Thesis for the degree of Doctorate in Clinical Psychology (ClinPsyD)

Volume I

Research Papers

Dr. Donna Reid
Doctoral Course in Clinical Psychology
School of Psychology
University of Birmingham
Edgbaston
Birmingham
B15 2TT

Authors Declaration Form

At no time during the registration for the degree of Doctor in Clinical Psychology has the author been registered for any other university award.

Overview

This thesis is submitted in partial fulfilment of the requirements for the degree of Doctorate in Clinical Psychology (ClinPsyD) at the school of Psychology, University of Birmingham, UK. This thesis is presented in two volumes. Volume I consists of the research component of the thesis and Volume II contains the written clinical component.

Volume I is comprised of two papers: a literature review and a research paper. The literature review examines research into executive functioning in individuals with developmental disorders. The experimental research paper is entitled 'Executive Functioning in Cornelia de Lange Syndrome'. Both papers are prepared as if for submission to the Journal of Intellectual Disability Research (JIDR). Some changes have been made to the formatting of these papers to comply with thesis regulations.

Volume II contains five Clinical Practice Reports (CPR's). The first details the assessment and formulation from two perspectives of a young man with Post Traumatic Stress Disorder (PTSD). CPR two is a small-scale service related research report, investigating user satisfaction in a Child and Adolescent Mental Health Service (CAMHS). The third CPR is a case study outlining the work carried out with a 45 year old lady with Body Dysmorphic Disorder (BDD). CPR four is a single case experimental design that evaluates the effectiveness of a behavioural intervention as part of a proof of concept study with a 10 year old girl with Cri Du Chat syndrome. The final report was presented orally and the abstract and slides are presented here for reference. It focussed on the case of a 65 year old gentleman with fronto-temporal dementia demonstrating disruptive vocalisation behaviour.

Dedication

This thesis is dedicated to my Grandad: Gordon James Hardcastle Reid. In my heart and memories you are with me every day. Thank you for always believing in me and for teaching me to be a fighter x

Acknowledgements

I would like to take this opportunity to thank the many people who have helped over the last three years. There are too many people to mention by name, who have offered their support, advice and friendship throughout the duration of the course and the thesis. Thanks to my research supervisor Professor Chris Oliver for offering me the opportunity to join the Cerebra Centre for Neurodevelopmental Disorders, I have learnt so much and it has been an honour being part of such an amazing research team. The greatest thanks is owed to my research partner, Lisa Nelson who allowed me to join her research programme under the supervision of Professor Chris Oliver. Her vast knowledge of CdLS and useful guidance, encouragement and pep talks from start to finish were gratefully received. Lisa has been a great colleague and my best friend. This thesis hopefully reflects the great synergistic relationship we had on the project. Thanks to Leah Bull for her assistance in the data inputting, and the rest of the Cerebra Centre for Neurodevelopmental Disorders for being such a welcoming team. This research would not have taken place if it were not to the participants and their families who kindly volunteered their time to participate in the project- thank you all so much.

I have been lucky to have some great clinical supervisors who have aided my learning in formulation, assessment and therapy skills. These have included Dr Judith Bond, Dr Thomas Patterson, Dr Phil Ray and Professor Chris Oliver.

There are many other people within the school who deserve mentioning, and without whom the research and clinical volumes would not have gone as smoothly. Thanks to Michelle O'Shea, Gary Law and Heather Bennett for their tutoring and placement advice. A special thanks is owed to all the administration staff who were always so helpful- Angie, Barbara, Joyce and Karen.

Huge thanks are given to my mum, Ian, and little brother James who were there when I needed them the most, and allowed me to believe in myself. As well as giving me support through the toughest parts, they gave me the opportunities to switch off and keep sane, putting up with the ups and downs along the way. Similarly, thanks to Laura, Chris and Narinda (Nina) for being great friends and offering many an encouraging word. I will be forever thankful to you all.

The last few years have been an amazing journey, and I am grateful to you all for being there for me.

THESIS CONTENTS

VOLUME I: ACADEMIC RESEARCH COMPONENT

VOLUME II: CLINICAL PRACTICE REPORTS

1. Literature Review

Executive Functioning in Developmental Disorders

-A Review of the Literature

6891 words

CONTENTS

FIGURES

TABLES

APPENDICES

ABSTRACT

The term 'executive functioning' refers to the 'higher order, self-regulatory, cognitive processes that aid in the monitoring and control of thought and action. These skills include inhibitory control, planning, attentional flexibility, error correction and detection, and resistance to interference' (Carlson, 2005, p595). It is widely known that executive functioning is typically impaired in patients with frontal lobe damage (Baron-Cohen & Moriarty, 1995), however in recent years there has been a growing focus on whether executive functioning is impaired in neurodevelopmental disorders associated with congenital deficits in the frontal lobe. This paper reviews research of executive functioning in three neurodevelopmental disorders: Fragile X, Williams and Prader Willi syndromes. Whilst there has been plenty of research examining the behavioural phenotype of these disorders (e.g. Russell & Oliver, 2003; Oliver *et al*., 2007; Woodcock, Oliver & Humphreys, 2009a), there is a paucity of research examining how deficits in executive functioning may explain such behaviours. Research was found to show some indication of executive functioning deficits in all three of the syndromes however specific information as to how these related to the behavioural phenotype was generally lacking. Methodological issues regarding sample size and measures were highlighted, with recommendations for more longitudinal studies with consistent comprehensive executive functioning measures (encompassing both hot and cold executive functioning) proposed for future research.

Key Words: Executive Function, inhibition, working memory, switching, cognitive flexibility, fluency, neurodevelopmental disorders, Fragile X syndrome, Prader Willi syndrome, Williams syndrome, hot executive function, cool executive function, measures of executive function, cognitive phenotype, behaviour phenotype, Autism.

1.0. EXECUTIVE FUNCTIONING

There are a plethora of definitions and models existing for the psychological construct of 'executive functioning' (see Anderson, 2008 for a comprehensive review). Early models defined executive functioning as an umbrella concept, attributed to the frontal lobes and limited to the cognitive domain (Baddeley & Della Sala, 1998; Shallice, 1990). However this definition was found to be far too simplistic as executive functioning was acknowledged to encompass a 'highly complex, interrelated set of cognitive abilities....critical for adaptive function' (Anderson *et al*., 2008, p.xxviii). It is proposed that the main function of executive functioning is to help an individual to engage in goal-directed self-serving behaviours (Lezak, 1995).

The general consensus now is that executive functioning is a collection of interrelated processes responsible for goal-directed behaviours, controlling, organising and directing other cognitive activites, emotions and behaviours (De Luca & Leventer, 2008; Gioia, Isquith & Guy, 2001). Gioia *et al*. identify the main elements of executive functioning to include working memory, initiation, planning, mental flexibility, impulse control, selection of appropriate problem solving strategies and anticipation and deployment of attention.

