**Executive Functioning in Children with Unilateral Cerebral Palsy: Study Protocol**

<table>
<thead>
<tr>
<th>Journal</th>
<th><em>BMJ Open</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID</td>
<td>bmjopen-2012-002500</td>
</tr>
<tr>
<td>Article Type</td>
<td>Protocol</td>
</tr>
<tr>
<td>Date Submitted by the Author</td>
<td>15-Dec-2012</td>
</tr>
<tr>
<td>Complete List of Authors</td>
<td>Brodimede, Harriett; The University of Queensland, Queensland Cerebral Palsy Research Centre Whittingham, Koa; The University of Queensland, Queensland Cerebral Palsy Research Centre Lloyd, Owen; Queensland Childrens Hospital, Department of Rehabilitation Boyd, Roslyn; The University of Queensland, Queensland Cerebral Palsy and Rehabilitation Research Centre; The University of Queensland, Queensland Children’s Medical Research Institute</td>
</tr>
<tr>
<td>Primary Subject Heading</td>
<td>Rehabilitation medicine</td>
</tr>
<tr>
<td>Secondary Subject Heading</td>
<td>Paediatrics, Rehabilitation medicine, Neurology</td>
</tr>
<tr>
<td>Keywords</td>
<td>Paediatric neurology &lt; NEUROLOGY, Stroke &lt; NEUROLOGY, Developmental neurology &amp; neurodisability &lt; PAEDIATRICS, REHABILITATION MEDICINE</td>
</tr>
</tbody>
</table>
Executive Functioning in Children with Unilateral Cerebral Palsy: Study Protocol

Authors:

Harriet L. Bodimeade\textsuperscript{1,2} DPsych (Clin & Clin Neuro), BPsySc (Hons)

Koa Whittingham\textsuperscript{1,2} PhD (Clinical Psychology), BSc (Hons), BA

Owen Lloyd\textsuperscript{3} MPsych (Clin Neuro), BSc (Hons)

Roslyn N. Boyd\textsuperscript{1} PhD, MSc (PT), BSc (Anatomy), BA, BAppSc (PT), Pgrad (Biomech)

\textsuperscript{1} Queensland Cerebral Palsy and Rehabilitation Research Centre, Discipline of Paediatrics and Child Health, School of Medicine, The University of Queensland, Brisbane, Australia;

\textsuperscript{2} School of Psychology, Faculty of Social and Behavioural Sciences, The University of Queensland, Brisbane, Australia;

\textsuperscript{3} Queensland Paediatric Rehabilitation Service, Royal Children’s Hospital, Brisbane, Australia.

Address for Correspondence:

Professor Roslyn Boyd

Queensland Cerebral Palsy and Rehabilitation Research Centre

Department of Paediatrics and Child Health, School of Medicine

The University of Queensland

Level 7, Block 6, Royal Brisbane and Women’s Hospital

Herston, Brisbane, Australia, 4029

Phone: + 61 3365 5315

Email: r.boyd@uq.edu.au

Word count: 5018

Keywords: Cerebral palsy, unilateral cerebral palsy, executive function, psychological functioning
ABSTRACT

Introduction: Early brain injury, as found in children with unilateral cerebral palsy (CP), may cause deficits in higher-order cognitive tasks known as executive functions (EF). This study aims to examine EF in children with unilateral CP and compare their performance to a typically developing reference group (TDC). Exploration of potential laterality effects of unilateral CP on EF will be explored, as will the relationship between cognitive measures of EF, behavioural manifestations of EF, psychological functioning, and clinical features of unilateral CP.

Methods and analysis: This cross-sectional study aims to recruit a total of 42 children with unilateral CP (21 right unilateral CP and 21 left unilateral CP) and 21 TDC aged between 8 to 16 years. Clinical severity will be described for gross motor function (GMFCS) and manual ability (MACS). Outcomes for cognitive EF measures will include subtests from the Wechsler Intelligence Scale for Children – Fourth Edition, Delis-Kaplan Executive Function System, Rey Complex Figure Test, and the Test of Everyday Attention for Children. Behavioural manifestations of EF will be assessed using the Behaviour Rating Inventory of Executive Function, Parent and Teacher versions. Psychological functioning will be examined using the Strengths and Difficulties Questionnaire. Between-groups differences will be examined in a series of one-way analyses of covariance and followed up using linear comparisons. An overall composite of cognitive EF measures will be created. Relationships between EF and psychological measures will be examined using regression analyses.

Ethics and dissemination: This protocol describes a study that, to our knowledge, is the first to examine multiple components of EF using a cohort of children with unilateral CP. Exploration of potential laterality effects of EF amongst children with a congenital, unilateral brain injury is also novel. Possible relationships between EF and psychological functioning will also be investigated. Australian New Zealand Clinical Trials Registration
article focuses:

1) To our knowledge, this protocol outlines the first study to examine multiple components of EF using a cohort of children with unilateral Cerebral Palsy.

2) Exploration of potential laterality effects of EF amongst children with a congenital, unilateral brain injury is also novel.

3) Possible relationships between EF and psychological functioning will also be investigated.

key messages

1) Early brain injury, as found in children with unilateral cerebral palsy (CP), may cause deficits in higher-order cognitive tasks known as executive functions (EF).

2) Executive Function has been conceptualised as comprised of four distinct, yet inter-related components: (i) attentional control, (ii) cognitive flexibility, (iii) goal setting, and (iv) information processing.

3) Executive Function will be examined for the four domains of EF in children with both right and left sided unilateral CP and compared to an age and gender matched group of typically developing children.

strengths and limitations:

4) Study design of prospectively recruited cohort of children with right and left sided unilateral CP and compared to an age and gender matched group of typically developing children.

5) Use of a strong conceptual model of Executive Function as comprised of four distinct, yet inter-related components: (i) attentional control, (ii) cognitive flexibility, (iii) goal setting, and (iv) information processing.
6) Potential Limitations: the sample size is powered to detect differences in EF between unilateral CP and TDC but may not be sufficient to determine differences according to the laterality of the brain lesion in congenital hemiplegia if such differences exist.
INTRODUCTION

Cerebral Palsy (CP) is the leading cause of childhood physical disability in Australia with an incidence of 1 in 500 live births (1). It is estimated that over 17 million people have CP worldwide, with approximately 34,000 in Australia (2). It is projected that 47,000 people will have CP in Australia by 2050 (2). Unilateral CP, with a presumed brain lesion occurring congenitally prior to 28 days old corrected age, is the most common type of CP among children born full term and the second most common type of CP in children born pre term, with an incidence of 1 in 1,300 live births (1, 3). Since the 1950s, there has been an increasing worldwide trend in the diagnosis of unilateral CP, mainly due to decreasing perinatal mortality and a higher survival rate of preterm infants (3).

Caring for people with CP is costly on both the health care system and families. In 2007, the overall financial expenditure for persons with CP in Australia was AUD $1.47 billion (4). It is estimated that it costs AUD $115,000 per annum to care for a person with CP (4). Families, friends, and individuals with CP cover 43% of these costs, with the Australian government bearing the remainder (4). These statistics highlight that sufficiently managing this life-long disability is vital given that there is no cure.

Cerebral palsy is not a single diagnosis but rather an umbrella term that defines a group of conditions with differing levels of motor and postural abnormalities. The most commonly used and acknowledged CP definition is one generated by a committee from the American Academy for CP and Developmental Medicine – “a group of disorders of the development of movement and posture ...that is attributed to non-progressive disturbances that occurred in the developing foetal or infant brain...often accompanied by disturbances of...cognition” (5).

From this definition, the presence of motor and movement impairments is the clinical hallmark of CP; however, many children with CP experience comorbidities such as cognitive,
behavioural, and emotional difficulties (6-10). A population-based register study of children with CP in Australia identified that 45% of children with CP experience cognitive difficulties (2). In later life, CP is related to reduced educational and employment opportunities (11). In comparison to research on motor and movement impairments in CP, there is a lack of literature examining cognitive and psychological difficulties faced by children with CP (12). This is concerning given that these factors are essential to the well-being and overall development of children with CP (13).

Another diagnostic marker for CP is damage to the developing foetal or infant brain. A key systematic review by Krageloh-Mann and colleagues (14) analysed MRI brain scan findings for children with CP and found that in children with unilateral CP, periventricular white matter damage was the most common brain injury, occurring in 36% of children, followed by cortical deep grey matter lesions in 31%, brain malformations (e.g., schizencephaly) in 16%, and miscellaneous lesions in 7% of children. Given that children with unilateral CP have sustained a brain injury, and the fact that research has illustrated a link between brain injuries and reduced cognitive and psychological functioning (15), examination of neuropsychological and psychological functioning in this population is warranted.

Executive Function

‘Executive function’ is an umbrella term that encompasses skills necessary for novel, goal-directed, and complex activity (16-20) including: abstract thinking; problem solving; analysing and reasoning; initiating, monitoring, sustaining, and shifting attention/behaviour; organisation and planning; mental flexibility; goal selection; self-control and regulation; feedback utilisation; and metacognition (21-26). Everyday functioning relies on executive skills and deficits in EF may manifest as: disorganisation and poor planning; inability to focus and attend to tasks; disinhibition; perseveration; careless responding to tasks;
impulsivity and reduced self-control; increased errors without subsequent self-correction, even in the context of feedback; taking longer to complete tasks; and inflexible thinking and behavioural patterns (27, 28).

It has been argued that executive skills are only triggered in unfamiliar or novel situations where previously learned and instinctive behaviours/plans are no longer relevant (29, 30). Among children, it is difficult to define what tasks are novel, as what may be complex for one child may be relatively easy for another (21). Others have found that executive abilities are required to successfully complete most daily activities (31). Use of the executive system is therefore not solely restricted to situations that produce novelty, particularly in children; rather, they are pivotal in almost all areas of adaptive day-to-day functioning.

As well as being important for cognitive functioning, executive skills are also involved in emotional responses, behavioural actions, and social skills (32). Consequently, a distinction between the traditional cognitive or ‘cold’ and affective or ‘hot’ EF has been proposed (33). ‘Cold’ EF refers to classic cognitive difficulties ascribed to executive dysfunction, such as organisation, problem solving, and inhibition (34). In comparison, EF that involve emotional aspects, regulation of one’s own social behaviour, empathy, and theory of mind are ‘hot’ executive skills (35). Despite the seemingly dichotomous separation of cognitive and affective executive components, these two aspects are thought to be intimately associated and invariably used in conjunction for daily functions (36).

Findings from functional neuroimaging studies, predominantly in adult brain-injured populations, have indicated that EF is principally mediated by the frontal lobes, particularly the prefrontal cortex (23, 31). The frontal lobes demonstrate rich efferent and afferent connections with nearly all other posterior and subcortical cerebral regions (26, 37). It is thought that the frontal lobes integrate and coordinate information and in essence work as the
‘control master’ of the brain (38). As a consequence, the frontal lobes are important for EF but it is the integrity of the entire brain that is pivotal for successful executive skills (27, 39). In children and adolescents, the frontal lobes are the last brain region to reach maturity, typically by the end of the second decade of life (40). The refinement of intricate white matter tracts from these underlying brain regions to the frontal lobes and ongoing myelination are also important aspects of prefrontal maturation and in turn, the progression of executive skills (40).

There is some evidence suggesting lateralisation of verbal and spatial aspects of executive functioning amongst adults. For example, utilising position emission tomography (PET), asymmetrical organisation of visual and verbal working memory skills, a component of executive function, was shown amongst a cohort of female adults aged 18 to 30 years. Predominantly left lateralisation occurred during a verbal memory task whereas right lateralisation was shown during a spatial working memory task (41). However, within paediatric literature, there is a paucity of research exploring possible laterality of EFs amongst children, and findings from adult cohorts cannot be extrapolated to children given their ongoing development. Moreover, amongst unilateral CP, a congenital brain injury has occurred, rather than one acquired later during development. This may also change the picture of potential lateralisation given the possibility for functional re-organisation in the developing brain (42). There is some evidence of functional re-lateralisation of lower level cognitive functions in children, particularly related to visuospatial and language skills, following early brain injury (43). Research by Lidzba and colleagues (43) has highlighted that children with both left and right unilateral CP show preserved language functions at the cost, however, of poorer visuospatial skills. It appears that visuospatial deficits in children with early left hemispheric lesions are a consequence of lesion-induced right hemispheric language re-organisation. This phenomenon is known as the cognitive crowding hypothesis.
(42). It is unknown whether this functional re-lateralisation would apply to EFs.

Development of Executive Functions

As executive skills show a prolonged development through childhood and adolescence, it is important to understand the normal development of these skills in order to identify deviations from projected maturational patterns. An analogous relationship between the maturing frontal lobes and the unfolding of executive skills is seen (16). This parallel relationship typically emerges along a hierarchical developmental trajectory often in growth ‘spurts’ rather than developing in a uniform fashion (44, 45). Major neurophysiological growth spurts occur from birth to 2 years, 7 to 9 years, and again in adolescence from 16 to 19 years (16, 25, 46). These timeframes involve peak periods of synaptogenesis and increased myelination with corresponding improvements in specific EF domains (44).

A conceptual framework of EF in typically developing children, proposed by P. Anderson (47), operationalises EF as an overall control system that is comprised of four distinct, yet inter-related, executive components: (1) attentional control, the earliest EF domain to emerge, involves the ability to maintain and focus attention for extended periods of time and the capability to selectively focus one’s attention towards target stimuli; (2) cognitive flexibility, the ability to correct and learn from errors, flexibly shift from one response set to another, and generate multiple and alternative strategies to problems; (3) goal setting, the ability to generate novel goals and initiatives, plan actions and strategies, and complete tasks in an organised and proficient manner; and (4) information processing, the ability to fluently and efficiently complete tasks and the overall processing speed and speed of output (Figure 1). This model of EF is unique in the paediatric neuropsychological literature as it incorporates a developmental context, highlights that each executive component operates in an integrative manner, and considers each component as having a separate developmental trajectory.
Executive Functions in Cerebral Palsy

In spite of the importance of executive skills for the successful achievement of academic, behavioural, social, and adaptive day-to-day functions, there is a paucity of research examining EF in children and adolescents with unilateral CP. Research among other paediatric populations, such as in childhood stroke (48) and focal frontal lobe lesions (49), has shown EF is particularly susceptible to early brain insult during the prenatal and perinatal periods. Recent research has also established that executive difficulties are present following early brain insult to any region of the brain—it does not need to be a frontal lesion for executive deficits to be seen (50-52). Brain injury sustained early in development (i.e. before age 3) has been shown to result in global executive deficits across several executive components (50, 53).

