing adverse effects on educational and academic attainment.

The main aim of the current study was to examine the association of social and perinatal risk factors with cognitive functioning in preschoolers born preterm, with a focus on executive functioning. We measured a range of executive function components, and utilized both performance-based and questionnaire outcomes. On the basis of previous findings with school-aged children, we hypothesised that earlier gestational age, higher social risk, male sex, and longer hospital stay would be predictive of lower IQ and poorer executive functioning. An additional aim was to assess the magnitude of the cognitive deficits in the preterm group by comparing them to a term comparison group.

Participants and assessment process

Preterm children eligible for this study were born at less than 33 weeks' gestation and cared for at the Royal Hobart Hospital (RHH) (n=184) in 2007-2009. After University ethics committee approval, 141 children (77%) were recruited from the routine follow-up of preterm infants offered by the RHH Neonatal Intensive Care Unit Follow-up Clinic as close as possible to their fourth birthday. As this study had a strongly clinical focus, age was not corrected for prematurity. In clinical practice, age is corrected

for prematurity up to two to three years but not beyond (11), and generally there is no extra consideration for degree of prematurity in the education system. Ten children were not contactable or had moved away, six declined to participate in the study, and 27 did not attend after multiple reminders. The mean gestational age of the participating preterm children was 29.69 weeks (range 23.6-32.5 weeks), and none had congenital syndromes. Children who could not participate in subtests due to significant global delay or sensorimotor issues (n=5) were given the minimum score on those subtests.

The four- to five-year-old comparison group participants (*N*=77) were recruited from local schools (pre-kindergarten groups and kindergarten, i.e., prior to compulsory formal schooling), and by advertising at the RHH. All were born at or over 38 weeks' gestation and had no diagnosed disabilities. The preterm and comparison groups were matched for the age at the time of the questionnaire completion, sex distribution and social risk. However, the preterm group was younger at the time of the performance-based assessment. This was partly mitigated by using age-standardized scores or controlling for age. Table 1 shows the preterm group and comparison group characteristics.

The children's socioeconomic risk was determined by a social risk index (12). The six risk factors are maternal age at the time of birth, family structure, main carer education level, main income earner occupation, main income earner employment status, and language spoken at home, all of which have a risk scale from 0 (low risk) to 2 (high risk). The total score was calculated by combining the six factors. We used the length of hospital stay as an overall indicator of medical risk. There were insufficient numbers in this study to compare separate medical complications such as brain injury or infections.

Performance based assessment (four years)

At four years, the preterm children underwent performance-based intellectual and executive function assessment. General intelligence was assessed with the *Wechsler Preschool and Primary Scale of Intelligence, 3rd edition* (WPPSI-III) (13), and the cognitive functioning of the preterm and comparison group was compared on the subtests of Block Design, Matrix Reasoning, Information and Coding. Due to logistical issues, a small number of term comparison children (*n*=9) were older than four years when completing the performance-based assessments.

To assess executive functioning, subtests from the *Developmental Neuropsychological Assessment battery* (NEPSY-II; 14) were administered to both groups (narrative memory recall, sentence recall and word generation), along with the *Shape School Task* (15), and the *Day-Night Stroop* (16). The *Shape School Task* is a measure of inhibition, switching set and combination of both skills. It is a storybook-like assessment tool for pre-schoolers with human-like coloured shape figures. In condition A (control measure for baseline naming speed), the child is told that the figure's name is the colour, and the child has to say the name (colour) as quickly as possible without making any errors. In Condition B (Switch), the figures have both happy and sad faces. The child is told to name only the shape of the figures that are happy and inhibit saying the names of the sad shapes. In conditions C and D, some figures are wearing hats. In condition C, the child has to say the colour of the figures with hats

and the shape for figures without hats, measuring cognitive shifting. Both conditions B and C require keeping two rules in mind, placing demands on working memory. The *Day-Night Stroop* can be used with young children to measure switching and inhibition abilities. In this test, the child is required to say "day" when presented a page showing a night-time sky and "night" when shown a picture of a sun (16 trials). The WPPSI-III and NEPSY-II provide standardized age norms. For the Day-Night and Shape School tasks we used raw scores, but age-controlled scores when comparing the preterm and term groups.