Research has proposed that executive functioning may operate differently in different contexts (Hongwanishkul *et al*., 2005). The two aspects of executive functioning implicated are 'cool' cognitive executive functioning (associated with the dorsolateral prefrontal cortex) elicited by abstract decontextualised problems, and 'hot' affective executive functioning (associated with the ventral medial prefrontal cortex) elicited by problems associated with social and emotional decision making, affect regulation and motivation (Zelazo, Qu & Müller, 2004; Zalazo & Müller, 2002). The majority of research on executive functioning has used tasks focussed almost exclusively on cool executive functioning (eg. tasks associated

with working memory and rule flexibility), although it may be argued that there is a combination of hot and cool needed to complete the task. There is increasing interest in the development of hot executive functioning and how it affects making decisions that have emotionally significant consequences (Hongwanishkul *et al*., 2005).

Just as executive functioning is not a unitary concept, neither is executive *dysfunction*. Individuals rarely show global executive dysfunction (Pennington & Ozonoff, 1996). Disinhibition, perseverative behaviour, planning and initiation difficulties, and resisting change are all examples of impairments in executive functioning. Individuals with executive functioning impairments may present as being socially inappropriate, being ignorant of social and moral rules, demonstrating impulsiveness, lacking initiative or may appear to not think through the consequences of their actions. As Anderson (2008) highlights, such behaviours are considered deviant for adults but would not be the case for an infant. Therefore it is important to understand the 'developmental expectations of executive processes' (p. 4).

1.1. Models of Executive Functioning

In his review of executive functioning models, Anderson (2008) concludes that as of yet there is no universal model. Anderson (2008) states that for a model to be useful it needs to be valid theoretically, integrate all elements of executive functioning, be able to account for impairment patterns, postulate brain-behaviour relationships and to be able to be tested using appropriate assessments. Much more research needs to be conducted before such a model can be generated.

1.2. Executive Functioning and Intelligence

Friedman *et al* (2006) reviewed the claim that executive functioning is unrelated to general intelligence. Several case reports have described individuals with executive functioning impairments with normal intelligence (Duncan, Burgess & Emslie, 1995). Friedman *et al*., using a combination of crystallized and fluid intelligence measures, demonstrated that whilst some executive functioning processes correlate with intelligence (e.g. updating working memory), others show far weaker relationships (e.g. switching, inhibition and flexibility). It has been shown in some studies (e.g. Jauregi *et al*., 2007) that higher levels of intellectual development do not necessarily protect against neuropsychological deficits.

1.3. Executive Functioning and the Frontal Lobes

In relation to the biological basis of executive functioning, examining the impact of injury to different areas of the brain through fMRI scans and clinical observations has revealed that some executive functioning components, such as working memory, inhibition and social processing, are indeed localised to the frontal lobes and prefrontal cortex (e.g. Fuster, 2002; Goldman-Rakic & Leung, 2002). There has however also been evidence that other regions are also involved (Anderson *et al*., 2008). It is now considered that executive function's rely on the whole brain, with the Prefrontal cortex (PFC) being a necessary but not sufficient component for effective executive functioning. The PFC is proposed to fulfil a monitoring capacity (Stuss & Alexander, 2000). More research looking at the development of executive functioning is needed to better understand the executive functioning-frontal lobe relationship. There is a parallel between frontal lobe development and executive functioning (Zelazo, 2008; Phillips & Henry, 2008). The frontal lobe is the last region of the brain to

mature, with protracted development into early adulthood (Steinberg, 2005). Throughout the development of the frontal lobes, executive functioning also develops with performance on many measures of executive functioning hitting ceiling levels at this time. Once development of the frontal lobes has peaked, they then start to degenerate in old age. Executive functioning abilities also decline. This development of executive functioning is represented in Figure 1.

Frontal lobe development is determined by genetics and responses to environmental stimuli (De Luca & Leventer, 2008). These control gray matter development (proliferation and differentiation of neurons) and white matter development (axonal and dendritic arborisation) alongside myelination, synaptic pruning and apoptosis (Kuan, Roth, Flavell & Rakic, 2000). Appendix A documents the structural and functional changes in brain development and executive functioning across child hood to early adulthood (see De Luca and Leventer for a detailed review of frontal lobe development).

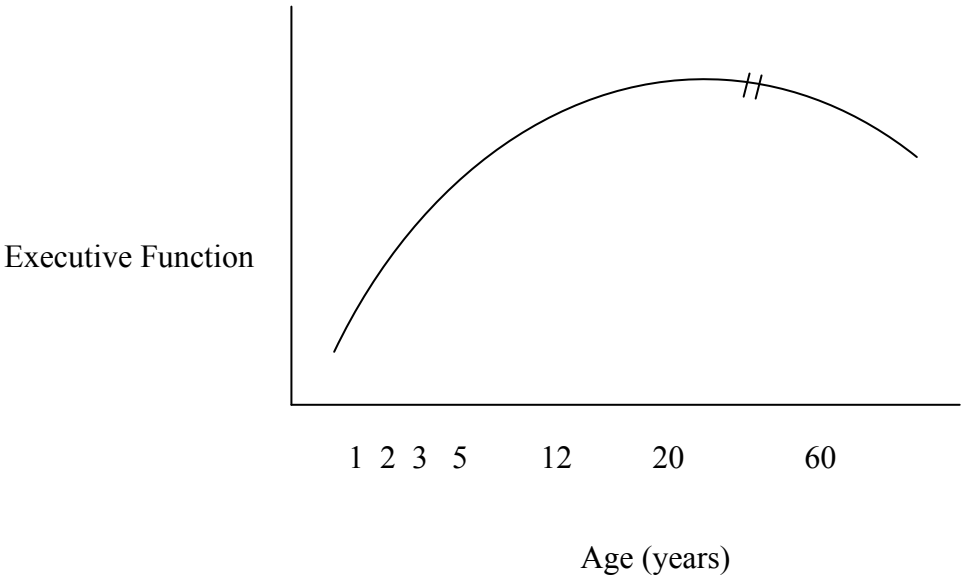


Figure 1. Typical executive functioning development across the lifespan (Zelazo, 2010)

Generally, young children lack the capacity to plan, monitor, update and shift their goal-oriented behaviours, struggling with more complex tasks that increase cognitive demands. As they age and their brain develops, these higher-order skills come 'online', and individuals demonstrate more independent and purposeful behaviour. However with such a complex system of development, there is a risk of dysfunction if one element of brain development goes awry. Neurodevelopmental disorders, diseases and psychological disorders (such as depression) may lead to executive dysfunction. As highlighted by De Luca and Leventer (2008): 'from the primitive reflexes of the immature and helpless newborn, to the development of imaginative play and self-autonomy of the young child, on to the planning and organization of a career and family in adulthood, and finally to the decline of one's self-sufficiency in later life. When executive development follows its projected route we see the creation of unique individuals, but when disrupted, either through biological or environmental insults, havoc is wreaked on cognitive, social, academic and vocational growth.....the timing, extent and location of this disruption is important in defining the type and severity of the deficits suffered' (p. 24).