Recent research has noted EF deficits among children and adolescents with CP (54-57). In Bottcher and colleague’s (54) study, children (9-13 years old) with either unilateral CP (n=14) or diplegia (n=18) were found to have attentional deficits, as measured by subtests from the Test of Everyday Attention for Children (TEA-Ch), EF deficits, as measured by the Contingency Naming Test (CNT), and deficits in behavioural manifestations of EF in everyday life as measured by the BRIEF. It was found that both the unilateral and diplegia CP groups scored significantly below aged based norms on all measures and there was a non-significant trend for children with diplegia to perform poorer than those with unilateral CP (54). In a similar study, a smaller cohort of children (8-17 years old), again with either unilateral CP (n=8) or diplegia (n=9), were rated as showing clinically significant impairments on measures of attention, impulsivity, and vigilance from the Conners’ Continuous Performance Test (CCPT), with children with diplegia showing significantly higher impairments than those with unilateral CP (57).

The relationship between arithmetic difficulties and EF in children with CP has also
been investigated (55, 56). In one study, first graders (mean age of 7 years) with CP were split into two groups—those attending a mainstream school \( (n = 16) \) and those attending a special school \( (n = 41) \) (56). A control group of 16 first graders without CP, again with a mean age of 7 years, who were attending a mainstream school, were also included. Within the CP mainstream school group, 12 children had unilateral CP, 3 had diplegia, and one had ataxia, while the CP special school group comprised of 10 children with unilateral CP, 29 with diplegia, and 2 with ataxia (56). Executive skills, specifically verbal and visuospatial working memory, were assessed using a Digits Forwards and Backwards task and the Knox Blocks test.

Interestingly, the CP mainstream group had the lowest score on the Digits Forwards tasks, followed by the CP special school group and then the controls. Even though the CP mainstream group performed more poorly than the CP special school group and the CP special school group lower than the controls, neither of these differences reached clinical significance. On the Digits Backwards task, the CP special school group performed significantly worse than the CP mainstream group and the CP mainstream group performed significantly poorer than the control group. Finally, on the Knox Blocks task, the CP special school group performed significantly worse than the CP mainstream group; however, there was no difference in performance between the CP mainstream and control groups (56). Structural equation modelling revealed that tasks assessing working memory skills (i.e. Digits Forwards/Backwards and Knox Blocks) mediated arithmetic ability in both CP groups, such that poorer working memory abilities predicted a lower arithmetic ability (56). A follow-on study by the same authors confirmed that EF, particularly working memory skills, are lower in children with CP (CP types included hemiplegia, diplegia, and ataxia) compared to their typically developing peers and that these predict poorer arithmetic ability (55).

Executive functions have also been examined in a study of 21 school age children
(mean age of 8 years) who had been born preterm with a periventricular haemorrhagic infarction (58). Of these children, 13 had unilateral CP, 3 had diplegia, 1 had minor neurologic dysfunction, and 4 were neurologically normal. The BRIEF was used as the outcome measure for executive skills with results showing executive impairments in 18% (parent report) and 29% (teacher report) of the sample (58). Other research has used the Wisconsin Card Sorting Test (WCST) to examine executive skills among 37 children with unilateral CP and 15 children with diplegia (mean age 11 years old) and 50 matched typically developing peers (59). Results found that children with CP, compared to controls, made more non-preservative errors, completed fewer categories, required more trials to complete the first category, and gave fewer conceptual responses.

This current literature is limited as all existing studies examine mixed groups of CP and/or investigate only one discrete component of EF; thus, the heterogeneous nature of CP and the multidimensional nature of EF is not accounted for and the results may be misleading. Furthermore, the majority of studies lack a typically developing reference group and also do not include both cognitive and behavioural measures of EF. Furthermore the relationship between cognitive EF and behavioural manifestations of EF and psychological functioning has also not previously been explored. This study aims to remedy these gaps in the literature.

**Executive functions following early brain injury**

Research among children who had sustained an early brain injury has also uncovered EF deficits (50, 60). Using a cross-sectional, retrospective group design, Anderson and colleague’s (50) examined EF amongst 164 children (aged 10 to 16 years old) who had sustained a brain injury at varying developmental time points: congenital, perinatal, infancy, preschool, middle childhood, and late childhood. Children with diverse focal pathologies and diagnoses were included across all study groups, such as stroke, penetrating head injury and
contusions, tumour, cysts, and abscesses (50). The study utilised P. Anderson’s (47) conceptual model of EF to assess these skills in children across four components—attentional control, cognitive flexibility, goal setting, and processing speed. Subtests from the Delis-Kaplan Executive Function System (D-KEFS), TEA-Ch, and the Rey Complex Figure were used to assess the four executive domains. Behavioural manifestations of EF in everyday life were also examined using the BRIEF.

Results showed that compared to normative expectations, children who sustained a brain injury before the age of 3 years experienced the most severe and global EF deficits across all domains (50). Regardless of location (i.e. frontal versus non-frontal regions), the presence of brain pathology was found to lead to executive dysfunction. These findings lend further support for the early vulnerability hypothesis of brain insult sustained early in development, as children with earlier lesions were most at risk for global EF impairments. The study findings also support the notion that injury to any part of the brain may disrupt neural circuits involved in EF and that there appears to be a lack of functional specificity in the immature brain (50). Even though children with unilateral CP, by definition, have sustained damage to the developing foetal or infant brain there is a paucity of research specifically on EF and unilateral CP.

**Aims and hypotheses**

The broad aim of this prospective cohort study of children with unilateral CP (21 right, 21 left sided unilateral CP) was to examine their performance on the four domains of EF and to compare this with a group of typically developing age and gender matched children. The primary aim of the current study is to determine the pattern of EF in children and adolescents with unilateral CP with the following hypotheses and research questions:

1. It was hypothesised that children with unilateral CP will demonstrate poorer performance on tasks assessing the following EF components:
(a) Attentional control;
(b) Cognitive flexibility;
(c) Goal setting;
(d) Information processing; and
(e) In everyday life.

2. It was hypothesised that children with higher levels of EF (i.e. better executive skills) would show fewer difficulties across the following domains:
(a) Behavioural manifestations of executive dysfunction in everyday life, as measured by the Behaviour Rating Inventory of Executive Function (32);
(b) Emotional functioning, as measured by the Strengths and Difficulties Questionnaire (61, 62);
(c) Behavioural functioning, as measures by the Strengths and Difficulties Questionnaire (61, 62); and
(d) Social functioning, as measured by the Strengths and Difficulties Questionnaire (61, 62).

3. Finally, the profile EF across the EF components (i.e. attentional control, cognitive flexibility, goal setting, information processing, and in everyday life) will be explored for children with left unilateral CP versus right unilateral CP in order to ascertain potential laterality effects of EF following a congenital brain injury.

METHODS AND ANALYSES

Ethics

Ethics approvals have been gained through the University of Queensland School of Psychology Ethics Committee (10-PSYCH-DCP-32-JM) and the Queensland Children’s Health Services Human Research Ethics Committee (HREC/10/QRCH/31). There is no known safety risks associated with any aspect of the study. All parents or legal guardians will
give written informed consent and children aged ≥12 will provide assent, and will be able to withdraw from the study at any time without penalty or any effect on the child’s care. Data collected in this study will be stored in a coded re-identifiable form by ID number. Each child will have one appointment during which all assessment measures will be completed. If desired by parents, all children will receive a brief neuropsychological report outlining their results on EF measures and general strategies to assist any identified cognitive weaknesses.

Recruitment

Children will be recruited from the research database of the Queensland Cerebral Palsy & Rehabilitation Research Centre and from the Queensland Cerebral Palsy Health Service at the Royal Children’s Hospital, Brisbane, Australia. Participants will be assessed for eligibility using a brief parent telephone-screening interview based on study criteria. Typically developing children (age and gender matched) will be recruited as a reference sample. Siblings and friends of children with unilateral CP will be invited to take part in the study, as well as recruitment through staff newsletters and from other studies within the centre.

Selection criteria

Inclusion criteria

Children will be invited to participate in the study if they have a confirmed unilateral CP diagnosis that was diagnosed within 28 days postnatally, are aged 8 to 16 years at study entry, have English as their first language, are able to communicate through spoken language, and live within Queensland.

Exclusion criteria

Children will be excluded from the study if they have an uncontrolled seizure disorder or if CP was acquired postnatally.
Typically developing reference sample

Children are eligible to participate in the reference sample if they are aged between 8 to 16 years, have English as their first language, and do not have a history of developmental, neurological, physical, or psychiatric conditions.

Sample size

A power analysis was conducted and revealed that at least 21 children per group needed to be recruited in order to have sufficient power (0.80) to detect a large effect size utilising an Analysis of Variance with three comparison groups (63). Large effect sizes have been found in previous research comparing the performance of children with CP on tests of attention and EF, such as the TEA-Ch (54).

Classification measures

Family Background Questionnaire (FBQ) (64). Parents will complete an adapted version of the FBQ that gathers basic demographic and background information pertaining to both the parent and child.

Gross Motor Function Classification System (GMFCS) (65). This measure will enable classification of the unilateral CP participants’ gross motor functioning (e.g., the ability to sit, stand, walk, and climb stairs) over a five-level classification system. Research has found strong construct validity between the GMFCS and the Gross Motor Function Measure ($r = 0.91$), a criterion-referenced measure that evaluates change in gross motor function in children with CP (66). High test–retest reliability ($r = 0.79$) (67), inter–rater reliability between professionals (kappa = 0.74) (68), and intra–rater reliability between professionals and parents ($r = 0.94$) (69) has also been documented.

Manual Ability Classification System (MACS) (70). This measure will be used to classify the manual ability of children with unilateral CP to use their hands when handling objects in daily activities over a five-level classification system. Research has shown good construct validity between the MACS and the GMFCS ($r = 0.79$) and high inter–rater reliability between therapists ($r = 0.97$) and intra–rater reliability between parents and therapists ($r = 0.96$) (70).

Strengths and Difficulties Questionnaire–Extended Version (SDQ) (61, 62). Parents will complete the SDQ, a 33 item questionnaire measuring parents’ perceptions of prosocial
and difficult behaviours in their child. The SDQ is able to discriminate well between community and clinic samples and has good construct validity in associations with the Achenbach Child Behaviour Checklist (CBCL; \( r = 0.87 \) and \( r = 0.81 \)) (71, 72). The SDQ total difficulties score has high internal consistency (\( \alpha = 0.73 \)) and high test–retest reliability (\( r = 0.85 \)) (73). The SDQ total scale scores (i.e. Emotional Symptoms, Conduct Problems, Inattention/Hyperactivity, Peer Problems, and Prosocial Behaviour) and the overall total difficulties score will be used as outcome measures for children’s emotional, behavioural, and social functioning.

**Behaviour Rating Inventory of Executive Function–Parent Form and Teacher Form (BRIEF–Parent Form and BRIEF–Teacher Form)** (32). Parents and schoolteachers will complete the BRIEF—an 86 item behavioural measure of EF in their child’s everyday life. The BRIEF yields two index scores: the behavioural regulation index (including initiate, working memory, plan/organise, organisation of materials, and monitor) and the metacognition index (including inhibit, shift, and emotional control). The behavioural regulation index and metacognition index combined form a global executive composite score. Both indexes and composite score can be converted into \( T \) scores with higher \( T \) scores indicating a greater level of executive dysfunction and a \( T \) score of 65 and above indicative of an abnormal elevation (32).

The BRIEF has good convergent and divergent validity with the CBCL and the Behaviour Assessment System for Children (74). High internal consistency, with Cronbach’s \( \alpha \) coefficients ranging from .80 to .98 for both the parent and teacher forms, has also been shown (32, 75). Moderate intra–rater reliability between parents and teachers has been found (\( r = .32 \)), as have high test–retest reliability statistics for the parent form on the BRI (\( r = 0.84 \)), MCI (\( r = 0.88 \)), and the GEC (\( r = 0.86 \)), and for the teacher form on the BRI (\( r = 0.92 \)), MCI (\( r = 0.90 \)), and the GEC (\( r = 0.91 \)) (32, 75).
Outcome Measures of Executive Function

Peter Anderson’s (47) conceptual model of EF will be used to operationalise EF. Ten neuropsychological measures were selected to evaluate the four components (i.e. attentional control, cognitive flexibility, goal setting, and information processing) of this model. The model of EF and list of the neuropsychological measures is reported in Figure 3.

Digit Span Backward from the Wechsler Intelligence Scale for Children–Fourth Edition (WISC-IV) (76). Digit Span Backwards (range 0–16) is a verbal working memory task that requires children to temporarily store and manipulate information. The child has to repeat a number string that increases from 2 to 8 digits in the reverse order. Higher scores indicate a greater level of the cognitive flexibility. Good internal consistency has been documented for Digit Span Backward ($\alpha = 0.80$) and it has high test–retest reliability ($r = 0.74$) (77).

Trail Making Test from the Delis-Kaplan Executive Function System (D-KEFS) (78). The Number Sequencing subtest and the Number–Letter Switching subtest from the Trail Making Test will be used as measures of attentional control and cognitive flexibility, respectively. These pencil and paper tasks require children to connect numbers in numerical order from 1 to 16 (Number Sequencing) or to switch back and forth between connecting numbers in numerical order and letters in alphabetical order (Number–Letter Switching). Outcome is the time taken to complete. Higher scores indicate greater difficulty with attentional control (for Number Sequencing) or cognitive flexibility (for Number–Letter Switching). High test–retest reliability for Number Sequencing ($r = .77$) and moderate test–retest reliability for Number–Letter Switching ($r = 0.20 – 0.55$) has been reported (79).