Questionnaire assessment (four to five years)

The year following the performance-based cognitive assessment, when the preterm children were four to five years old and had started kindergarten, their parents and teachers were sent the *Behavior Rating Inventory of Executive Function – Preschool Version* questionnaires (BRIEF-P; 17). This is a rating scale developed to measure everyday behaviours associated with specific areas of executive functioning in children aged two to five years. It has five subscales: Inhibit, Shift, Emotional Control, Working Memory and Plan/Organize. The scales have three summary indexes: the Inhibitory Self-Control Index, the Flexibility Index, and the Emergent Metacognition Index. Age-standardized scores were used in the study. The questionnaires were not provided at the time of the performance-based assessments as the children were not yet at school and we wanted concurrent reports from parents and teachers. Parents and teachers of both groups were informed that the study's aim was to compare the higher cognitive functioning of preterm and term children. While the teachers were not specifically informed if the child was born preterm, they may have had that knowledge. The teacher questionnaires were completed three to five months after the start of the school year. We had high return rates: 95% of parent and 75% of teacher questionnaires.

Results

Between-group comparisons (preterm vs. comparison) on standardized measures of IQ and EF were assessed on all measures using independent-groups t-tests, with Bonferroni correction for multiple comparisons and controlling for the effects of age where necessary. The preterm group performed significantly more poorly than the comparison group on all intelligence and executive function tests (effect size g=0.49 to 1.5; see Table 2). As standardized scores are not available for the Day-Night and Shape School tasks, analyses of covariance were performed, controlling for age. All statistical differences persisted (Table 2). Based on parental report, there were no significant group differences on the BRIEF-P (g=0.00 to 0.24). However, the teachers reported elevated difficulties for the preterm group on several subscales: inhibition, working memory, planning/organizational skills, self-control and overall emergent metacognitive skills (g=0.42 to 0.64; see Table 3).

Simultaneous multiple regression analysis was used to examine factors that may predict IQ and EF in the preterm group (gestational age, birthweight, social risk, sex, and length of hospital stay).

Due to issues of multicollinearity, we assessed the effects of gestational age and length of stay separately, using two regression models. Gestational age is a well-known predictor for outcomes of preterm children, but length of stay in hospital had the highest number of correlations with the IQ and EF outcomes in our study. Thus, we first investigated the associations of gestational age, sex and overall social risk level with the cognitive and executive function outcome measures by using simultaneous regression analysis. Next, we used the length of hospital stay instead of gestational age. Higher social risk was independently associated with all intellectual measures (standardized β=-0.22 to -0.52), performance-based executive function assessment results (standardized β=-0.24 to -0.42), and most parent and teacher questionnaire results in both models (standardized β=0.30 to 0.51). Male sex independently predicted poorer outcome on four mainly verbal subscales on the WPPSI-III, lower verbal and full scale IQ and memory (standardized β=0.16 to 0.32). Gestational age was independently associated with only five out of 18 performance-based measures (mainly those including naming and processing speed; standardized β =0.16 to 0.25), and it had some association with the questionnaire scores (standardized β=-0.24 to 0.38). Length of hospital stay was independently associated with some IQ measures (standardized β =-0.17 to -0.30), two performance-based EF measures (standardized β =-0.24 to -0.25), and some reported EF difficulties (standardized β=0.22 to 0.37). To investigate social risk in more detail, we conducted a further multiple regression analysis in which we entered all the separate social risk factors simultaneously. The analysis indicated that the main carer education level was the strongest predictor for executive function (standardized β =-0.22 to 0.40).

Discussion

The current study aimed to identify predictors of executive function difficulties in school-entry preterm children. The preterm group performed significantly more poorly than the term comparison group on direct measures of IQ and EF. These results are similar to those reported in older preterm children (2, 18). This robust finding supports our premise that cognitive difficulties in preterm children are evident at preschool age, and emphasises the need to develop preventive and remedial measures to reduce the discrepancy between preterm and full-term children. However, there were conflicting results between parents and teachers who rated executive functioning in everyday settings. Specifically, the parents in the preterm group and the parents in the comparison group reported their children as having similar rates of difficulty. In contrast, the teachers of the preterm children reported the children as having more difficulties with inhibition, working memory, planning/organizational skills and self-control than did the teachers of the comparison group. A possible explanation for this discrepancy is that parents of the preterm children may feel encouraged by the early developmental outcomes of their children, who may have been given initially a cautious or negative prognosis, and thus they may overestimate the higher-level cognitive abilities of their children. Alternatively, executive function difficulties may not be evident in the preterm four- to five-year-olds at home, but they may be more evident in the school setting in which children are required to be more focussed and organized and to

comply with group rules and instructions. The teachers may be more perceptive of mild cognitive and behavioural difficulties than parents, given teachers' more extensive experience.