2.0. NEURODEVELOPMENTAL DISORDERS AND EXECUTIVE FUNCTIONING

Executive functioning difficulties have been found in many developmental disorders, such as autism and Down syndrome. Different disorders may involve impairments in different aspects of executive functioning (Zelazo, 2010). Studying children who have had head injuries suggest disrupted executive functioning development can result not only in cognitive difficulties but also in problems with social, emotional and moral development (Anderson *et al*., 1999). Poor executive functioning is associated with emotional difficulties (e.g. aggression, mood swings), risk taking (e.g. alcohol, drugs), compulsive behaviour (OCD

type symptoms) and attentional difficulties (e.g. distractibility, poor academic planning) (Zelazo *et al*., 2008).

Developmental disability is a clinically significant cognitive and adaptive function impairment with an onset before 18 years old and is clinically manifested in 1228 genetic syndromes (Gothelf *et al*., 2005). 'Given that so many different genetic disorders can result in [developmental disability] and that brain development is the result of myriad genes and complex environmental interactions, it is not surprising that many different brain abnormalities have been found in subjects diagnosed with [developmental delay]' (Gothelf *et al*, 2005, p 331). The executive deficits characteristic of acquired and developmental disorders are considered to be a result of disruption or developmental impairment of the PFC (Luna *et al*., 2002).

What follows is a brief review of executive functioning in three neurodevelopmental disorders: Fragile X syndrome, Williams syndrome and Prada Willi. Each syndrome has an associated behavioural phenotype- a predisposition towards a characteristic pattern of behaviour that may affect social adaptation (Jauregi, *et al*.,2007; Liss *et al*., 2001). A considerable amount of research has been conducted examining the genetic and behavioural phenotypes of neurodevelopmental syndromes (e.g. Russell & Oliver, 2003; Oliver *et al*., 2007; Woodcock, Oliver & Humphreys, 2009a), however there is comparatively little on the cognitive phenotypes that mediate between these. Research over the last decade has started to examine how behavioural phenotypes and the capacity for social adaptation, may be linked to deficits in executive functioning.

Autism is one of the most well researched disorders in relation to executive functioning deficits, Executive dysfunction has been used as an explanation of the behaviours associated with autism (Ozonoff, Pennington & Rogers, 1991; Turner, 1997, Happé, Booth, Charlton &

Hughes, 2006). Early research into executive functioning in autism looked for a single factor that would explain the autistic triad of impairments (communication, imagination, social interaction), however recent thinking has moved on and instead it is considered that autism may entail multiple impairments in different areas of the brain and functional systems (Bishop & Norbury, 2005b). As such, the combination may produce a variety of different autistic symptom profiles and explain the variability in research findings (e.g. some studies have found fluency to be impaired in autism, others have not). This means that research needs to examine which specific executive function's are associated with which symptoms. Findings generally point to deficits with cognitive flexibility and planning, with relative strengths in working memory (Bishop & Norbury, 2005b). One aspect of behaviour these deficits have been used to explain are the restricted, repetitive behaviours in people with autism (Lopez *et al*., 2005). Turner (1997) has proposed two dissociable hypotheses regarding executive functioning and its relation to repetitive behaviour in autism. One is that there is a failure to inhibit behaviour due to lack of attention control. This is due to frontal lobe dysfunction influencing the tendency to perseverate and to become 'stuck' or 'locked into' a behaviour. The second is related to the ability to generate novel responses-Turner suggests the people with autism lack the ability to do so which then leads to repetitive behaviours. Attention deficit hyperactivity disorder (ADHD) is another widely researched disorder, with findings showing a different pattern of executive function skills with relative strengths in planning and weaknesses in inhibition (Pennington, 1997; Corbett et al., 2008).

The finding that executive functioning deficits may be present in many developmental disorders has raised a question of discriminant validity – how can disorders with different behavioural phenotypes have the same cognitive underpinnings? (Ozonoff & Jensen, 1999; Ozonoff, Pennington & Rogers, 1991). Ozonoff & Jensen argue that as executive functioning is comprised of many elements (e.g. planning, inhibition, fluency), it is possible that

disruptions in different combinations of these elements may explain the differences in presented behaviours. It is important to examine if behavioural phenotypes can be explained by underlying executive functioning deficits as it will help improve understanding of behaviours and also help inform treatment/rehabilitation strategies.

2.1. Fragile X syndrome (FXS)

Fragile X (or Martin Bell) Syndrome is the second most common genetic cause of intellectual disability (Dykens *et al*., 2000; the first is Down syndrome). It is a genetic disorder caused by a mutation in the FMR1 gene on the X chromosome (Batshaw, 1997), and is more prevalent in males (1 in 3600) than females (1 in 8000; Hagerman, 1999). FMR1 is responsible for the synthesis of a protein (FMRP) that is important in learning and memory, aiding with synapse and axon development (Bassell & Warren, 2008). Females with Fragile X tend to demonstrate less penetrance as there is a high chance that the other FMR1 allele on their other X chromosome is intact. Males on the other hand only have one X chromosome so if this is mutated the penetrance is much higher. Males tend to have IQs around 40-60, whereas females tend to show a much milder intellectual disability (Abbeduto *et al*., 2001).

In relation to behaviour, individuals with FXS are reported to have difficulties with social interaction, similar to that seen in autism (Garner, Callias & Turk, 1999). They are socially anxious and have difficulties initiating social contact (Holsen, Dalton, Johnston & Davidson, 2008). Also, they have been found to have an increased likelihood of obsessive compulsive symptoms, which is more pronounced in males (Bourgeois, *et al*., 2007). Repetitive behaviour (defined by Turner (1997) as being behaviours characterised by frequency of repetition, inappropriateness and invariance) are also reported. Autistic features may also be present (Hooper *et al*., 2008).

Other characteristics displayed by individuals with FXS include short attention span, hyperactivity, hypersensitivity (visual, auditory, tactile and/or olfactory stimuli) and perseveration in behaviour and speech (Goldstein & Reynolds, 1999). Individuals with FXS show strengths in verbal relative to performance IQ and in short-term memory for simple, meaningful information relative to complex sequential information (Cornish, Sudhalter, & Turk, 2004).

Cornish and colleagues have reported individuals with FXS as having difficulties with inhibition and visual attention switching (Cornish, Munir, & Cross, 2001; Wilding, Cornish, & Munir, 2002). Similarly Woodcock, Oliver and Humphreys (2009b) found evidence of difficulties in switching which correlate with repetitive behaviours in males.