Verbal Fluency from the D-KEFS (78). Letter Fluency and Category Fluency subtests from Verbal Fluency will be used as measures of attentional control, cognitive flexibility, and goal setting. In Letter Fluency, children are told that they have 60 seconds to name as many
words as they can think of that begin with a specified letter (F, then A, then S) while following specified rules (e.g. do not say names of people). In Category Fluency, children are informed that they again have 60 seconds but that this time they have to name as many different animals and then boy’s names as they can think of.

The total number of words generated for Letter Fluency and Category Fluency will be used as outcomes for goal setting; the total number of repetition errors across both Letter Fluency and Category Fluency will be used as a measure of attentional control; and the total number of set-loss errors (i.e. saying a word that does not belong in the specific category) across Letter Fluency and Category Fluency will be used as a measure of cognitive flexibility. Higher scores for the total number of words generated and fewer numbers of repetition and set-loss errors indicate greater levels of goal setting, attentional control, and cognitive flexibility, respectively. Moderate to high levels of internal consistency for Letter Fluency and Category Fluency in children and adolescents is documented ($\alpha = 0.53 – .80$) (79). Test–retest reliability for people aged 8 to 19 years is high for Letter Fluency ($r = 0.67$) and Category Fluency ($r = 0.70$) (79).

*Colour–Word Interference Test from the D-KEFS* (78). Inhibition and Inhibition/Switching subtests from the Colour–Word Interference Test will be used as measures of attentional control and cognitive flexibility. For Inhibition, children have to name the ink colour that colour words (i.e. “red”, “green”) are printed in. The total time taken in seconds to complete the task and the total number of errors will be used as outcome measures for cognitive flexibility, with higher scores indicating a greater difficulty with cognitive flexibility. For Inhibition/Switching, children have to switch between reading the word and saying the colour of the ink in which the colour word is printed. The total time in seconds to complete the task will be used as a measure of cognitive flexibility while the total number of errors will be used as a measure of attentional control. For people aged 8 to 19
For peer review only

years, an excellent level of test–retest reliability has been shown ($r = .90$) (79). Divergent validity between Inhibition and a measure of verbal memory, the California Verbal Learning Test–Second Edition (CVLT-II: $r = 0.90$) has been documented ($r = 0.27$) (79).

Tower Test from the D-KEFS (78). Tower Test will be used as a measure of goal setting. Across nine items, children move five disks across three pegs to build a target tower shown in a picture within a specified time limit following specified rules (e.g. use the fewest number of moves possible). The total achievement score, which is based on the number of moves needed to make the tower, and the total number of rule violations will be used as outcome measures of goal setting. A higher total achievement score and a lower number of rule violations score indicates higher goal setting ability. Moderate to high levels of internal consistency has been found for the Tower Test for people aged 8 to 19 years old ($\alpha = 0.43 – .84$) (79). Adequate test–retest reliability has also been shown for people aged 8 to 19 years ($r = 0.51$) (79). Evidence for divergent validity has been demonstrated by a low correlation ($r = 0.19$) between the Tower Test total achievement score and the CVLT-II (79).

Rey-Osterrieth Complex Figure Test (80-82). The Rey Figure will be used as a measure of goal setting. Children are instructed to copy a complex geometric figure. The examiner records the order that the child drew the figure, which will allow for the child’s strategic decision-making and organisation to be rated on a scale from 1 (unrecognisable or substitution) to 7 (excellent organisation), as per P. Anderson and colleagues (83).

Osterrieth’s (81) accuracy scoring procedure (score range: 0 – 36, with higher scores indicating greater spatial organisation; $M = 32, SD = 4.2$) and the organisational strategy score will be used as measures of goal setting. Higher scores on both measures indicate a greater goal setting ability.

The Rey Figure accuracy score has good convergent and divergent validity with significant correlations with related tests such as the Hooper Visual Organization and no
significant correlations with language measures such as the Benton Sentence Repetition Test (84). A moderate level of convergent validity between the organisational strategy score and other measures of EF has also been documented (83). High test–retest reliability has been shown for the accuracy scores on the immediate recall trial \( r = 0.76 \) and the delayed recall trial \( r = 0.89 \), as well as for the organisational strategy score \( r = 0.79 – 0.94 \) (83, 84).

Using Osterrieth’s (81) scoring procedure, an excellent level of inter–rater reliability for the copy trial \( r = 0.96 \) has been documented (85). Similarly, the organisational strategy score has shown a high level of inter–rater reliability \( r = 0.85 – 0.92 \) (83).

**Code Transmission Test from the Test of Everyday Attention for Children (TEA-Ch)** (86). The Code Transmission Test will be used as a measure of attentional control. This auditory sustained attention task requires children to listen to a tape recording that recites 360 consecutive numbers (40 targets) that are heard at regular intervals. The child had to identify when they hear two number fives in a row (e.g., “5 – 5”) and then say out loud the number that came before the two number fives. The total number of correctly identified targets will be used as the outcome measure, with a higher number indicating great attentional control (range = 0 to 40). A high level of test–retest reliability has been documented for the Code Transmission Test \( r = 0.78 \) (86). Overall, the TEA-Ch has been shown to be a valid assessment instrument, based on its factor structure, correlation with other measures, and utility in clinical populations (86).

**Symbol Search from the WISC-IV** (Wechsler, 2004). Symbol Search will be used as a measure of information processing. Children are required to visually scan a search group of symbols and indicate, by placing a line through the word ‘yes’ or ‘no’, whether or not a target symbol is in the search group. Children are instructed to work as quickly as they can and are given a two-minute time limit. A total score is generated by subtracting the total number of incorrectly identified symbols from the total number of correctly identified symbols. A higher
score (range = 0 – 60) indicates a greater level of information processing. Raw scores can also be converted into scaled scores ($M = 10$, $SD = 3$). Good internal consistency has been shown for Symbol Search ($\alpha = 0.79$) as has a high level of test–retest reliability ($r = 0.80$) (77).

Cancellation from the WISC-IV (76). Cancellation will also be used as a measure of information processing. In this task, children have to visually scan both a random and structured arrangement of pictures and place a mark through all of the animals. They are instructed to work as quickly as they can and are given 45 seconds for each of the picture arrangements. The total score will be calculated by subtracting the number of incorrectly identified pictures from the number of correctly identified pictures, with higher scores indicating a higher level of information processing (range = 0 – 136). Good internal consistency has been demonstrated for both Cancellation random ($\alpha = 0.70$) and Cancellation structured ($\alpha = 0.75$) (77). Similarly, a high level of test–retest reliability has been shown for Cancellation random ($r = 0.72$) and Cancellation structured ($r = 0.76$) (77). The WISC-IV’s overall validity has been demonstrated, based on the test’s content, response processes, internal structure, and relationships to other variables (77).

Statistical considerations

To test study hypotheses and research questions 1 (a) – (e) and 3, a series of one-way Analyses of Covariance (ANCOVA) will be conducted for each of the neuropsychological assessment measures, controlling for age. If significant between-groups differences are found, each will be followed-up using two a priori linear contrasts: the first comparing the control group with all the unilateral CP participants and the second comparing the left are right unilateral CP participants. An overall composite of the cognitive EF measures will be created by standardising all measures, reversing selected items so that higher scores equalled
better performance, and then aggregating all measures. A series of multiple regressions will be used to test hypotheses 2 (a) - (d).

CONCLUSION

This study protocol describes a prospective cohort study of children with unilateral CP purposely sampled for age and gender for an equal group of children with right and left sided brain lesion to examine their executive functions and compare them to a group of typically developing children. To our knowledge, this is the first study to examine multiple components of EF amongst a cohort of children solely with unilateral CP and the first study to explore possible laterality effects of EF amongst children with a congenital brain injury. In addition, this study examines the relationship between cognitive EF measures, behavioral manifestations of EF in everyday life, and psychological functioning. Results of this study are planned to be published in peer reviewed publications and will be presented at national and international conferences.

Contributions

HB is the chief investigator and together with KW, OL, and RB designed and established this research study as part of HB’s clinical doctorate study. HB, KW, and RB were responsible for ethics applications and reporting. All authors were responsible for the selection of measures. HB will be responsible for recruitment and data collection and HB and KW will be responsible for data analysis. All authors have read and approved the final manuscript.

Funding

This work was supported by the National Health and Medical Research Council (NHMRC) Research Grant (1003887– COMBIT), Career Development Fellowship (10037220–RB) and an NHMRC Hospital Training Fellowship (631712–KW)

Competing interests

The authors declare that they have no competing interests.
Ethics approval

University of Queensland School of Psychology Ethics Committee (10-PSYCH-DCP-32-JM) and the Queensland Children’s Health Services (Royal Children’s Hospital) Human Research Ethics Committee (HREC reference number: HREC/10/QRCH/31).

Provenance and peer review

This protocol has been reviewed as part of HB’s Doctor of Psychology (Clinical Psychology and Clinical Neuropsychology) dissertation, which was awarded on 17.07.2012.

Data sharing statement

Further details of the study protocol can be requested from the corresponding author.

REFERENCES


81. Osterrieth P. Le test de copie d'une figure complexe. Archives de Psychologie. 1944;30:206-56.
84. Meyers JE, Meyers KR. Rey Complex Figure and the recognition trial: Professional manual. Supplemental norms for children and adolescents. Odessa, Fla.: Psychological Assessment Resources; 1996.
Figure 1. Model of EF in children proposed by P. Anderson (47).
Figure 2. Study flow chart
**Figure 3:** Model of EF with corresponding neuropsychological assessments.
STROBE Statement—Checklist of items that should be included in reports of *cohort studies* for  

**Executive Functioning in Children with Unilateral Cerebral Palsy: Study Protocol**

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td><em>(a) Indicate the study’s design with a commonly used term in the title or the abstract (Page 2)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Provide in the abstract an informative and balanced summary of what was done and what was found (page 2)</em></td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported (P5-13)</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses (P13-14)</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Present key elements of study design early in the paper (P15-16)</td>
</tr>
<tr>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (p15)</td>
</tr>
<tr>
<td>6</td>
<td><em>(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (p15-16)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) For matched studies, give matching criteria and number of exposed and unexposed (NA)</em></td>
</tr>
<tr>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (P16)</td>
</tr>
<tr>
<td>8*</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (P17-22)</td>
</tr>
<tr>
<td><strong>Bias</strong></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Describe any efforts to address potential sources of bias (NA)</td>
</tr>
<tr>
<td><strong>Study size</strong></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Explain how the study size was arrived at (P16)</td>
</tr>
<tr>
<td><strong>Quantitative variables</strong></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (P22)</td>
</tr>
<tr>
<td><strong>Statistical methods</strong></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td><em>(a) Describe all statistical methods, including those used to control for confounding (P22)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Describe any methods used to examine subgroups and interactions (P22)</em></td>
</tr>
<tr>
<td></td>
<td><em>(c) Explain how missing data were addressed (P22)</em></td>
</tr>
<tr>
<td></td>
<td><em>(d) If applicable, explain how loss to follow-up was addressed (NA)</em></td>
</tr>
<tr>
<td></td>
<td><em>(e) Describe any sensitivity analyses (NA)</em></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td></td>
</tr>
<tr>
<td>13*</td>
<td><em>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Give reasons for non-participation at each stage (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(c) Consider use of a flow diagram (fig 2)</em></td>
</tr>
<tr>
<td>14*</td>
<td><em>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Indicate number of participants with missing data for each variable of interest (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(c) Summarise follow-up time (eg, average and total amount) (NA protocol)</em></td>
</tr>
<tr>
<td>15*</td>
<td>Report numbers of outcome events or summary measures over time (NA protocol)</td>
</tr>
</tbody>
</table>
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (NA protocol).
| (b) Report category boundaries when continuous variables were categorized (NA protocol).
| (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period (NA protocol).
| Other analyses | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses (NA protocol).

**Discussion**

| Key results | 18 | Summarise key results with reference to study objectives (P23).
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (NA protocol).
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (NA protocol).
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results (NA protocol).
| Other information | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (NA).

*Give information separately for exposed and unexposed groups.*

Executive Functioning in Children with Unilateral Cerebral Palsy: Study Protocol

<table>
<thead>
<tr>
<th>Journal:</th>
<th>BMJ Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID:</td>
<td>bmjopen-2012-002500.R1</td>
</tr>
<tr>
<td>Article Type:</td>
<td>Protocol</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>05-Feb-2013</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>Brodimede, Harriett; The University of Queensland, Queensland Cerebral Palsy Research Centre Whittingham, Koa; The University of Queensland, Queensland Cerebral Palsy Research Centre Lloyd, Owen; Queensland Children's Hospital, Department of Rehabilitation Boyd, Roslyn; The University of Queensland, Queensland Cerebral Palsy and Rehabilitation Research Centre; The University of Queensland, Queensland Children's Medical Research Institute</td>
</tr>
<tr>
<td>Primary Subject Heading:</td>
<td>Rehabilitation medicine</td>
</tr>
<tr>
<td>Secondary Subject Heading:</td>
<td>Paediatrics, Rehabilitation medicine, Neurology</td>
</tr>
<tr>
<td>Keywords:</td>
<td>Paediatric neurology &lt; NEUROLOGY, Stroke &lt; NEUROLOGY, Developmental neurology &amp; neurodisability &lt; PAEDIATRICS, REHABILITATION MEDICINE</td>
</tr>
</tbody>
</table>
Executive Functioning in Children with Unilateral Cerebral Palsy: Cross-Sectional Study Protocol

Authors:

Harriet L. Bodimeade\textsuperscript{1,2} DPsych (Clin & Clin Neuro), BPsySc (Hons)
Koa Whittingham\textsuperscript{1,2} PhD (Clinical Psychology), BSc (Hons), BA
Owen Lloyd\textsuperscript{3} MPsych (Clin Neuro), BSc (Hons)
Roslyn N. Boyd\textsuperscript{1} PhD, MSc (PT), BSc (Anatomy), BAppSc (PT), Pgrad (Biomech)

\textsuperscript{1} Queensland Cerebral Palsy and Rehabilitation Research Centre, Discipline of Paediatrics and Child Health, School of Medicine, The University of Queensland, Brisbane, Australia;

\textsuperscript{2} School of Psychology, Faculty of Social and Behavioural Sciences, The University of Queensland, Brisbane, Australia;

\textsuperscript{3} Queensland Paediatric Rehabilitation Service, Royal Children’s Hospital, Brisbane, Australia.