Contrary to our expectations, only social risk was strongly associated with all executive functions. Low educational level of the main caregiver (i.e. less than 11 years of education) was the strongest social predictor of poorer executive function. This finding is in agreement with general population studies of children from higher social risk backgrounds having less proficient executive functions (6, 19), and with reports that socio-economic environment has a greater impact on cognitive outcomes than the genetic profile of the child (20). There is some previous evidence of lower parental education level impacting negatively on the development of children's executive functions (21, 22), with the current study contributing in this regard. However, more studies are needed, especially in the preterm preschoolers, to investigate the association. Also, we did not assess the intellectual and executive functioning of the caregivers of the children in the current study. Such further research could clarify how much impact the genetically inherited intellectual capacity and the caregivers' executive function skills may have on the development of preterm children's executive functions compared to other social, medical and educational factors. We did not separately control the preterm children's IQ as IQ overlaps with EF, and using it as a co-variate can produce overcorrected findings about neurocognitive function (23).

Unexpectedly, gestational age and the length of hospital stay were not independent predictors of executive function difficulties in our preterm group. Many studies have shown that the risk of developmental and cognitive difficulties increases with decreasing gestational age (5, 24). Nevertheless, some researchers have not found gestational age to be such a strong predictor (25, 26). While gestational age has been shown to have a clear association with survival rates and severe neurodevelopmental delays of preterm children, it is possible there is more variability in how the gestational age impacts on higher cognitive processes, especially in younger children. Commonly recognized risk factors like gestational age, medical complications, and sex of a child cannot be modified. However, our findings offer a more positive message for parents of preterm children and professional working with them: there are other factors, such as social risk, that can be possibly be mitigated, providing better outcomes for preterm children.

The question remains as to whether children born in recent decades have a different outcome to the children born in the previous century, due to improvements in medical and therapeutic care. It should be noted that all preterm children in our study had access to regular medical/allied health surveillance and free preschool educational/allied health therapies provided by the state. Further studies on the effect of preterm child follow-up and associated interventions could strengthen understanding of its relevance to EF outcomes.

In summary, these results emphasize the importance of the social environment on the development of preterm pre-schoolers' executive functions. There is a need for research examining why the children from families at greater social risk have poorer outcomes, to enable the establishment of

possible interventions to assist these vulnerable children. There are psycho-social, parenting and educational intervention programmes that have been shown to have a positive impact on cognitive and behavioural development, and to improve executive functioning of children living in high social risk families in general populations (27, 28). Nevertheless, intervention programs aiming to improve the cognitive and executive function outcomes of preterm children have not generally been proven to have long-term effects (29, 30). There is a clear need for more effective identification of higher-level cognitive difficulties prior to preterm children entering school, especially when they come from families with high social risk. Such identification would allow for intervention, remediation and support prior to schoolentry, thereby reducing potential effects on educational and academic attainment.



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Conflict of interest statement

There are no conflicts of interest

Ethics committee approval

This study was approved by the Tasmanian Human Research Ethics Committee (H0011567) and the Tasmanian Social Science Ethics Committee (H0014174).

Abbreviations

BRIEF-P Behavior Rating Inventory of Executive Function–Preschool Version

EF executive functions

IQ intelligence quotient

NEPSY-II Developmental Neuropsychological Assessment battery, 2nd edition

RHH Royal Hobart Hospital

WPPSI-III Wechsler Preschool and Primary Scale of Intelligence, 3rd edition

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Table 1 Preterm and control group characteristics

Boys, <i>n</i> (%)	70.00 (49.6)	45.00 (58.4)	1.55
Girls, <i>n</i> (%)	71.00 (50.4)	32.00 (41.6)	1.55
Age (months)at IQ/EF assessment (mean,	49.10 (48-58)	54.86 (48-67)	11.40***
range) ^a			
Age (months) at parent questionnaires (mean,	58.33 (48-66)	57.35 (48-64)	-2.18
range)			
Age (months) at teacher questionnaires	58.40 (48-68)	58.41 (48-68)	-0.41
(mean, range)			
	M SD	M SD	t
Social risk index (the below risks combined)	2.98 2.61	3.26 2.62	0.74
Maternal age ^b	0.17 0.38	0.03 0.16	-3.94***
Family structure ^b	0.36 0.75	0.42 0.71	0.54
Main carer education levelb	1.03 0.75	0.90 0.82	-1.20
Main income earner occupation ^b	1.01 0.91	1.03 0.85	0.14
Main income earner work status b	0.63 0.85	0.81 0.81	1.42
Language spoken at home b	0.07 0.12	0.07 0.34	1.57