In a comparison of boys with FXS and boys with an intellectual disability of unknown etiology, Garner *et al*. (1999) found both groups were at floor level on the assessments used, suggesting impairment in executive functioning was not specific to FXS, rather it is impaired in all children with an intellectual disability. However they only used one measure of executive functioning- the modified Wisconsin Card Sort Task (WCST-M), which may not have been sensitive enough to detect subtle changes between the groups.

Grigsby *et al* (2007) and Brega *et al*. (2008) reported their results of a series of studies into FXS and executive functioning. They found executive functioning deficits in behavioural self-regulation, working memory, verbal fluency, inhibition and attention control in the male participants that they studied. Through a mediation analysis, they demonstrated that executive functioning deficits impacted on performance on other cognitive measures such as verbal and performance IQ measures.

Scerif *et al*, (2004) found male toddlers with FXS showed inhibition deficits, in comparison to participants with Williams syndrome and mental/chronologically aged matched

participants who were typically developing. Hopper *et al*. (2008) found that boys with FXS demonstrated impairments in working memory, shifting, inhibition, planning and cognitive flexibility. Mental age was a significant predictor of working memory and shift tasks.

Hoopper *et al.* (2008) are in the process of conducting a longitudinal study over five years to examine executive functioning in 54 7-13 year old boys with FXS. A year into the project, they have reported evidence of flexibility/shift, inhibition, planning/problem solving and working memory impairments in FXS. These impairments were present even when mental age was controlled for, suggesting there are impairments that are not just explained by developmental delay. The authors propose that as males with FXS get older, they will face challenges in problem solving and strategy deployment in their learning as cognitive demands increase.

Research examining executive functioning in women with FXS has found impaired cognitive flexibility and planning (Pennington, 1997), and impaired working memory (Kirk, Mazzocco & Kover, 2005; Mazzocco & Kover, 2005) and inhibition (Cornish, Sudhalter & Turk, 2004) not to be attributed solely to IQ. Lightbody, Hall & Reiss (2006) found evidence that executive functioning deficits (specifically inhibition, fluency and switching) in girls with FXS increased with age, in contrast to verbal and visual-spatial abilities when compared to unaffected siblings and a developmental age-matched group.

Mazzocco, Pennington & Hagerman (1993) reported 'specific deficits in skills thought to be monitored by the frontal lobes' (p328). They have found evidence of deficits in executive functioning in women with FXS in comparison with women who were obligate carriers of the gene. The obligate carriers did not differ from a control group who did not have the gene. Women with FXS demonstrated more perseveration/shifting errors, and had inhibition

difficulties. This is consistent with the behavioural phenotype of difficulties with transitions and in perseverative thinking and language.

So these findings demonstrate that there are executive functioning impairments in FXS, and Woodcock *et al*. (2009b) showed impairment in one element of executive functioning (inhibition) was related to a measure of repetitive behaviour (lining up objects and repetitive actions), providing evidence for an executive functioning-behaviour link.

It has been proposed that FXS may be associated with the damage of crucial neural pathways involved in executive functioning. This may then explain weakness in executive functioning capabilities. This damage to specific executive functioning pathways can also then explain why abilities unrelated to executive functioning (such as face processing and vocabulary) may be more preserved (Cornish *et al*., 2004). Indeed, the use of fMRI scanning of individuals with FXS has showed reduced activation in the prefrontal cortex (Holsen *et al*., 2008) which suggests there may be executive functioning impairments.

Research using brain imaging techniques has also informed executive functioning knowledge. Menon, Leroux, White & Reiss, (2004; cited in Hoopper, 2008) have found evidence from fMRI scanning that implicates dysfunction in the prefrontal cortex to self-monitoring and inhibition difficulties in FXS. Cornish *et al*. (2004) used fMRI to examine neural activity in females with FXS on executive functioning tasks of response inhibition and switching. They found the prefrontal cortex had significantly more activation in FXS than controls.

Structural MRI studies have shown tissue volume of the caudate nucleus (which receives afferent fibres from the prefrontal cortex and is has efferent connections to subcortical regions) is larger in the brains of both males and females with FXS. Studies of lesions within this circuit have found damage in this area to be associated with deficits in response

inhibition, cognitive flexibility, attentional and goal-oriented behaviour - behaviours associated with FXS. The caudate nucleus is also implicated in FXS, with imaging studies finding that lower FMRP affects this component of the brain. This leads to the possibility that pharmacological treatments may be developed to increase FMRP to alleviate some of the cognitive difficulties associated with FXS, or even with other syndromes with executive functioning deficits (Gothelf *et al*., 2005).

2.2. Williams Syndrome (WS)

Williams syndrome is a neurodevelopmental disorder caused by the deletion of at least 25 genes from chromosome 7 (Korenberg *et al*., 2000). It has a prevalence rate of 1 in 7,500-20,000 births (Martens, Wilson, & Reutens, 2008). Individuals with WS typically fall within the mild to moderate range of intellectual impairment (Bellugi *et al*., 2000).

There are many brain abnormalities that have been detected in WS, including abnormalities in the cerebellum, right parietal cortex, and left frontal cortical regions. Reiss *et al*. (2000) reported the results of an MRI study of WS compared to typically developing individuals. They found that individuals with WS had brains that were 13% lower in volume. This decrease was mainly located in the lower brain stem regions.

These abnormalities manifest themselves in the visual-spatial disabilities and problems with behavioural timing. Dorsal-frontal abnormalities manifest themselves with difficulties in inhibition. WS is associated with a characteristic behavioural phenotype which main characteristics include individuals being hyperverbal- failing to wait their turn in conversations and 'blurting' (Järvinen-Pasley *et al*., 2008). They present as overly sociable, friendly and empathetic, with low intelligence and poor emotion regulation. They are also

reported to experience high levels of anxiety (Jones *et al*., 2000). Verbal skills are relatively intact, whereas visual-cognition and spatial skills are shown to be impaired (Reiss *et al*., 2000). It is this 'uneven' cognitive profile that has fuelled research interest into the syndrome (Bellugi *et al*. 2000).

Researchers including Mervis *et al*. (2000), Karmiloff-Smith *et al*. (2003), and Udwin and Yule (1991) identified a cognitive profile of WS which include slow processing speeds, and relative strengths in verbal working memory and auditory processing (Don, Schellenberg & Rourke, 1999). Mervis *et al*. report that despite variability in IQ, the majority of studies have found a consistent pattern of cognitive strengths and weaknesses in individuals with WS. Gothelf *et al*. (2005) reviewed the findings of relative strengths and difficulties in different areas and concluded that the data indicated that they are indicative of modular cognitive development, with different developmental trajectories.