Address for Correspondence:
Professor Roslyn Boyd
Queensland Cerebral Palsy and Rehabilitation Research Centre
Department of Paediatrics and Child Health, School of Medicine
The University of Queensland
Level 7, Block 6, Royal Brisbane and Women’s Hospital
Herston, Brisbane, Australia, 4029
Phone: + 61 3365 5315
Email: r.boyd@uq.edu.au

Word count: 5018
Keywords: Cerebral palsy, unilateral cerebral palsy, executive function, psychological functioning

ABSTRACT

Introduction: Early brain injury, as found in children with unilateral cerebral palsy (CP), may cause deficits in higher-order cognitive tasks known as executive functions (EF). Executive Function has been conceptualised as comprised of four distinct, yet inter-related components: (i) attentional control, (ii) cognitive flexibility, (iii) goal setting, and (iv) information processing. The aim of this study is to examine EF in children with unilateral CP and compare their performance to a typically developing reference group (TDC). Exploration of potential laterality effects of unilateral CP on EF will be explored, as will the relationship between cognitive measures of EF, behavioural manifestations of EF, psychological functioning, and clinical features of unilateral CP.

Methods and analysis: This cross-sectional study aims to recruit a total of 42 children with unilateral CP (21 right unilateral CP and 21 left unilateral CP) and 21 TDC aged between 8 to 16 years. Clinical severity will be described for gross motor function (GMFCS) and manual ability (MACS). Outcomes for cognitive EF measures will include subtests from the Wechsler Intelligence Scale for Children – Fourth Edition, Delis-Kaplan Executive Function System, Rey Complex Figure Test, and the Test of Everyday Attention for Children. Behavioural manifestations of EF will be assessed using the Behaviour Rating Inventory of Executive Function, Parent and Teacher versions. Psychological functioning will be examined using the Strengths and Difficulties Questionnaire. Between-groups differences will be examined in a series of one-way analyses of covariance and followed up using linear comparisons. An overall composite of cognitive EF measures will be created. Bivariate correlations between the EF composite and psychological measures will be calculated.

Ethics and dissemination: This protocol describes a study that, to our knowledge, is the first
to examine multiple components of EF using a cohort of children with unilateral CP.

Exploration of potential laterality effects of EF amongst children with a congenital, unilateral brain injury is also novel. Possible relationships between EF and psychological functioning will also be investigated. Ethics have been obtained through the University of Queensland School of Psychology Ethics Committee and the Queensland Children’s Health Services Human Research Ethics Committee. Results will be disseminated in peer reviewed publications and presentations at national and international conferences. This study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12611000263998).

Abstract word count: 378
INTRODUCTION

Cerebral Palsy (CP) is the leading cause of childhood physical disability in Australia with an incidence of 1 in 500 live births (1). Unilateral CP, with a presumed brain lesion occurring congenitally prior to 28 days old corrected age, is the most common type of CP among children born full term and the second most common type of CP in children born preterm, with an incidence of 1 in 1,300 live births (1, 3).

Caring for people with CP is costly on both the health care system and families. In 2007, the overall financial expenditure for persons with CP in Australia was AUD $1.47 billion (4).

Cerebral palsy has been defined as “a group of disorders of the development of movement and posture ...that is attributed to non-progressive disturbances that occurred in the developing foetal or infant brain...often accompanied by disturbances of...cognition” (5).

A population-based register study of children with CP in Australia identified that 45% of children with CP experience cognitive difficulties (2). In later life, CP is related to reduced educational and employment opportunities (6). In comparison to research on motor and movement impairments in CP, there is a lack of literature examining cognitive and psychological difficulties faced by children with CP (7). This is concerning given that these factors are essential to the well-being and overall development of children with CP (8).

Another diagnostic marker for CP is damage to the developing foetal or infant brain. A key systematic review by Krageloh-Mann and colleagues (9) analysed MRI brain scan findings for children with CP and found that in children with unilateral CP, periventricular white matter damage was the most common brain injury, occurring in 36% of children, followed by cortical deep grey matter lesions in 31%, brain malformations (e.g., schizencephaly) in 16%, and miscellaneous lesions in 7% of children. Given that children with unilateral CP have sustained a brain injury, and the fact that research has illustrated a
link between brain injuries and reduced cognitive and psychological functioning (10), examination of neuropsychological and psychological functioning in this population is warranted.

**Executive Function**

‘Executive function’ is an umbrella term that encompasses skills necessary for novel, goal-directed, and complex activity (11-15). Everyday functioning relies on executive skills and deficits in EF may manifest as: disorganisation and poor planning; inability to focus and attend to tasks; careless responding to tasks; reduced self-control; and taking longer to complete tasks (16, 17).

Findings from functional neuroimaging studies, predominantly in adult brain-injured populations, have indicated that EF is principally mediated by the frontal lobes, particularly the prefrontal cortex (18, 19). The frontal lobes demonstrate rich efferent and afferent connections with nearly all other posterior and subcortical cerebral regions (20, 21). It is thought that the frontal lobes integrate and coordinate information and in essence work as the ‘control master’ of the brain (22). As a consequence, the frontal lobes are important for EF but it is the integrity of the entire brain that is pivotal for successful executive skills (16, 23).

In children and adolescents, the frontal lobes are the last brain region to reach maturity, typically by the end of the second decade of life (24). The refinement of intricate white matter tracts from these underlying brain regions to the frontal lobes and ongoing myelination are also important aspects of prefrontal maturation and in turn, the progression of executive skills (24).

There is some evidence suggesting lateralisation of verbal and spatial aspects of executive functioning amongst adults. For example, utilising position emission tomography (PET), asymmetrical organisation of visual and verbal working memory skills, a component of
executive function, was shown amongst a cohort of female adults aged 18 to 30 years. Predominantly left lateralisation occurred during a verbal memory task whereas right lateralisation was shown during a spatial working memory task (25). However, within paediatric literature, there is a paucity of research exploring possible laterality of EFs amongst children, and findings from adult cohorts cannot be extrapolated to children given their ongoing development. Moreover, amongst unilateral CP, a congenital brain injury has occurred, rather than one acquired later during development. This may also change the picture of potential lateralisation given the possibility for functional re-organisation in the developing brain (26).

Specifically, there is some evidence of functional re-lateralisation of lower level cognitive functions in children, particularly related to visuospatial and language skills, following early brain injury (27). Research by Lidzba and colleagues (27) has highlighted that children with both left and right unilateral CP show preserved language functions at the cost, however, of poorer visuospatial skills. It appears that visuospatial deficits in children with early left hemispheric lesions are a consequence of lesion-induced right hemispheric language re-organisation. This phenomenon is known as the cognitive crowding hypothesis (26).

**Development of Executive Functions**

As executive skills show a prolonged development through childhood and adolescence, it is important to understand the normal development of these skills in order to identify deviations from projected maturational patterns. An analogous relationship between the maturing frontal lobes and the unfolding of executive skills is seen (11). This parallel relationship typically emerges along a hierarchical developmental trajectory often in growth ‘spurts’ rather than developing in a uniform fashion (28, 29). Major neurophysiological growth spurts occur from birth to 2 years, 7 to 9 years, and again in adolescence from 16 to 19 years (11, 30, 31). These timeframes involve peak periods of synaptogenesis and increased
myelination with corresponding improvements in specific EF domains (28).

A conceptual framework of EF in typically developing children, proposed by P. Anderson (32), operationalises EF as an overall control system that is comprised of four distinct, yet inter-related, executive components: (1) attentional control, the earliest EF domain to emerge, involves the ability to maintain and focus attention for extended periods of time and the capability to selectively focus one’s attention towards target stimuli; (2) cognitive flexibility, the ability to correct and learn from errors, flexibly shift from one response set to another, and generate multiple and alternative strategies to problems; (3) goal setting, the ability to generate novel goals and initiatives, plan actions and strategies, and complete tasks in an organised and proficient manner; and (4) information processing, the ability to fluently and efficiently complete tasks and the overall processing speed and speed of output (Figure 1). This model of EF is unique in the paediatric neuropsychological literature as it incorporates a developmental context, highlights that each executive component operates in an integrative manner, and considers each component as having a separate developmental trajectory.

Executive Functions in Cerebral Palsy

In spite of the importance of executive skills for the successful achievement of academic, behavioural, social, and adaptive day-to-day functions, there is a paucity of research examining EF in children and adolescents with unilateral CP. Research among other paediatric populations, such as in childhood stroke (33) and focal frontal lobe lesions (34), has shown EF is particularly susceptible to early brain insult during the prenatal and perinatal periods. Recent research has also established that executive difficulties are present following early brain insult to any region of the brain—it does not need to be a frontal lesion for executive deficits to be seen (35-37). Brain injury sustained early in development (i.e. before age 3) has been shown to result in global executive deficits across several executive
components (35, 38).

Recent research has noted EF deficits among children and adolescents with CP (39-42). In Bottcher and colleague’s (39) study, children (9-13 years old) with either unilateral CP (n=14) or diplegia (n=18) were found to have attentional deficits, as measured by subtests from the Test of Everyday Attention for Children (TEA-Ch), EF deficits, as measured by the Contingency Naming Test (CNT), and deficits in behavioural manifestations of EF in everyday life as measured by the BRIEF. It was found that both the unilateral and diplegia CP groups scored significantly below aged based norms on all measures and there was a non-significant trend for children with diplegia to perform poorer than those with unilateral CP (39). In a similar study, a smaller cohort of children (8-17 years old), again with either unilateral CP (n=8) or diplegia (n=9), were rated as showing clinically significant impairments on measures of attention, impulsivity, and vigilance from the Conners’ Continuous Performance Test (CCPT), with children with diplegia showing significantly higher impairments than those with unilateral CP (42).

The relationship between arithmetic difficulties and EF in children with CP has also been investigated (40, 41). In one study, first graders (mean age of 7 years) with CP were split into two groups—those attending a mainstream school (n = 16) and those attending a special school (n = 41) (41). A control group of 16 first graders without CP, again with a mean age of 7 years, who were attending a mainstream school, were also included. Within the CP mainstream school group, 12 children had unilateral CP, 3 had diplegia, and one had ataxia, while the CP special school group comprised of 10 children with unilateral CP, 29 with diplegia, and 2 with ataxia (41). Executive skills, specifically verbal and visuospatial working memory, were assessed using a Digits Forwards and Backwards task and the Knox Blocks test.

 Interestingly, the CP mainstream group had the lowest score on the Digits Forwards
tasks, followed by the CP special school group and then the controls. Even though the CP mainstream group performed more poorly than the CP special school group and the CP special school group lower than the controls, neither of these differences reached clinical significance. On the Digits Backwards task, the CP special school group performed significantly worse than the CP mainstream group and the CP mainstream group performed significantly poorer than the control group. Finally, on the Knox Blocks task, the CP special school group performed significantly worse than the CP mainstream group; however, there was no difference in performance between the CP mainstream and control groups (41).

Structural equation modelling revealed that tasks assessing working memory skills (i.e. Digits Forwards/Backwards and Knox Blocks) mediated arithmetic ability in both CP groups, such that poorer working memory abilities predicted a lower arithmetic ability (41). A follow-on study by the same authors confirmed that EF, particularly working memory skills, are lower in children with CP (CP types included hemiplegia, diplegia, and ataxia) compared to their typically developing peers and that these predict poorer arithmetic ability (40).

Executive functions have also been examined in a study of 21 school age children (mean age of 8 years) who had been born preterm with a periventricular haemorrhagic infarction (43). Of these children, 13 had unilateral CP, 3 had diplegia, 1 had minor neurologic dysfunction, and 4 were neurologically normal. The BRIEF was used as the outcome measure for executive skills with results showing executive impairments in 18% (parent report) and 29% (teacher report) of the sample (43). Other research has used the Wisconsin Card Sorting Test (WCST) to examine executive skills among 37 children with unilateral CP and 15 children with diplegia (mean age 11 years old) and 50 matched typically developing peers (44). Results found that children with CP, compared to controls, made more non-preservative errors, completed fewer categories, required more trials to complete the first category, and gave fewer conceptual responses.
This current literature is limited as all existing studies examine mixed groups of CP and/or investigate only one discrete component of EF; thus, the heterogeneous nature of CP and the multidimensional nature of EF is not accounted for and the results may be misleading. Furthermore, the majority of studies lack a typically developing reference group and also do not include both cognitive and behavioural measures of EF. Furthermore the relationship between cognitive EF and behavioural manifestations of EF and psychological functioning has also not previously been explored. This study aims to remedy these gaps in the literature.

**Executive functions following early brain injury**

Research among children who had sustained an early brain injury has also uncovered EF deficits (35, 45). Using a cross-sectional, retrospective group design, Anderson and colleague’s (35) examined EF amongst 164 children (aged 10 to 16 years old) who had sustained a brain injury at varying developmental time points: congenital, perinatal, infancy, preschool, middle childhood, and late childhood. Children with diverse focal pathologies and diagnoses were included across all study groups, such as stroke, penetrating head injury and contusions, tumour, cysts, and abscesses (35). The study utilised P. Anderson’s (32) conceptual model of EF to assess these skills in children across four components—attentional control, cognitive flexibility, goal setting, and processing speed. Subtests from the Delis-Kaplan Executive Function System (D-KEFS), TEA-Ch, and the Rey Complex Figure were used to assess the four executive domains. Behavioural manifestations of EF in everyday life were also examined using the BRIEF.