^{*}p<.05, **p<.01, ***p<.001

Table 2 Intelligence and executive function assessment

	Preterm (<i>n</i> =141)		Comparison						
			(<i>n</i> =77)						
	M	SD	M	SD	t/F*	p	df	g	
WPPSI-III									
Block Design ^a	8.11	3.17	10.55	3.10	4.82	<.001	184	0.77	
Informationa	9.05	4.10	11.05	2.64	3.96	<.001	152	0.54	
Matrix Reasoning ^a	8.47	3.17	10.46	2.91	4.03	<.001	184	0.64	
Coding ^a	7.05	3.55	10.95	2.37	8.72	<.001	149	1.20	
<u>NEPSY-II</u>									
Narrative Recalla	5.23	2.33	8.77	3.25	8.17	<.001	170	1.35	
Sentence Recalla	7.21	3.86	11.25	2.90	7.40	<.001	129	1.12	

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^a scaled scores/scores adjusted by age utilised for comparison

^b social risk scores scaled 0(low)-2(high), e.g. maternal age <18 years=2, 18-21years=1, >21years=0

Word Generation ^a	8.04	3.38	12.07	2.34	9.08	<.001	140	1.29
D N: 11 F#:	0.40	0.40	0.07	0.45	0.00	004	400	4.50
Day-Night Efficiency ^b	0.18	0.12	0.37	0.15	8.60	<.001	136	1.50
(adjusted by age)	0.18	0.02	0.37	0.02	37.2	<.001	136	0.95
Shape A Efficiency ^b	0.55	0.24	0.78	0.28	5.30	<.001	145	0.49
(adjusted by age)	0.58	0.03	0.73	0.04	6.15	.014	145	0.44
Shape B Efficiency ^b	0.44	0.22	0.66	0.30	4.73	<.001	135	0.88
(adjusted by age)	0.46	0.03	0.63	0.04	8.67	.004	135	0.50
Shape C Efficiency ^b	0.18	0.09	0.28	0.12	5.00	<.001	116	0.92
(adjusted by age)	0.19	0.01	0.28	0.02	12.2	.001	116	0.59

^{*}F-values provided for age-adjusted scores, analysed by ANCOVA

Table 3 Parent and teacher reporting of executive functioning (BRIEF-P, scaled scores)

	Preterm		Compari	Comparison				
	M	SD	М	SD	t	p	df	g
<u>Parents</u>	(n=81)		(n=49)					
Inhibit	52.50	12.06	51.00	11.37	-0.71	.478	128	0.13
Shift	49.63	11.15	47.98	8.62	-0.89	.376	128	0.16
Emotional Control	50.90	12.69	50.65	11.69	-0.11	.912	128	0.02
Working Memory	55.48	15.61	52.04	11.68	-1.33	.155	122	0.24
Plan/Organize	51.62	13.97	51.61	13.12	-0.00	.998	128	0.00
Self-Control	51.88	13.18	50.04	11.07	-0.82	.416	128	0.15
Flexibility	49.99	12.62	49.06	10.69	-0.43	.669	128	80.0
Emergent	54.23	15.64	51.61	12.38	-1.06	.293	119	0.18
Metacognitive								
<u>Teachers</u>	(<i>n</i> =105)		(<i>n</i> =46)					
Inhibit	50.92	11.89	45.43	8.80	-2.81	.006	149	0.50
Shift	47.48	9.11	45.83	7.01	-1.09	.276	149	0.19
Emotional Control	46.15	7.31	45.46	7.39	-0.54	.592	149	0.09
Working Memory	54.09	12.34	47.00	7.57	-4.32	<.001	132	0.64
Plan/Organize	52.92	14.13	45.20	8.76	-4.09	<.001	132	0.60

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^ascaled scores, ^braw scores

Self-Control	48.86	10.14	44.65	9.49	-2.39	.018	149	0.42
Flexibility	46.92	8.57	44.83	7.35	-1.44	.151	149	0.25
Emergent	53.87	13.50	46.11	7.95	-4.40	<.001	136	0.64
Metacognitive								