Studies on the cognitive elements of WS have focussed on language skills (e.g. Bellugi *et al*., 2000). There is little reported work on executive functioning, although some researchers comment that impairments in reasoning and decision making may also be a part of the profile (Namihira, Hirayasu & Koga, 2004). Zhao *et al*. (2008) reported individuals with WS in their study to demonstrate poorer switching skills and more repetitive errors than controls (a group with Down Syndrome, a group matched for mental age and a group matched for chronological age) on a visual search task and visual sort task. They concluded that executive functioning was developing atypically in WS.

Porter and Colheart (2005) make the important point that, just as cognitive profiles in a typically developing population vary, so do individuals with WS (and indeed all syndromes). In reviewing research on the cognitive profile of WS they identified many flaws, including the range of different tests used and the lack of specificity of individual tests.

In summary, the paucity of research into executive functioning in WS suggests an important future research agenda. As well as looking at traditional 'cold' EF, this author proposes another direction for research- to address how the excessive sociability may be related to executive functioning. It has been proposed in the literature that hot executive functions are responsible for the social-affective parts of human behaviour (Hongwanishkul *et al*., 2005). A literature search failed to show any articles examining hot executive functioning in WS. Deficits in hot executive functioning may explain the reported lack of inhibition when individuals with WS meet strangers (Jones *et al*, 2000). This is something that needs to be investigated in future.

2.3. Prader Willi Syndrome (PWS)

Prader Willi syndrome has a prevalence rate of 1 in 10,000-15,000 births (Kileen, 2004). It is caused by a deletion or uniparental disomy of seven genes on the paternal chromosome 15 (Walley & Davidson, 2005). There is a 1:1 male to female ratio. Intellectual disability and the behavioural phenotype of behavioural issues (Dykens & Shah, 2003), particularly compulsive behaviours (such as skin-picking, perseverative speech), impulsivity, anxiety, emotional lability and temper tantrums are common in this disorder (Clark, Boer & Webb, 1995; Wigren & Hansen, 2005). Individuals with PWS are often reported to have difficulty forming and maintaining social relationships (Water, 1999). PWS is associated with an extreme and insatiable appetite, which often leads to obesity (Cassidy, 1997). Hiraiwa *et al*. (2007) found that the behavioural phenotype is unique to PWS when compared to other individuals with intellectual disabilities matched for intelligence and age.

In relation to cognitive profiles, the majority of individuals with PWS fall within the mild/borderline/low average intelligence range (Cassidy, 1997). One study found that 5% of individuals with PWS have average-low average IQ, 66% have borderline-mild intellectual disability and 29% have mild-moderate intellectual disability (Curfs & Fryns, 1992). In contrast to WS, individuals with PWS often demonstrate strong visual-spatial skills but poorer vocabulary skills. (Holm *et al*., 1993). They are also likely to have poor short-term memory (Curfs *et al*., 1991).

Studies of typical developing patients with frontal lesions of the brain have shown some of these same behaviours, leading researchers to hypothesise that processes requiring the prefrontal cortex such as executive functioning, may hold the answer to explaining the behavioural phenotype of PWS (Jauregi *et al*., 2007). Kenichi *et al*. (2006) used MRI scans and found that participants with PWS had developmental abnormalities in frontal white matter and the left dorsomedial thalamus, areas important for cognitive, visual and spatial functions.

To examine whether executive functions could underlie the behavioural phenotype, researchers have began to examine different elements of executive functioning. This has revealed that individuals with PWS show impairments in flexibility, response inhibition, social understanding and shifting (Wigren & Hansen, 2005). Walley and Donaldson (2005) conducted an investigation of executive functioning abilities in adults with PWS. They found a lack of executive functioning deficits when comparing the group to one matched for verbal ability and chronological age, concluding that differences in executive functioning did not account for the behavioural phenotype of the PWS group. Impairments in the phonological loop were found, leading them to tentatively suggest that another area of the frontal cortex, the orbitofrontal cortex (OFC), may be involved. This is thought to be tied to the modulation of emotion, with dysfunction manifesting in inappropriate emotional responses. Although the

authors do not mention it, the modulation of emotion fall into the 'hot' executive functioning category (Hongwanishkul, Happaney, Lee & Zelazo, 2005), so rather than the results indicating a lack of executive functioning deficits, their tasks specifically looked at cold executive functions (initiation, planning, rule-shift and working memory). It could be hypothesised that deficits in hot executive functioning could explain some of the behaviours demonstrated by PWS: compulsions, temper tantrums etc.

Jauregi *et al*. (2007) examined attention, working memory, and a number of other aspects of executive functioning to see how they differed compared to standard scores from the typically developing population. They found that individuals with PWS were significantly impaired in shifting, fluency, mental flexibility, and planning.

Other studies have shown there to be difficulties with inhibition (Stauder *et al*., 2005) and attention switching (Woodcock *et al*., 2009b) in PWS. Woodcock *et al*. (2009b) found repetitive behaviour in PWS (e.g. strict routines, skin picking, repetitive questioning/phrasing, hoarding, obsessions with order, cleaning) correlated with deficits in task switching. This suggests that repetitive behaviours may be caused by failure to inhibit the present behaviour, or by individuals lacking the ability to deal with the cognitive complexity of switching tasks, sticking with the ease of pre-learned behaviours. They go on to suggest that the deficit in task switching (also found in FXS) can lead to challenging behaviour following unexpected environment changes, postulated to place a greater demand on the individuals task switching capacity. Of all the studies reviewed this is the only one that has identified a direct link between a specific deficit in an executive function and a clinical pattern of behaviour in PWS or FXS. More research examining different executive functions and their relationship to behaviour is warranted.

As with all of the three neurodevelopmental disorders discussed, the degree to which the executive functioning deficits reported by researchers contribute to the behavioural phenotype of each disorder has yet to be determined. Sample sizes have been very small (< 20 in a clinical population in all studies reviewed) and age ranges restricted. What is needed is a review of executive functioning development over time so that developmental trajectories of executive functioning and behavioural phenotype can be examined and links between them analysed.

In summary of the discussion so far, Table 1 provides an overview of brain abnormalities, behavioural and executive functioning phenotypes in Fragile X, Williams and Prader Willi syndromes.

3.0. DISCUSSION

It is clear from the research discussed that there are some executive functioning deficits associated with each syndrome which may account for the emergence of the behavioural phenotype demonstrated. However it remains unclear which particular executive functions, if any, are critical in behaviour development. Also, as highlighted by Jauregi *et al*. (2007), executive processes may be multicomponential and therefore could selectively dissociate. More research needs to be conducted to identify which executive functions are critical in behaviour development.

What follows is a discussion of some of the limitations of the study of executive functioning generally, the studies of executive functioning in neurodevelopmental disorders and some suggestions for future research agendas.