Results showed that compared to normative expectations, children who sustained a brain injury before the age of 3 years experienced the most severe and global EF deficits across all domains (35). Regardless of location (i.e. frontal versus non-frontal regions), the presence of brain pathology was found to lead to executive dysfunction. These findings lend further support for the early vulnerability hypothesis of brain insult sustained early in
development, as children with earlier lesions were most at risk for global EF impairments. The study findings also support the notion that injury to any part of the brain may disrupt neural circuits involved in EF and that there appears to be a lack of functional specificity in the immature brain (35). Even though children with unilateral CP, by definition, have sustained damage to the developing foetal or infant brain there is a paucity of research specifically on EF and unilateral CP.

Aims and hypotheses

The broad aim of this prospective cross-sectional study of children with unilateral CP (21 right, 21 left sided unilateral CP) is to examine their performance on the four domains of EF and to compare this with a group of typically developing age and gender matched children. The primary aim of the current study is to determine the pattern of EF in children and adolescents with unilateral CP with the following hypotheses and research questions:

1. It is hypothesised that children with unilateral CP will demonstrate poorer performance on tasks assessing the following EF components:
   (a) Attentional control;
   (b) Cognitive flexibility;
   (c) Goal setting;
   (d) Information processing; and
   (e) In everyday life.

2. It is hypothesised that children with higher levels of EF (i.e. better executive skills) would show fewer difficulties across the following domains:
   (a) Behavioural manifestations of executive dysfunction in everyday life, as measured by the Behaviour Rating Inventory of Executive Function (46);
   (b) Emotional functioning, as measured by the Strengths and Difficulties Questionnaire (47, 48);
(c) Behavioural functioning, as measured by the Strengths and Difficulties Questionnaire (47, 48); and

(d) Social functioning, as measured by the Strengths and Difficulties Questionnaire (47, 48).

3. Finally, the profile EF across the EF components (i.e. attentional control, cognitive flexibility, goal setting, information processing, and in everyday life) will be explored for children with left unilateral CP versus right unilateral CP in order to ascertain potential laterality effects of EF following a congenital brain injury.

METHODS AND ANALYSES

Ethics

Ethics approvals have been gained through the University of Queensland School of Psychology Ethics Committee (10-PSYCH-DCP-32-JM) and the Queensland Children’s Health Services Human Research Ethics Committee (HREC/10/QRCH/31). There is no known safety risks associated with any aspect of the study. All parents or legal guardians will give written informed consent and children aged ≥12 will provide assent, and will be able to withdraw from the study at any time without penalty or any effect on the child’s care. Data collected in this study will be stored in a coded re-identifiable form by ID number. Each child will have one appointment during which all assessment measures will be completed. If desired by parents, all children will receive a brief neuropsychological report outlining their results on EF measures and general strategies to assist any identified cognitive weaknesses.

Recruitment

Children will be identified from the research database of the Queensland Cerebral Palsy & Rehabilitation Research Centre and from the Queensland Cerebral Palsy Health Service at the Royal Children’s Hospital, Brisbane, Australia. Parents of potential suitable children identified will be asked by their treating clinician if they seek further information
about the study. After expressing interest and providing consent to be contacted informed consent will proceed with the researchers. Participants will be assessed for eligibility using a brief parent telephone-screening interview based on study criteria (see below). A provisional psychologist will conduct all telephone-screening interviews. If the participant meets the study selection criteria, they will be invited to take part in the study and will be emailed/posted a study information sheet/consent form. A time will then been made for them to take part in the study.

Typically developing children (age and gender matched) will be recruited as a reference sample. Siblings and friends of children with unilateral CP will be invited to take part in the study, as well as recruitment through staff newsletters and from other studies within the centre. A provisional psychologist will again conduct a brief telephone-screen interview to ensure they meet the study selection criteria (see below).

Selection criteria

Inclusion criteria

Children will be invited to participate in the study if they have a confirmed unilateral CP diagnosis that was diagnosed within 28 days postnatally, are aged 8 to 16 years at study entry, have English as their first language, are able to communicate through spoken language, and live within Queensland.

Exclusion criteria

Children will be excluded from the study if they have an uncontrolled seizure disorder or if CP was acquired postnatally.

Typically developing reference sample

Children are eligible to participate in the reference sample if they are aged between 8 to 16 years, have English as their first language, and do not have a history of developmental, neurological, physical, or psychiatric conditions.
Sample size

A power analysis was conducted using g power and revealed that at least 21 children per group needed to be recruited in order to have sufficient power (0.80) to detect a large effect size (0.80) utilising an Analysis of Variance with three comparison groups (49). Large effect sizes have been found in previous research comparing the performance of children with CP on tests of attention and EF, such as the TEA-Ch (39).

Classification measures

*Family Background Questionnaire* (FBQ) (50). Parents will complete an adapted version of the FBQ that gathers basic demographic and background information pertaining to both the parent and child. This includes the presence or absence of seizures and if present whether they are controlled by medication.

*Gross Motor Function Classification System* (GMFCS) (51). This measure will enable classification of the unilateral CP participants’ gross motor functioning (e.g., the ability to sit, stand, walk, and climb stairs) over a five-level classification system. Research has found strong construct validity between the GMFCS and the Gross Motor Function Measure ($r = 0.91$), a criterion-referenced measure that evaluates change in gross motor function in children with CP (52). High test–retest reliability ($r = 0.79$) (53), inter–rater reliability between professionals (kappa = 0.74) (54), and intra–rater reliability between professionals and parents ($r = 0.94$) (55) has also been documented.

*Manual Ability Classification System* (MACS) (56). This measure will be used to classify the manual ability of children with unilateral CP to use their hands when handling objects in daily activities over a five-level classification system. Research has shown good construct validity between the MACS and the GMFCS ($r = 0.79$) and high inter–rater reliability between therapists ($r = 0.97$) and intra–rater reliability between parents and therapists ($r = 0.96$) (56).
**Strengths and Difficulties Questionnaire–Extended Version (SDQ)** (47, 48). Parents will complete the SDQ, a 33 item questionnaire measuring parents’ perceptions of prosocial and difficult behaviours in their child. The SDQ is able to discriminate well between community and clinic samples and has good construct validity in associations with the Achenbach Child Behaviour Checklist (CBCL; \( r = 0.87 \) and \( r = 0.81 \)) (57, 58). The SDQ total difficulties score has high internal consistency (\( \alpha = 0.73 \)) and high test–retest reliability (\( r = 0.85 \)) (59). The SDQ total scale scores (i.e. Emotional Symptoms, Conduct Problems, Inattention/Hyperactivity, Peer Problems, and Prosocial Behaviour) and the overall total difficulties score will be used as outcome measures for children’s emotional, behavioural, and social functioning.

**Behaviour Rating Inventory of Executive Function–Parent Form and Teacher Form** (BRIEF–Parent Form and BRIEF–Teacher Form) (46). Parents and schoolteachers will complete the BRIEF—an 86 item behavioural measure of EF in their child’s everyday life. The BRIEF yields two index scores: the behavioural regulation index (including initiate, working memory, plan/organise, organisation of materials, and monitor) and the metacognition index (including inhibit, shift, and emotional control). The behavioural regulation index and metacognition index combined form a global executive composite score. Both indexes and composite score can be converted into \( T \) scores with higher \( T \) scores indicating a greater level of executive dysfunction and a \( T \) score of 65 and above indicative of an abnormal elevation (46).

The BRIEF has good convergent and divergent validity with the CBCL and the Behaviour Assessment System for Children (60). High internal consistency, with Cronbach’s \( \alpha \) coefficients ranging from .80 to .98 for both the parent and teacher forms, has also been shown (46, 61). Moderate intra–rater reliability between parents and teachers has been found (\( r = .32 \)), as have high test–retest reliability statistics for the parent form on the BRI (\( r = \))
0.84), MCI ($r = 0.88$), and the GEC ($r = 0.86$), and for the teacher form on the BRI ($r = 0.92$), MCI ($r = 0.90$), and the GEC ($r = 0.91$) (46, 61).

**Outcome Measures of Executive Function**

Peter Anderson’s (32) conceptual model of EF will be used to operationalise EF. Ten neuropsychological measures were selected to evaluate the four components (i.e. attentional control, cognitive flexibility, goal setting, and information processing) of this model. The model of EF and list of the neuropsychological measures is reported in Figure 3.

*Digit Span Backward from the Wechsler Intelligence Scale for Children–Fourth Edition* (WISC-IV) (62). Digit Span Backwards (range 0–16) is a verbal working memory task that requires children to temporarily store and manipulate information. The child has to repeat a number string that increases from 2 to 8 digits in the reverse order. Higher scores indicate a greater level of the cognitive flexibility. Good internal consistency has been documented for Digit Span Backward ($\alpha = 0.80$) and it has high test–retest reliability ($r = 0.74$) (63).

*Trail Making Test from the Delis-Kaplan Executive Function System* (D-KEFS) (64). The Number Sequencing subtest and the Number–Letter Switching subtest from the Trail Making Test will be used as measures of attentional control and cognitive flexibility, respectively. These pencil and paper tasks require children to connect numbers in numerical order from 1 to 16 (Number Sequencing) or to switch back and forth between connecting numbers in numerical order and letters in alphabetical order (Number–Letter Switching). Outcome is the time taken to complete. Higher scores indicate greater difficulty with attentional control (for Number Sequencing) or cognitive flexibility (for Number–Letter Switching). High test–retest reliability for Number Sequencing ($r = .77$) and moderate test–retest reliability for Number–Letter Switching ($r = 0.20 – 0.55$) has been reported (65).

*Verbal Fluency from the D-KEFS* (64). Letter Fluency and Category Fluency subtests from Verbal Fluency will be used as measures of attentional control, cognitive flexibility, and...
goal setting. In Letter Fluency, children are told that they have 60 seconds to name as many words as they can think of that begin with a specified letter (F, then A, then S) while following specified rules (e.g. do not say names of people). In Category Fluency, children are informed that they again have 60 seconds but that this time they have to name as many different animals and then boy’s names as they can think of.

The total number of words generated for Letter Fluency and Category Fluency will be used as outcomes for goal setting; the total number of repetition errors across both Letter Fluency and Category Fluency will be used as a measure of attentional control; and the total number of set-loss errors (i.e. saying a word that does not belong in the specific category) across Letter Fluency and Category Fluency will be used as a measure of cognitive flexibility. Higher scores for the total number of words generated and fewer numbers of repetition and set-loss errors indicate greater levels of goal setting, attentional control, and cognitive flexibility, respectively. Moderate to high levels of internal consistency for Letter Fluency and Category Fluency in children and adolescents is documented ($\alpha = 0.53 - .80$) (65). Test–retest reliability for people aged 8 to 19 years is high for Letter Fluency ($r = 0.67$) and Category Fluency ($r = 0.70$) (65).

*Colour–Word Interference Test from the D-KEFS* (64). Inhibition and Inhibition/Switching subtests from the Colour–Word Interference Test will be used as measures of attentional control and cognitive flexibility. For Inhibition, children have to name the ink colour that colour words (i.e. “red”, “green”) are printed in. The total time taken in seconds to complete the task and the total number of errors will be used as outcome measures for cognitive flexibility, with higher scores indicating a greater difficulty with cognitive flexibility. For Inhibition/Switching, children have to switch between reading the word and saying the colour of the ink in which the colour word is printed. The total time in seconds to complete the task will be used as a measure of cognitive flexibility while the total number of
errors will be used as a measure of attentional control. For people aged 8 to 19 years, an excellent level of test–retest reliability has been shown \( (r = .90) \) (65). Divergent validity between Inhibition and a measure of verbal memory, the California Verbal Learning Test–Second Edition (CVLT-II; \( r = 0.90 \)) has been documented \( (r = 0.27) \) (65).

**Tower Test from the D-KEFS** (64). Tower Test will be used as a measure of goal setting. Across nine items, children move five disks across three pegs to build a target tower shown in a picture within a specified time limit following specified rules (e.g. use the fewest number of moves possible). The total achievement score, which is based on the number of moves needed to make the tower, and the total number of rule violations will be used as outcome measures of goal setting. A higher total achievement score and a lower number of rule violations score indicates higher goal setting ability. Moderate to high levels of internal consistency has been found for the Tower Test for people aged 8 to 19 years old \( (\alpha = 0.43 – .84) \) (65). Adequate test–retest reliability has also been shown for people aged 8 to 19 years \( (r = 0.51) \) (65). Evidence for divergent validity has been demonstrated by a low correlation \( (r = 0.19) \) between the Tower Test total achievement score and the CVLT-II (65).

**Rey-Osterrieth Complex Figure Test** (66-68). The Rey Figure will be used as a measure of goal setting. Children are instructed to copy a complex geometric figure. The examiner records the order that the child drew the figure, which will allow for the child’s strategic decision-making and organisation to be rated on a scale from 1 (unrecognisable or substitution) to 7 (excellent organisation), as per P. Anderson and colleagues (69). Osterrieth’s (67) accuracy scoring procedure (score range: 0 – 36, with higher scores indicating greater spatial organisation; \( M = 32, SD = 4.2 \)) and the organisational strategy score will be used as measures of goal setting. Higher scores on both measures indicate a greater goal setting ability.
The Rey Figure accuracy score has good convergent and divergent validity with significant correlations with related tests such as the Hooper Visual Organization and no significant correlations with language measures such as the Benton Sentence Repetition Test (70). A moderate level of convergent validity between the organisational strategy score and other measures of EF has also been documented (69). High test–retest reliability has been shown for the accuracy scores on the immediate recall trial ($r = 0.76$) and the delayed recall trial ($r = 0.89$), as well as for the organisational strategy score ($r = 0.79 – 0.94$) (69, 70).

Using Osterrieth’s (67) scoring procedure, an excellent level of inter–rater reliability for the copy trial ($r = 0.96$) has been documented (71). Similarly, the organisational strategy score has shown a high level of inter–rater reliability ($r = 0.85 – 0.92$) (69).

**Code Transmission Test from the Test of Everyday Attention for Children (TEA-Ch)**

(72). The Code Transmission Test will be used as a measure of attentional control. This auditory sustained attention task requires children to listen to a tape recording that recites 360 consecutive numbers (40 targets) that are heard at regular intervals. The child had to identify when they hear two number fives in a row (e.g., “5 – 5”) and then say out loud the number that came before the two number fives. The total number of correctly identified targets will be used as the outcome measure, with a higher number indicating great attentional control (range = 0 to 40). A high level of test–retest reliability has been documented for the Code Transmission Test ($r = 0.78$) (72). Overall, the TEA-Ch has been shown to be a valid assessment instrument, based on its factor structure, correlation with other measures, and utility in clinical populations (72).

**Symbol Search from the WISC-IV** (Wechsler, 2004). Symbol Search will be used as a measure of information processing. Children are required to visually scan a search group of symbols and indicate, by placing a line through the word ‘yes’ or ‘no’, whether or not a target symbol is in the search group. Children are instructed to work as quickly as they can and are
given a two-minute time limit. A total score is generated by subtracting the total number of incorrectly identified symbols from the total number of correctly identified symbols. A higher score (range = 0 – 60) indicates a greater level of information processing. Raw scores can also be converted into scaled scores ($M = 10$, $SD = 3$). Good internal consistency has been shown for Symbol Search ($\alpha = 0.79$) as has a high level of test–retest reliability ($r = 0.80$) (63).

Cancellation from the WISC-IV (62). Cancellation will also be used as a measure of information processing. In this task, children have to visually scan both a random and structured arrangement of pictures and place a mark through all of the animals. They are instructed to work as quickly as they can and are given 45 seconds for each of the picture arrangements. The total score will be calculated by subtracting the number of incorrectly identified pictures from the number of correctly identified pictures, with higher scores indicating a higher level of information processing (range = 0 – 136). Good internal consistency has been demonstrated for both Cancellation random ($\alpha = 0.70$) and Cancellation structured ($\alpha = 0.75$) (63). Similarly, a high level of test–retest reliability has been shown for Cancellation random ($r = 0.72$) and Cancellation structured ($r = 0.76$) (63). The WISC-IV’s overall validity has been demonstrated, based on the test’s content, response processes, internal structure, and relationships to other variables (63).

Statistical considerations

To test study hypotheses and research questions 1 (a) – (e) and 3, a series of one-way Analyses of Covariance (ANCOVA) will be conducted for each of the neuropsychological assessment measures, controlling for age and presence/absence of seizure disorders. If significant between-groups differences are found, each will be followed-up using two a priori linear contrasts: the first comparing the control group with all the unilateral CP participants and the second comparing the left are right unilateral CP participants. An overall composite of the cognitive EF measures will be created by standardising all measures, reversing selected
items so that higher scores equalled better performance, and then aggregating all measures. A series of multiple regressions will be used to test hypotheses 2 (a) - (d).

CONCLUSION

This study protocol highlights a prospective cross-sectional study of children with unilateral CP purposely sampled for age and gender for an equal group of children with right and left sided brain lesion to examine their executive functions and compare them to a group of typically developing children. To our knowledge, this protocol outlines the first study to examine multiple components of EF amongst a cohort of children solely with unilateral CP and explores possible laterality effects of EF amongst children with a congenital brain injury. In addition this study examines the relationship between cognitive EF measures, behavioral manifestations of EF in everyday life, and psychological functioning. Results of this study are planned to be published in peer reviewed publications and will be presented at national and international conferences.

Contributions

HB is the chief investigator and together with KW, OL, and RB designed and established this research study as part of HB’s clinical doctorate study. HB, KW, and RB were responsible for ethics applications and reporting. All authors were responsible for the selection of measures. HB will be responsible for recruitment and data collection and HB and KW will be responsible for data analysis. All authors have read and approved the final manuscript.

Funding

This work is supported by the National Health and Medical Research Council (NHMRC) Research Grant (1003887– COMBIT), Career Development Fellowship (10037220–RB) and an NHMRC Hospital Training Fellowship (631712–KW)

Competing interests

The authors declare that they have no competing interests.
Ethics approval

University of Queensland School of Psychology Ethics Committee (10-PSYCH-DCP-32-JM) and the Queensland Children’s Health Services (Royal Children’s Hospital) Human Research Ethics Committee (HREC reference number: HREC/10/QRCH/31).

Provenance and peer review

This protocol has been reviewed as part of HB’s Doctor of Psychology (Clinical Psychology and Clinical Neuropsychology) dissertation, which was awarded on 17.07.2012

Data sharing statement

Further details of the study protocol can be requested from the corresponding author.

REFERENCES


70. Meyers JE, Meyers KR. Rey Complex Figure and the recognition trial: Professional manual. Supplemental norms for children and adolescents. Odessa, Fla.: Psychological Assessment Resources; 1996.
Figure 1. Model of EF in children proposed by P. Anderson (32).
Figure 2. Study flow chart
Figure 3: Model of EF with corresponding neuropsychological assessments.
Executive Functioning in Children with Unilateral Cerebral Palsy: Cross-Sectional Study Protocol

Authors:

Harriet L. Bodimeade¹,² DPsysch (Clin & Clin Neuro), BPsysc (Hons)

Koa Whittingham¹,² PhD (Clinical Psychology), BSc (Hons), BA

Owen Lloyd³ MPsych (Clin Neuro), BSc (Hons)

Roslyn N. Boyd¹ PhD, MSc (PT), BSc (Anatomy), BAppSc (PT), Pgrad (Biomech)

¹ Queensland Cerebral Palsy and Rehabilitation Research Centre, Discipline of Paediatrics and Child Health, School of Medicine, The University of Queensland, Brisbane, Australia;

² School of Psychology, Faculty of Social and Behavioural Sciences, The University of Queensland, Brisbane, Australia;

³ Queensland Paediatric Rehabilitation Service, Royal Children’s Hospital, Brisbane, Australia.

Address for Correspondence:

Professor Roslyn Boyd

Queensland Cerebral Palsy and Rehabilitation Research Centre

Department of Paediatrics and Child Health, School of Medicine

The University of Queensland

Level 7, Block 6, Royal Brisbane and Women’s Hospital

Herston, Brisbane, Australia, 4029

Phone: + 61 3365 5315

Email: r.boyd@uq.edu.au

Word count: 5018
Keywords: Cerebral palsy, unilateral cerebral palsy, executive function, psychological functioning

ABSTRACT

Introduction: Early brain injury, as found in children with unilateral cerebral palsy (CP), may cause deficits in higher-order cognitive tasks known as executive functions (EF). Executive Function has been conceptualised as comprised of four distinct, yet inter-related components: (i) attentional control, (ii) cognitive flexibility, (iii) goal setting, and (iv) information processing. The aim of this study is to examine EF in children with unilateral CP and compare their performance to a typically developing reference group (TDC). Exploration of potential laterality effects of unilateral CP on EF will be explored, as will the relationship between cognitive measures of EF, behavioural manifestations of EF, psychological functioning, and clinical features of unilateral CP.

Methods and analysis: This cross-sectional study aims to recruit a total of 42 children with unilateral CP (21 right unilateral CP and 21 left unilateral CP) and 21 TDC aged between 8 to 16 years. Clinical severity will be described for gross motor function (GMFCS) and manual ability (MACS). Outcomes for cognitive EF measures will include subtests from the Wechsler Intelligence Scale for Children – Fourth Edition, Delis-Kaplan Executive Function System, Rey Complex Figure Test, and the Test of Everyday Attention for Children. Behavioural manifestations of EF will be assessed using the Behaviour Rating Inventory of Executive Function, Parent and Teacher versions. Psychological functioning will be examined using the Strengths and Difficulties Questionnaire. Between-groups differences will be examined in a series of one-way analyses of covariance and followed up using linear comparisons. An overall composite of cognitive EF measures will be created. Bivariate correlations between the EF composite and psychological measures will be calculated.

Ethics and dissemination: This protocol describes a study that, to our knowledge, is the first
to examine multiple components of EF using a cohort of children with unilateral CP.

Exploration of potential laterality effects of EF amongst children with a congenital, unilateral brain injury is also novel. Possible relationships between EF and psychological functioning will also be investigated. Ethics have been obtained through the University of Queensland School of Psychology Ethics Committee and the Queensland Children’s Health Services Human Research Ethics Committee. Results will be disseminated in peer reviewed publications and presentations at national and international conferences. This study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12611000263998).

Abstract word count: 378
INTRODUCTION

Cerebral Palsy (CP) is the leading cause of childhood physical disability in Australia with an incidence of 1 in 500 live births (1). Unilateral CP, with a presumed brain lesion occurring congenitally prior to 28 days old corrected age, is the most common type of CP among children born full term and the second most common type of CP in children born preterm, with an incidence of 1 in 1,300 live births (1, 3).

Caring for people with CP is costly on both the health care system and families. In 2007, the overall financial expenditure for persons with CP in Australia was AUD $1.47 billion (4).

Cerebral palsy has been defined as “a group of disorders of the development of movement and posture ...that is attributed to non-progressive disturbances that occurred in the developing foetal or infant brain...often accompanied by disturbances of...cognition” (5).

A population-based register study of children with CP in Australia identified that 45% of children with CP experience cognitive difficulties (2). In later life, CP is related to reduced educational and employment opportunities (6). In comparison to research on motor and movement impairments in CP, there is a lack of literature examining cognitive and psychological difficulties faced by children with CP (7). This is concerning given that these factors are essential to the well-being and overall development of children with CP (8).

Another diagnostic marker for CP is damage to the developing foetal or infant brain. A key systematic review by Krageloh-Mann and colleagues (9) analysed MRI brain scan findings for children with CP and found that in children with unilateral CP, periventricular white matter damage was the most common brain injury, occurring in 36% of children, followed by cortical deep grey matter lesions in 31%, brain malformations (e.g., schizencephaly) in 16%, and miscellaneous lesions in 7% of children. Given that children with unilateral CP have sustained a brain injury, and the fact that research has illustrated a
link between brain injuries and reduced cognitive and psychological functioning (10), examination of neuropsychological and psychological functioning in this population is warranted.

**Executive Function**

‘Executive function’ is an umbrella term that encompasses skills necessary for novel, goal-directed, and complex activity (11-15). Everyday functioning relies on executive skills and deficits in EF may manifest as: disorganisation and poor planning; inability to focus and attend to tasks; careless responding to tasks; reduced self-control; and taking longer to complete tasks (16, 17).

Findings from functional neuroimaging studies, predominantly in adult brain-injured populations, have indicated that EF is principally mediated by the frontal lobes, particularly the prefrontal cortex (18, 19). The frontal lobes demonstrate rich efferent and afferent connections with nearly all other posterior and subcortical cerebral regions (20, 21). It is thought that the frontal lobes integrate and coordinate information and in essence work as the ‘control master’ of the brain (22). As a consequence, the frontal lobes are important for EF but it is the integrity of the entire brain that is pivotal for successful executive skills (16, 23). In children and adolescents, the frontal lobes are the last brain region to reach maturity, typically by the end of the second decade of life (24). The refinement of intricate white matter tracts from these underlying brain regions to the frontal lobes and ongoing myelination are also important aspects of prefrontal maturation and in turn, the progression of executive skills (24).

There is some evidence suggesting lateralisation of verbal and spatial aspects of executive functioning amongst adults. For example, utilising position emission tomography (PET), asymmetrical organisation of visual and verbal working memory skills, a component of
executive function, was shown amongst a cohort of female adults aged 18 to 30 years. Predominantly left lateralisation occurred during a verbal memory task whereas right lateralisation was shown during a spatial working memory task (25). However, within paediatric literature, there is a paucity of research exploring possible laterality of EFs amongst children, and findings from adult cohorts cannot be extrapolated to children given their ongoing development. Moreover, amongst unilateral CP, a congenital brain injury has occurred, rather than one acquired later during development. This may also change the picture of potential lateralisation given the possibility for functional re-organisation in the developing brain (26).

Specifically, there is some evidence of functional re-lateralisation of lower level cognitive functions in children, particularly related to visuospatial and language skills, following early brain injury (27). Research by Lidzba and colleagues (27) has highlighted that children with both left and right unilateral CP show preserved language functions at the cost, however, of poorer visuospatial skills. It appears that visuospatial deficits in children with early left hemispheric lesions are a consequence of lesion-induced right hemispheric language re-organisation. This phenomenon is known as the cognitive crowding hypothesis (26).

**Development of Executive Functions**

As executive skills show a prolonged development through childhood and adolescence, it is important to understand the normal development of these skills in order to identify deviations from projected maturational patterns. An analogous relationship between the maturing frontal lobes and the unfolding of executive skills is seen (11). This parallel relationship typically emerges along a hierarchical developmental trajectory often in growth ‘spurts’ rather than developing in a uniform fashion (28, 29). Major neurophysiological growth spurts occur from birth to 2 years, 7 to 9 years, and again in adolescence from 16 to 19 years (11, 30, 31). These timeframes involve peak periods of synaptogenesis and increased
myelination with corresponding improvements in specific EF domains (28).

A conceptual framework of EF in typically developing children, proposed by P. Anderson (32), operationalises EF as an overall control system that is comprised of four distinct, yet inter-related, executive components: (1) attentional control, the earliest EF domain to emerge, involves the ability to maintain and focus attention for extended periods of time and the capability to selectively focus one’s attention towards target stimuli; (2) cognitive flexibility, the ability to correct and learn from errors, flexibly shift from one response set to another, and generate multiple and alternative strategies to problems; (3) goal setting, the ability to generate novel goals and initiatives, plan actions and strategies, and complete tasks in an organised and proficient manner; and (4) information processing, the ability to fluently and efficiently complete tasks and the overall processing speed and speed of output (Figure 1). This model of EF is unique in the paediatric neuropsychological literature as it incorporates a developmental context, highlights that each executive component operates in an integrative manner, and considers each component as having a separate developmental trajectory.