Table 1. *Overview of brain abnormalities, behavioural and executive functioning phenotypes in Fragile X, Williams and Prader Willi syndromes.*

Syndrome	Brain regions implicated	Behaviours demonstrated	Executive Function Impairment
Fragile X	Caudate Nucleus Prefrontal cortex	Repetitive behaviour (hand flapping) Difficulties initiating social contact Social anxiety Obsessive compulsive symptoms Short attention spans Perseverative thinking and language Transition difficulties	Inhibition Visual attention Switching/Shifting Working memory Verbal fluency Planning Cognitive flexibility
Williams	Cerebellum, Right parietal cortex Left frontal cortical regions Dorsal-frontal lobe	Hypersociability Behavioural timing difficulties Hyperverbal Hypersocial Poor emotion regulation Anxiety Visual-Spatial disabilities	Inhibition Slow processing speed Problem solving skills Switching Hot executive functioning??
Prader-Willis	Left frontal white matter Left dorsomedial Thalamus	Repetitive behaviour (repetitive speech) Impulsivity Anxiety Emotional lability Difficulties with social relationships Extreme insatiable appetite Poor short term memory	Inhibition Flexibility Shifting Fluency Planning Attention switching Hot executive functioning??

3.1. Limitations in the Study of Executive Functioning

Anderson *et al*. (2008) highlight several important limitations within this field of research. These include there not being a consensus on the precise definition of executive functioning, the assessments are limited in their ability to quantify the striking clinical observations of executive dysfunction and in generalizing from a clinical to real-world context.

In relation to tests of executive functioning, they are criticised as being artificial and not simulating day-to-day life They are also limited in detecting specific abilities as they do not test executive functioning in isolation of other cognitive abilities- i.e. there is no such thing as a pure measure of executive functioning (Walley & Donaldson, 2005) as any test will tap other cognitive abilities (Burgess, 1997). In addition, they are reported to be insensitive to subtle deficits in executive functioning (Anderson, 2008). For these reasons a combination of self- and other- reported measures of behaviour and executive functioning and clinical observations are important.

3.2. Limitations in the Research Reviewed and Directions for Future Research

Several things were salient from conducting the literature review on executive functioning in the three syndromes discussed. These included the small sample sizes, the lack of consistent test use across the studies (both within and between syndromes) and the bias towards examining cold executive functions, something that may be particularly important when studying WS.Table 2 provides a brief overview of the sample size, control groups and tests used in the studies discussed. It can be seen from Table 2 that in the majority of cases the sample sizes

Table 2. *Sample size, comparison groups and tests used in some of the studies reviewed examining EF in neurodevelopmental disorders.*

Authors	Sample size	Comparison group	Tests used
Porter & Coltheart (2007)	31 WS (5-43 years)	None	Cognitive abilities: Woodcock-Johnson Tests of Cognitive Ability-Revised (WJ-R COG; Woodcock & Johnson, 1989)
Zhao, Z. *et al*. (2008)	21 WS	25 DS, 45CA, 41 MA	Inhibition, Flexibility: Monster Sorting Task
Garner *et al* (1999)	8 FXS, aged 10-16	8 mixed etiology (10-16 years)	Set maintenance, inhibition: Modified Wisconsin Card Sorting Test (WCST-M; Nelson, 1976).
Brega *et al*. (2008)	47 FXS, mean age: 68	32 asymptomatic, mean age 60 41 normal population, mean 64	Behaviour self-regulation: Behavioral Dyscontrol Scale (BDS; Grigsby *et al*., 1992) Working memory: Digit span forwards & backwards (WAIS-III; Weschler, 1997), Rey Auditory Verbal Learning Test (RVALT; Spreen & Strauss, 1998) Verbal fluency: Controlled Oral Word Association Test (Spreen & Benton, 1977) Verbal learning and memory: RAVLT

Hooper *et al*. (2008)	54 FXS (males), 7-13	48 typically developing males (aged 4-8)	Inhibition: The Day-Night Task (Diamond & Taylor, 1996) Contingency Naming Test (CNT; Anderson *et al*, 2000) Working Memory: subtests from Woodcock-Johnson Tests of Cognitive Abilities (WJ-III). Flexibility/set-shifting: CNT Planning: Tower task from NEPSY (Korpman, Kirk & Kemp, 1998) & Planning from WJ-III
Mazzocco, Pennington & Hagerman (1993)	22 FXS, mean 31 years (women)	35 women, obligate FXS carrier, mean 35 years 60 women, mean 32 years, family affected by X	Inhibition, switching: Contingency Naming Test (CNT) Mental flexibility: Wisconsin Card Sort Test (WCST), Visual Verbal Test
Lightbody *et al*.(2006)	46 FXS females (5-23)	46 unaffected siblings(28 females, 18 males, 6-20 years), 33 non-specific developmental disorders(12 females, 21 males, 7-18 years)	Inhibition, switching: Contingency Naming Task (Taylor, 1988) Fluency: F,A,S. Test (Spreen & Benton, 1977) Visual-spatial ability: subtest of Woodcock-Johnson battery (Woodcock & Johnson, 1990).

Kirk, Mazzocc & Kover (2005)	12 FXS females aged 7.8-11.4	12 typically developing females aged 8.0-9.2 20 turner females aged 8-9.9,	Verbal inhibition, switching: Contingency Naming Test (CNT; Anderson *et al*., 2000):
Woodcock, Oliver & Humphreys (2009)	28 participants (aged 9-19)paternal deletion subtype PWS (aged 6-18) 28 FXS boys with full FMR1 mutation	28 typically developing children (aged 5-11)	Simon spatial interference task (Simon, 1969)-response inhibition and task switching Attention, Inhibition, Switching: TEA-Ch subtests (Sky Search, Walk Don't walk, Opposite Worlds; Manly *et al*. 1999): Repetitive behaviour: Repetitive Behaviour Questionnaire (RBQ; Moss & Oliver, 2008) Childhood Routines Inventory (Evans *et al*., 1997)
Jauregi *et al*. (2007)	16 PWS (17-48 years)		Initiation, fluency: COWAT Mental flexibility, attention: Trail Making Test (TMT; Reinton, 1958) Perseveration: Wisconsin Card Sorting Test (WCST; Heaton, 1981) Working memory: Corsi Span (Milner, 1971), RAVLT, Bead memory (Thorndike *et al*. 1986)