Executive Functions in Cerebral Palsy

In spite of the importance of executive skills for the successful achievement of academic, behavioural, social, and adaptive day-to-day functions, there is a paucity of research examining EF in children and adolescents with unilateral CP. Research among other paediatric populations, such as in childhood stroke (33) and focal frontal lobe lesions (34), has shown EF is particularly susceptible to early brain insult during the prenatal and perinatal periods. Recent research has also established that executive difficulties are present following early brain insult to any region of the brain—it does not need to be a frontal lesion for executive deficits to be seen (35-37). Brain injury sustained early in development (i.e. before age 3) has been shown to result in global executive deficits across several executive
components (35, 38).

Recent research has noted EF deficits among children and adolescents with CP (39-42). In Bottcher and colleague’s (39) study, children (9-13 years old) with either unilateral CP (n=14) or diplegia (n=18) were found to have attentional deficits, as measured by subtests from the Test of Everyday Attention for Children (TEA-Ch), EF deficits, as measured by the Contingency Naming Test (CNT), and deficits in behavioural manifestations of EF in everyday life as measured by the BRIEF. It was found that both the unilateral and diplegia CP groups scored significantly below aged based norms on all measures and there was a non-significant trend for children with diplegia to perform poorer than those with unilateral CP (39). In a similar study, a smaller cohort of children (8-17 years old), again with either unilateral CP (n=8) or diplegia (n=9), were rated as showing clinically significant impairments on measures of attention, impulsivity, and vigilance from the Conners’ Continuous Performance Test (CCPT), with children with diplegia showing significantly higher impairments than those with unilateral CP (42).

The relationship between arithmetic difficulties and EF in children with CP has also been investigated (40, 41). In one study, first graders (mean age of 7 years) with CP were split into two groups—those attending a mainstream school (n = 16) and those attending a special school (n = 41) (41). A control group of 16 first graders without CP, again with a mean age of 7 years, who were attending a mainstream school, were also included. Within the CP mainstream school group, 12 children had unilateral CP, 3 had diplegia, and one 1 had ataxia, while the CP special school group comprised of 10 children with unilateral CP, 29 with diplegia, and 2 with ataxia (41). Executive skills, specifically verbal and visuospatial working memory, were assessed using a Digits Forwards and Backwards task and the Knox Blocks test.

Interestingly, the CP mainstream group had the lowest score on the Digits Forwards
tasks, followed by the CP special school group and then the controls. Even though the CP mainstream group performed more poorly than the CP special school group and the CP special school group lower than the controls, neither of these differences reached clinical significance. On the Digits Backwards task, the CP special school group performed significantly worse than the CP mainstream group and the CP mainstream group performed significantly poorer than the control group. Finally, on the Knox Blocks task, the CP special school group performed significantly worse than the CP mainstream group; however, there was no difference in performance between the CP mainstream and control groups (41).

Structural equation modelling revealed that tasks assessing working memory skills (i.e. Digits Forwards/Backwards and Knox Blocks) mediated arithmetic ability in both CP groups, such that poorer working memory abilities predicted a lower arithmetic ability (41). A follow-on study by the same authors confirmed that EF, particularly working memory skills, are lower in children with CP (CP types included hemiplegia, diplegia, and ataxia) compared to their typically developing peers and that these predict poorer arithmetic ability (40).

Executive functions have also been examined in a study of 21 school age children (mean age of 8 years) who had been born preterm with a periventricular haemorrhagic infarction (43). Of these children, 13 had unilateral CP, 3 had diplegia, 1 had minor neurologic dysfunction, and 4 were neurologically normal. The BRIEF was used as the outcome measure for executive skills with results showing executive impairments in 18% (parent report) and 29% (teacher report) of the sample (43). Other research has used the Wisconsin Card Sorting Test (WCST) to examine executive skills among 37 children with unilateral CP and 15 children with diplegia (mean age 11 years old) and 50 matched typically developing peers (44). Results found that children with CP, compared to controls, made more non-preservative errors, completed fewer categories, required more trials to complete the first category, and gave fewer conceptual responses.
This current literature is limited as all existing studies examine mixed groups of CP and/or investigate only one discrete component of EF; thus, the heterogeneous nature of CP and the multidimensional nature of EF is not accounted for and the results may be misleading. Furthermore, the majority of studies lack a typically developing reference group and also do not include both cognitive and behavioural measures of EF. Furthermore the relationship between cognitive EF and behavioural manifestations of EF and psychological functioning has also not previously been explored. This study aims to remedy these gaps in the literature.

Executive functions following early brain injury

Research among children who had sustained an early brain injury has also uncovered EF deficits (35, 45). Using a cross-sectional, retrospective group design, Anderson and colleague’s (35) examined EF amongst 164 children (aged 10 to 16 years old) who had sustained a brain injury at varying developmental time points: congenital, perinatal, infancy, preschool, middle childhood, and late childhood. Children with diverse focal pathologies and diagnoses were included across all study groups, such as stroke, penetrating head injury and contusions, tumour, cysts, and abscesses (35). The study utilised P. Anderson’s (32) conceptual model of EF to assess these skills in children across four components—attentional control, cognitive flexibility, goal setting, and processing speed. Subtests from the Delis-Kaplan Executive Function System (D-KEFS), TEA-Ch, and the Rey Complex Figure were used to assess the four executive domains. Behavioural manifestations of EF in everyday life were also examined using the BRIEF.

Results showed that compared to normative expectations, children who sustained a brain injury before the age of 3 years experienced the most severe and global EF deficits across all domains (35). Regardless of location (i.e. frontal versus non-frontal regions), the presence of brain pathology was found to lead to executive dysfunction. These findings lend further support for the early vulnerability hypothesis of brain insult sustained early in
development, as children with earlier lesions were most at risk for global EF impairments. The study findings also support the notion that injury to any part of the brain may disrupt neural circuits involved in EF and that there appears to be a lack of functional specificity in the immature brain (35). Even though children with unilateral CP, by definition, have sustained damage to the developing foetal or infant brain there is a paucity of research specifically on EF and unilateral CP.

Aims and hypotheses

The broad aim of this prospective cross-sectional study of children with unilateral CP (21 right, 21 left sided unilateral CP) is to examine their performance on the four domains of EF and to compare this with a group of typically developing age and gender matched children. The primary aim of the current study is to determine the pattern of EF in children and adolescents with unilateral CP with the following hypotheses and research questions:

1. It is hypothesised that children with unilateral CP will demonstrate poorer performance on tasks assessing the following EF components:
   (a) Attentional control;
   (b) Cognitive flexibility;
   (c) Goal setting;
   (d) Information processing; and
   (e) In everyday life.

2. It is hypothesised that children with higher levels of EF (i.e. better executive skills) would show fewer difficulties across the following domains:
   (a) Behavioural manifestations of executive dysfunction in everyday life, as measured by the Behaviour Rating Inventory of Executive Function (46);
   (b) Emotional functioning, as measured by the Strengths and Difficulties Questionnaire (47, 48);
(c) Behavioural functioning, as measured by the Strengths and Difficulties Questionnaire (47, 48); and

(d) Social functioning, as measured by the Strengths and Difficulties Questionnaire (47, 48).

3. Finally, the profile EF across the EF components (i.e. attentional control, cognitive flexibility, goal setting, information processing, and in everyday life) will be explored for children with left unilateral CP versus right unilateral CP in order to ascertain potential laterality effects of EF following a congenital brain injury.

METHODS AND ANALYSES

Ethics

Ethics approvals have been gained through the University of Queensland School of Psychology Ethics Committee (10-PSYCH-DCP-32-JM) and the Queensland Children’s Health Services Human Research Ethics Committee (HREC/10/QRCH/31). There is no known safety risks associated with any aspect of the study. All parents or legal guardians will give written informed consent and children aged ≥12 will provide assent, and will be able to withdraw from the study at any time without penalty or any effect on the child’s care. Data collected in this study will be stored in a coded re-identifiable form by ID number. Each child will have one appointment during which all assessment measures will be completed. If desired by parents, all children will receive a brief neuropsychological report outlining their results on EF measures and general strategies to assist any identified cognitive weaknesses.

Recruitment

Children will be identified from the research database of the Queensland Cerebral Palsy & Rehabilitation Research Centre and from the Queensland Cerebral Palsy Health Service at the Royal Children’s Hospital, Brisbane, Australia. Parents of potential suitable children identified will be asked by their treating clinician if they seek further information
about the study. After expressing interest and providing consent to be contacted informed consent will proceed with the researchers. Participants will be assessed for eligibility using a brief parent telephone-screening interview based on study criteria (see below). A provisional psychologist will conduct all telephone-screening interviews. If the participant meets the study selection criteria, they will be invited to take part in the study and will be emailed/posted a study information sheet/consent form. A time will then been made for them to take part in the study.

Typically developing children (age and gender matched) will be recruited as a reference sample. Siblings and friends of children with unilateral CP will be invited to take part in the study, as well as recruitment through staff newsletters and from other studies within the centre. A provisional psychologist will again conduct a brief telephone-screen interview to ensure they meet the study selection criteria (see below).

Selection criteria

Inclusion criteria

Children will be invited to participate in the study if they have a confirmed unilateral CP diagnosis that was diagnosed within 28 days postnatally, are aged 8 to 16 years at study entry, have English as their first language, are able to communicate through spoken language, and live within Queensland.

Exclusion criteria

Children will be excluded from the study if they have an uncontrolled seizure disorder or if CP was acquired postnatally.

Typically developing reference sample

Children are eligible to participate in the reference sample if they are aged between 8 to 16 years, have English as their first language, and do not have a history of developmental, neurological, physical, or psychiatric conditions.
Sample size

A power analysis was conducted using g power and revealed that at least 21 children per group needed to be recruited in order to have sufficient power (0.80) to detect a large effect size (0.80) utilising an Analysis of Variance with three comparison groups (49). Large effect sizes have been found in previous research comparing the performance of children with CP on tests of attention and EF, such as the TEA-Ch (39).

Classification measures

*Family Background Questionnaire* (FBQ) (50). Parents will complete an adapted version of the FBQ that gathers basic demographic and background information pertaining to both the parent and child.

*Gross Motor Function Classification System* (GMFCS) (51). This measure will enable classification of the unilateral CP participants’ gross motor functioning (e.g., the ability to sit, stand, walk, and climb stairs) over a five-level classification system. Research has found strong construct validity between the GMFCS and the Gross Motor Function Measure \(r = 0.91\), a criterion-referenced measure that evaluates change in gross motor function in children with CP (52). High test–retest reliability \(r = 0.79\) (53), inter–rater reliability between professionals (kappa = 0.74) (54), and intra–rater reliability between professionals and parents \(r = 0.94\) (55) has also been documented.

*Manual Ability Classification System* (MACS) (56). This measure will be used to classify the manual ability of children with unilateral CP to use their hands when handling objects in daily activities over a five-level classification system. Research has shown good construct validity between the MACS and the GMFCS \(r = 0.79\) and high inter–rater reliability between therapists \(r = 0.97\) and intra–rater reliability between parents and therapists \(r = 0.96\) (56).
Strengths and Difficulties Questionnaire–Extended Version (SDQ) (47, 48). Parents will complete the SDQ, a 33 item questionnaire measuring parents’ perceptions of prosocial and difficult behaviours in their child. The SDQ is able to discriminate well between community and clinic samples and has good construct validity in associations with the Achenbach Child Behaviour Checklist (CBCL; \( r = 0.87 \) and \( r = 0.81 \)) (57, 58). The SDQ total difficulties score has high internal consistency (\( \alpha = 0.73 \)) and high test–retest reliability (\( r = 0.85 \)) (59). The SDQ total scale scores (i.e. Emotional Symptoms, Conduct Problems, Inattention/Hyperactivity, Peer Problems, and Prosocial Behaviour) and the overall total difficulties score will be used as outcome measures for children’s emotional, behavioural, and social functioning.

Behaviour Rating Inventory of Executive Function–Parent Form and Teacher Form (BRIEF–Parent Form and BRIEF–Teacher Form) (46). Parents and schoolteachers will complete the BRIEF—an 86 item behavioural measure of EF in their child’s everyday life. The BRIEF yields two index scores: the behavioural regulation index (including initiate, working memory, plan/organise, organisation of materials, and monitor) and the metacognition index (including inhibit, shift, and emotional control). The behavioural regulation index and metacognition index combined form a global executive composite score. Both indexes and composite score can be converted into \( T \) scores with higher \( T \) scores indicating a greater level of executive dysfunction and a \( T \) score of 65 and above indicative of an abnormal elevation (46).

The BRIEF has good convergent and divergent validity with the CBCL and the Behaviour Assessment System for Children (60). High internal consistency, with Cronbach’s \( \alpha \) coefficients ranging from .80 to .98 for both the parent and teacher forms, has also been shown (46, 61). Moderate intra–rater reliability between parents and teachers has been found (\( r = .32 \)), as have high test–retest reliability statistics for the parent form on the BRI (\( r = \))
0.84), MCI ($r = 0.88$), and the GEC ($r = 0.86$), and for the teacher form on the BRI ($r = 0.92$), MCI ($r = 0.90$), and the GEC ($r = 0.91$) (46, 61).

### Outcome Measures of Executive Function

Peter Anderson’s (32) conceptual model of EF will be used to operationalise EF. Ten neuropsychological measures were selected to evaluate the four components (i.e. attentional control, cognitive flexibility, goal setting, and information processing) of this model. The model of EF and list of the neuropsychological measures is reported in Figure 3.

**Digit Span Backward from the Wechsler Intelligence Scale for Children–Fourth Edition (WISC-IV) (62).** Digit Span Backwards (range 0-16) is a verbal working memory task that requires children to temporarily store and manipulate information. The child has to repeat a number string that increases from 2 to 8 digits in the reverse order. Higher scores indicate a greater level of the cognitive flexibility. Good internal consistency has been documented for Digit Span Backward ($\alpha = 0.80$) and it has high test–retest reliability ($r = 0.74$) (63).

**Trail Making Test from the Delis-Kaplan Executive Function System (D-KEFS) (64).** The Number Sequencing subtest and the Number–Letter Switching subtest from the Trail Making Test will be used as measures of attentional control and cognitive flexibility, respectively. These pencil and paper tasks require children to connect numbers in numerical order from 1 to 16 (Number Sequencing) or to switch back and forth between connecting numbers in numerical order and letters in alphabetical order (Number–Letter Switching). Outcome is the time taken to complete. Higher scores indicate greater difficulty with attentional control (for Number Sequencing) or cognitive flexibility (for Number–Letter Switching). High test–retest reliability for Number Sequencing ($r = .77$) and moderate test–retest reliability for Number–Letter Switching ($r = 0.20 – 0.55$) has been reported (65).

**Verbal Fluency from the D-KEFS (64).** Letter Fluency and Category Fluency subtests from Verbal Fluency will be used as measures of attentional control, cognitive flexibility, and
goal setting. In Letter Fluency, children are told that they have 60 seconds to name as many words as they can think of that begin with a specified letter (F, then A, then S) while following specified rules (e.g. do not say names of people). In Category Fluency, children are informed that they again have 60 seconds but that this time they have to name as many different animals and then boy’s names as they can think of.

The total number of words generated for Letter Fluency and Category Fluency will be used as outcomes for goal setting; the total number of repetition errors across both Letter Fluency and Category Fluency will be used as a measure of attentional control; and the total number of set-loss errors (i.e. saying a word that does not belong in the specific category) across Letter Fluency and Category Fluency will be used as a measure of cognitive flexibility. Higher scores for the total number of words generated and fewer numbers of repetition and set-loss errors indicate greater levels of goal setting, attentional control, and cognitive flexibility, respectively. Moderate to high levels of internal consistency for Letter Fluency and Category Fluency in children and adolescents is documented ($\alpha = 0.53 - 0.80$) (65). Test–retest reliability for people aged 8 to 19 years is high for Letter Fluency ($r = 0.67$) and Category Fluency ($r = 0.70$) (65).

*Colour–Word Interference Test from the D-KEFS* (64). Inhibition and Inhibition/Switching subtests from the Colour–Word Interference Test will be used as measures of attentional control and cognitive flexibility. For Inhibition, children have to name the ink colour that colour words (i.e. “red”, “green”) are printed in. The total time taken in seconds to complete the task and the total number of errors will be used as outcome measures for cognitive flexibility, with higher scores indicating a greater difficulty with cognitive flexibility. For Inhibition/Switching, children have to switch between reading the word and saying the colour of the ink in which the colour word is printed. The total time in seconds to complete the task will be used as a measure of cognitive flexibility while the total number of
errors will be used as a measure of attentional control. For people aged 8 to 19 years, an excellent level of test–retest reliability has been shown \((r = .90)\) (65). Divergent validity between Inhibition and a measure of verbal memory, the California Verbal Learning Test–Second Edition (CVLT-II: \(r = 0.90\)) has been documented \((r = 0.27)\) (65).

**Tower Test from the D-KEFS** (64). Tower Test will be used as a measure of goal setting. Across nine items, children move five disks across three pegs to build a target tower shown in a picture within a specified time limit following specified rules (e.g. use the fewest number of moves possible). The total achievement score, which is based on the number of moves needed to make the tower, and the total number of rule violations will be used as outcome measures of goal setting. A higher total achievement score and a lower number of rule violations score indicates higher goal setting ability. Moderate to high levels of internal consistency has been found for the Tower Test for people aged 8 to 19 years old \((\alpha = 0.43 – 0.84)\) (65). Adequate test–retest reliability has also been shown for people aged 8 to 19 years \((r = 0.51)\) (65). Evidence for divergent validity has been demonstrated by a low correlation \((r = 0.19)\) between the Tower Test total achievement score and the CVLT-II (65).

**Rey-Osterrieth Complex Figure Test** (66-68). The Rey Figure will be used as a measure of goal setting. Children are instructed to copy a complex geometric figure. The examiner records the order that the child drew the figure, which will allow for the child’s strategic decision-making and organisation to be rated on a scale from 1 (unrecognisable or substitution) to 7 (excellent organisation), as per P. Anderson and colleagues (69).

Osterrieth’s (67) accuracy scoring procedure (score range: 0 – 36, with higher scores indicating greater spatial organisation; \(M = 32, SD = 4.2\)) and the organisational strategy score will be used as measures of goal setting. Higher scores on both measures indicate a greater goal setting ability.
The Rey Figure accuracy score has good convergent and divergent validity with significant correlations with related tests such as the Hooper Visual Organization and no significant correlations with language measures such as the Benton Sentence Repetition Test (70). A moderate level of convergent validity between the organisational strategy score and other measures of EF has also been documented (69). High test–retest reliability has been shown for the accuracy scores on the immediate recall trial \( r = 0.76 \) and the delayed recall trial \( r = 0.89 \), as well as for the organisational strategy score \( r = 0.79 – 0.94 \) (69, 70).

Using Osterrieth's (67) scoring procedure, an excellent level of inter–rater reliability for the copy trial \( r = 0.96 \) has been documented (71). Similarly, the organisational strategy score has shown a high level of inter–rater reliability \( r = 0.85 – 0.92 \) (69).

**Code Transmission Test from the Test of Everyday Attention for Children (TEA-Ch)**

The Code Transmission Test will be used as a measure of attentional control. This auditory sustained attention task requires children to listen to a tape recording that recites 360 consecutive numbers (40 targets) that are heard at regular intervals. The child had to identify when they hear two number fives in a row (e.g., “5 – 5”) and then say out loud the number that came before the two number fives. The total number of correctly identified targets will be used as the outcome measure, with a higher number indicating great attentional control (range = 0 to 40). A high level of test–retest reliability has been documented for the Code Transmission Test \( r = 0.78 \) (72). Overall, the TEA-Ch has been shown to be a valid assessment instrument, based on its factor structure, correlation with other measures, and utility in clinical populations (72).

**Symbol Search from the WISC-IV** (Wechsler, 2004). Symbol Search will be used as a measure of information processing. Children are required to visually scan a search group of symbols and indicate, by placing a line through the word ‘yes’ or ‘no’, whether or not a target symbol is in the search group. Children are instructed to work as quickly as they can and are
given a two-minute time limit. A total score is generated by subtracting the total number of incorrectly identified symbols from the total number of correctly identified symbols. A higher score (range = 0 – 60) indicates a greater level of information processing. Raw scores can also be converted into scaled scores ($M = 10$, $SD = 3$). Good internal consistency has been shown for Symbol Search ($\alpha = 0.79$) as has a high level of test–retest reliability ($r = 0.80$) (63).

Cancellation from the WISC-IV (62). Cancellation will also be used as a measure of information processing. In this task, children have to visually scan both a random and structured arrangement of pictures and place a mark through all of the animals. They are instructed to work as quickly as they can and are given 45 seconds for each of the picture arrangements. The total score will be calculated by subtracting the number of incorrectly identified pictures from the number of correctly identified pictures, with higher scores indicating a higher level of information processing (range = 0 – 136). Good internal consistency has been demonstrated for both Cancellation random ($\alpha = 0.70$) and Cancellation structured ($\alpha = 0.75$) (63). Similarly, a high level of test–retest reliability has been shown for Cancellation random ($r = 0.72$) and Cancellation structured ($r = 0.76$) (63). The WISC-IV’s overall validity has been demonstrated, based on the test’s content, response processes, internal structure, and relationships to other variables (63).

Statistical considerations

To test study hypotheses and research questions 1 (a) – (e) and 3, a series of one-way Analyses of Covariance (ANCOVA) will be conducted for each of the neuropsychological assessment measures, controlling for age. If significant between-groups differences are found, each will be followed-up using two a priori linear contrasts: the first comparing the control group with all the unilateral CP participants and the second comparing the left and right unilateral CP participants. An overall composite of the cognitive EF measures will be created by standardising all measures, reversing selected items so that higher scores equalled better
performance, and then aggregating all measures. A series of multiple regressions will be used to test hypotheses 2 (a) - (d).

CONCLUSION

This study protocol highlights a prospective cross-sectional study of children with unilateral CP purposely sampled for age and gender for an equal group of children with right and left sided brain lesion to examine their executive functions and compare them to a group of typically developing children. To our knowledge, this protocol outlines the first study to examine multiple components of EF amongst a cohort of children solely with unilateral CP and explores possible laterality effects of EF amongst children with a congenital brain injury. In addition this study examines the relationship between cognitive EF measures, behavioral manifestations of EF in everyday life, and psychological functioning. Results of this study are planned to be published in peer reviewed publications and will be presented at national and international conferences.

Contributions

HB is the chief investigator and together with KW, OL, and RB designed and established this research study as part of HB’s clinical doctorate study. HB, KW, and RB were responsible for ethics applications and reporting. All authors were responsible for the selection of measures. HB will be responsible for recruitment and data collection and HB and KW will be responsible for data analysis. All authors have read and approved the final manuscript.

Funding

This work is supported by the National Health and Medical Research Council (NHMRC) Research Grant (1003887–COMBIT), Career Development Fellowship (10037220–RB) and an NHMRC Hospital Training Fellowship (631712–KW)

Competing interests

The authors declare that they have no competing interests.
Ethics approval

University of Queensland School of Psychology Ethics Committee (10-PSYCH-DCP-32-JM) and the Queensland Children’s Health Services (Royal Children’s Hospital) Human Research Ethics Committee (HREC reference number: HREC/10/QRCH/31).

Provenance and peer review

This protocol has been reviewed as part of HB’s Doctor of Psychology (Clinical Psychology and Clinical Neuropsychology) dissertation, which was awarded on 17.07.2012

Data sharing statement

Further details of the study protocol can be requested from the corresponding author.

REFERENCES


70. Meyers JE, Meyers KR. Rey Complex Figure and the recognition trial: Professional manual. Supplemental norms for children and adolescents. Odessa, Fla.: Psychological Assessment Resources; 1996.

Figure 1. Model of EF in children proposed by P. Anderson (32).
Figure 2. Study flow chart

Unilateral CP Participants
Assessed for eligibility from the QCPRRC (n=188)
+ Referrals from QLD CP Health Service
  Telephone screen
  Informed consent then enrolment
  Analyses

TD Participants
Assessed for eligibility from staff newsletters/other centre studies
  Telephone screen
  Informed consent then enrolment
  Analyses

136x90mm (300 x 300 DPI)
Figure 3: Model of EF with corresponding neuropsychological assessments.

116x90mm (300 x 300 DPI)
STROBE Statement—Checklist of items that should be included in reports of *cohort studies* for

**Executive Functioning in Children with Unilateral Cerebral Palsy: Study Protocol**

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>(a) Indicate the study’s design with a commonly used term in the title or the abstract (Page 2)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Provide in the abstract an informative and balanced summary of what was done and what was found (page 2)</em></td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Explain the scientific background and rationale for the investigation being reported (P5-13)</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>State specific objectives, including any prespecified hypotheses (P13-14)</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Present key elements of study design early in the paper (P15-16)</td>
</tr>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (p15)</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td><em>(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (p15-16)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) For matched studies, give matching criteria and number of exposed and unexposed (NA)</em></td>
</tr>
<tr>
<td><strong>Variables</strong></td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (P16)</td>
</tr>
<tr>
<td><strong>Data sources/measurement</strong></td>
<td>8*</td>
</tr>
<tr>
<td></td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (P17-22)</td>
</tr>
<tr>
<td><strong>Bias</strong></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Describe any efforts to address potential sources of bias (NA)</td>
</tr>
<tr>
<td><strong>Study size</strong></td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Explain how the study size was arrived at (P16)</td>
</tr>
<tr>
<td><strong>Quantitative variables</strong></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (P22)</td>
</tr>
<tr>
<td><strong>Statistical methods</strong></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td><em>(a) Describe all statistical methods, including those used to control for confounding (P22)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Describe any methods used to examine subgroups and interactions (P22)</em></td>
</tr>
<tr>
<td></td>
<td><em>(c) Explain how missing data were addressed (P22)</em></td>
</tr>
<tr>
<td></td>
<td><em>(d) If applicable, explain how loss to follow-up was addressed (NA)</em></td>
</tr>
<tr>
<td></td>
<td><em>(e) Describe any sensitivity analyses (NA)</em></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>13*</td>
</tr>
<tr>
<td></td>
<td><em>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Give reasons for non-participation at each stage (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(c) Consider use of a flow diagram (fig 2)</em></td>
</tr>
<tr>
<td><strong>Descriptive data</strong></td>
<td>14*</td>
</tr>
<tr>
<td></td>
<td><em>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(b) Indicate number of participants with missing data for each variable of interest (NA protocol)</em></td>
</tr>
<tr>
<td></td>
<td><em>(c) Summarise follow-up time (eg, average and total amount) (NA protocol)</em></td>
</tr>
<tr>
<td><strong>Outcome data</strong></td>
<td>15*</td>
</tr>
<tr>
<td></td>
<td>Report numbers of outcome events or summary measures over time (NA protocol)</td>
</tr>
<tr>
<td>Main results</td>
<td>16</td>
</tr>
<tr>
<td>-------------</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Other analyses</td>
<td>17</td>
</tr>
<tr>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>Key results</td>
<td>18</td>
</tr>
<tr>
<td>Limitations</td>
<td>19</td>
</tr>
<tr>
<td>Interpretation</td>
<td>20</td>
</tr>
<tr>
<td>Generalisability</td>
<td>21</td>
</tr>
<tr>
<td>Other information</td>
<td>22</td>
</tr>
</tbody>
</table>
Executive functioning in children with unilateral cerebral palsy: protocol for a cross-sectional study
Harriet L Bodimeade, Koa Whittingham, Owen Lloyd and Roslyn N Boyd

BMJ Open 2013 3:
doi: 10.1136/bmjopen-2012-002500

Updated information and services can be found at:
http://bmjopen.bmj.com/content/3/4/e002500

These include:

References
This article cites 52 articles, 7 of which you can access for free at:
http://bmjopen.bmj.com/content/3/4/e002500#BIBL

Open Access
This is an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license. See: http://creativecommons.org/licenses/by-nc/3.0/ and http://creativecommons.org/licenses/by-nc/3.0/legalcode

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Neurology (320)
- Paediatrics (485)
- Rehabilitation medicine (232)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/