			Visuospatial functions: Rey-Osterrieth Complex Figure (ROCF, Rey, 1987)
Walley & Donaldson (2005)	18 PWS (16-49 years)	15 (aged 18-49) intellectual disability (14 unknown causes, 1 DS)	Initiation,fluency: FAS (Newcombe, 1969), Planning: Tower of London Drexel version (Culbertson & Zilmer, 1998) Inhibition, set/rule changing: Luria Hand Game (Hughes, 1996), Rule Shift Card Task (Wilson *et al*., 1996), Spatial Reverse Task (MacEnvoy *et al*., 1993), Day/Night Task (Gerstadt *et al*., 1994) Working memory: digit span from WAIS-R (Weschler, 1981), Self-ordered pointing test (Temple *et al*., 1996) Dysexecutive Questionnaire (DEX) (Wilson *et al*. 1996). Aberrant behaviour checklist (Aman *et al*., 1985)
Namihira, Hirayasu & Koga (2003)	1 PWS, aged 19	(case report)	WCST-Keio version (KWCST) Frontal assessment battery (Dubois *et al*., 2000)
Cornish *et al*. (2004)	3 women with FMR1 full mutation FXS (aged 19, 22, 32)		Switching task (Wilding *et al*, 2002)

Cornish *et al*. (2009)	40 males with FXS (18-69 years)	67 males with normal FMR1 Alleles matched on age (20-69 years)	Working memory: Subtests from WAIS-III: Forward & Backward Digit Span, Spatial Span, Letter-number sequencing (Wechsler, 1997). Dot Test of Visuo-Spatial Working Memory (Bollini *et al*., 2000)

are small. Consequently, the generalisability of results from the studies may be questioned. However findings are strengthened in some part by the replication of results across studies.

The nature of the control group used is an important consideration when researching executive functioning in individuals with a neurodevelopmental disorder. Although there is research to suggest executive functioning and IQ are not related (see Section 1.3.), there is evidence that mental age (MA) may correlate (e.g. Mervis *et al*., 2000). As a result, many studies (e.g. Hopper *et al*., 2008) have used groups matched on MA. Some studies have used typically developing comparison groups (eg. Hoopper, 2008), others have used a syndrome group (e.g. Zhao *et al*., 2008) and some have used both (e.g. Brega *et al*., 2008). The problem with using a typically developing population is that if there are differences in executive functioning this is all that can be concluded. It is not possible to determine which behaviours are associated with the executive function, or to find out how specific the dysfunction is to a syndrome. By comparing against other groups with some similar behaviours it is easier to try and tease out specific executive function-behaviour relationships (Bishop & Norbury, 2005a). One study that addressed this was Woodcock *et al.* (2009b). They examined whether repetitive behaviours in PWS and FXS could be explained by deficits in two specific executive functions-switching and inhibition, and found there were distinctive profiles associated with each disorder.

They were also able to find a direct link between the deficits and selective aspects of repetitive behaviour. This study provides a useful template for future research.

It was clear from the literature on FXS and PWS that there is considerable heterogeneity within each syndrome. These variants need to be kept in mind as subtypes clearly differ in their behavioural and brain activation phenotypes (Stauder *et al*., 2005). The use of single-case approaches, favoured by some researchers (e.g. Porter & Coltheart, 2005), may provide more insight into this variability. Alongside single-case approaches, longitudinal imaging studies are needed to see if changes in brain structure tie in with the development of executive functioning and changes in behaviour. Research would benefit from using the *same* participants (due to heterogeneity within syndromes) to assess cognitive abilities, neurophysiology, neuromorphology and molecular genetics to link phenotype to genotype (Bellugi *et al*., 2000). Research is also needed to develop tests of executive functioning that can be used throughout the lifespan and that are sensitive enough to assess executive functioning development.

Another important concern is the great variability in tasks selected to examine executive functioning. As can be seen from Table 2, there is a vast range of different tests that are being used to study the same executive function, with varying sampling of multiple executive domains. Mervis et al. (2000) note that the difficulty in using different tests is that they are normed on different samples. However, the fact that similar results are found in spite of the difference in tests shows how salient the deficits are.

Additional limitations concern the use of measures of executive functioning that were typically developed for populations with no intellectual disability (Wigren & Hansen, 2005). Researchers have noted difficulties that individuals with a developmental disability have in completing some of the executive functioning measures which typically developing

individuals normally complete without difficulty (see Hooper *et al*., 2008 for more of a review). So although the tasks may be developmentally appropriate for typically developing individuals, they are not for individuals with developmental disabilities.

Gioia et al. (2002) discuss how many of the performance based executive functioning tests are not realistic, ecologically valid measures of executive functioning in the real world as they do not encompass the 'integrated, multidimensional, relativistic, priority-based decision making' (p.122) demanded in many real-world situations. They point to test batteries such as the Test of Everyday Attention for Children (TEA-Ch; Manly, Robertson, Anderson & Nimmo Smith, 1999) as going someway to address these concerns. They recommend increasing measure veridicality by using measures such as the Behaviour Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy & Kenworthy, 2000) where parent and teacher rated scales are used to assess a child's behaviour in their natural setting.

A consistent, efficient way to assess the pattern of cognitive abilities across syndromes would greatly aid the comparability of studies and aid in interpretation of the results. Mervis *et al*. (2000) state a preference for the use of single standardized measures, identifying the main advantage as being that all of the components of the battery being normed on a single sample. This is in contrast to the use of multiple measures, each of which is standardized on a different sample. Carson (2005) argues that it is crucial that adequate developmentally sensitive measurement tools be available to further advance research into executive functioning.

Alongside measures of executive functioning, studies have also used brain imaging. As with any methodology, there are limitations associated with brain imaging. These include the need for large sample sizes and the resulting cost of scanning. Gothelf *et al*. (2005) also note that some individuals with a developmental disability, particularly the more impaired, struggle

with staying still which leads to unusable images due to movement artefact. Also the scans are only able to provide gross observations of the brain. As brain imagining technology develops, more in depth explorations of brain mechanisms associated with each syndrome may be possible (Gothelf *et al*., 2005)

Another limitation noticed from reviewing the literature is the lack of operationalisation concerning behaviours demonstrated by the syndrome groups. Behaviours are complex yet umbrella terms such as 'repetitive behaviour' do not portray this. Woodcock *et al*. (2009b) showed that FXS and PWS demonstrate repetitive behaviour however the types of repetitive behaviour are different. 'The profile in the children with PWS was characterized by insistence on the sameness (e.g. liking to eat in a particular way), as well as liking to have things completed and having persistent habits. The profile in the boys with FXS, however, was characterized by more lining up objects and repetitive actions' (p.186). They go on to suggest, in line with other authors (e.g. Bodfish, 2004), that these behaviours may be associated with distinct underlying cognitive mechanisms. It is important therefore to get precise operational definitions of behaviours so that executive function-behaviour links can be more specific. It may be for example that inhibition ability in PWS may explain their repetitive behaviour but not repetitive behaviour in FXS. If repetitive behaviour is left as such a blanket term then it may be concluded that inhibition ability does not explain repetitive behaviour, where as in fact it explains the type of repetitive behaviour demonstrated in PWS.

In relation to the findings of executive functioning deficits in the disorders discussed, it is recognised by several authors that any deficits found may be argued to be a direct result of delayed development in executive functioning rather than a concrete deficit. Individuals with a neurodevelopmental disability might follow the same developmental path as typically developing children but at a slower rate. To address this longitudinal research needs to be conducted to examine whether reductions in problematic behaviour assumed to be related to

executive functioning corresponds with improved performance on measures of that executive function. Dykens (2004) conducted a cross-sectional study of individuals with PWS and reported a reduction in repetitive behaviour in older adults. As noted by Woodcock *et al*. (2009b), it would be useful to see if this was associated with an improved performance in task switching.

Developmental trajectories of different executive functions vary (Anderson, 2002). As such there is a need to investigate the differences in trajectories between syndrome groups and also within syndrome groups. It was discussed by several authors that there is variability within syndromes, so as such it is worth investigating whether there is a specific profile for low versus high mental age or low versus high chronological age.

By continuing to build the knowledge base around the cognitive profile of different syndromes, it may one day be possible to identify the specific genes responsible for certain brain development that is needed to support certain executive functions. This would then allow for models of brain and neuropsychology changes for each syndrome. By having a greater insight into the profiles of executive functioning associated both with individuals with typical development and developmental disorders, early interventions and treatments can be tailored to optimise individual development. They can help inform educational and rehabilitation strategies, parent information and support.

CONCLUSIONS

The study of executive functioning is important to help understand human behaviour. By increasing our understanding of executive functioning and its impact on behaviour, intervention strategies can be developed to help optimise healthy development and reduce

problematic behaviours associated with executive dysfunction. However, there are many difficulties in achieving these goals. At a fundamental level, with so many proposed models and definitions of executive functioning, consensus is unlikely (Anderson, 2008). As a result vague umbrella terms are often used which may undermine research looking at specific executive function-behaviour links.

Another limitation is that research tends to focus on 'cold' aspects of executive functioning, with 'hot' executive functioning being neglected. This needs to be addressed in order to present a full picture of executive functioning and its relation to behaviour. With two different components, it could be imagined that different disorders may show different patterns of deficits across them e.g. Zelazo and Müller (2002) suggest that autism may be associated primarily with hot executive functioning impairments, with secondary cold executive functioning impairments. Further research into hot aspects of executive functioning is clearly warranted.

In relation to the question of discriminant validity, by operationalising behaviours with more care, executive functioning deficits may help explain the differences in presented behaviours. Executive functioning is comprised of many elements, and different combinations of deficits in these elements may cause different behavioural outcomes

Alongside helping inform knowledge on the cognitive and executive functioning profiles of neurodevelopmental disorders, this field of research can help inform the development of models of the behaviour of the typically developing population of heuristic value (Jauregi *et al*., 2007). It is important for theoretical frameworks of executive functioning to take account of developmental processes, so it is important to map changes in executive functioning across the lifespan (Anderson *et al*., 2008).

In conclusion, sampling and methodology problems mean the results have to be interpreted with care. Studies up to now have found some good evidence that executive functioning deficits exist in the syndromes discussed. Further research utilising a more comprehensive uniform battery of executive functioning tests across syndrome groups is needed in order to increase knowledge of gene-brain-behaviour relationships and to examine whether profiles are syndrome specific. Longitudinal data is also needed to examine the developmental profile of the different executive functions across syndromes in order to examine how the development of executive functioning is correlated with social functioning and learning. Traditional psychometric testing combined with newer genetic and neuroimaging techniques are postulated by Anderson *et al*. (2008) as being critical to reliably assess executive functioning and its development.

5.0. REFERENCES

Abbeduto, L., Pavetto, M., Kesin, E., Weissman, M., Karadottir, S., O'Brien, A. & Cawthon, S. (2001) The linguistic and cognitive profile of Down syndrome: Evidence from a comparison with Fragile X syndrome. *Down syndrome Research and Practice*,**7**, 1, 9-15.

Anderson, P. (2002) Assessment and development of executive function (EF) during childhood. *Child Neuropsychology* **8**, 2, 71-82.

Anderson, P.J. (2008) Towards a developmental model of executive function. In: *Executive functions and the frontal lobes: A lifespan perspective* (eds V. Anderson, R. Jacobs, & P.J. Anderson.), pp. 1-21. Taylor & Francis Group, Hove.

Anderson, S.W., Bechara, A., Damasio, H., Tranel, D. & Damasio, A.R. (1999) Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nature Neuroscience* **2**,11, 1032-38.

Baddeley, A. & Deella Sala, S. (1998) Working memory and executive control. In: *The prefrontal cortex: Executive and cognitive functions* (eds A.C. Roberts, T.W. Robbins & L. Weiskrantz), pp. 9-22. OUP, Oxford.

Baron-Cohen, S, & Moriarty, J, (1995) Developmental Dysexecutive Syndrome: does it exist? A neuropsychological perspective. In: *Movement and allied disorders in childhood* (eds M. Robertson & V. Eapen). John Wiley and Sons Ltd.

Bassell, G.J., & Warren, S.T. (2008) Fragile X syndrome: loss of local mRNA regulation alters synaptic development and function. *Neuron* **60**, 2, 201–14.

Batshaw, M. L. (1997) Fragile X syndrome. In: *Children with Disabilities,* 4th edition (Ed. M. L. Batshaw), pp. 377-88. Brookes, Baltimore.

Bellugi, U., Lichtenberger, L., Jones, W., Lai, Z., & St. George, M. (2000) The neurocognitive profile of Williams syndrome: A complex pattern of strengths and weaknesses. *Journal of Cognitive Neuroscience* **12**, 1–6.

Bellugi, U., Lichtenberger, L., Mills, D., Galaburda, A.,&Korenberg, J. R. (1999) Bridging cognition, the brain and molecular genetics: Evidence from Williams syndrome. *Trends in Neuroscience* **22**, 197–207.

Bishop, D.V.M. & Norbury, C.F. (2005a) Executive functions in children with communication impairments, in relation to autistic symptomatology: 1: Generativity. *Autism* **9**, 1, 7-27.

Bishop, D.V.M. & Norbury, C.F. (2005b) Executive functions in children with communication impairments, in relation to autistic symptomatology: 2: Response Inhibition. *Autism* **9**, 1, 29-43.

Bodfish, J. (2004) Phenomenology of repetitive behaviour in autism: Comparison to non-specific intellectual disability. *Journal of Intellectual Disability Research* **48**, 292–292.

Bourgeois, J.A., Coffey, S.M., Rivera, S.M., Hessl, D., Gane, L.W., Tassone, F., Greco, C., Finucane, B., Nelson, L., Berry-Kravis, E., Grigsby, J., Hagerman, P.J. & Hagerman, R.J. (2009) A review of fragile X premutation disorders: expanding the psychiatric perspective. *Journal of Clinical Psychiatry* **70**, 6, 852-62.

Bourgeois, J.A., Cogswell, J.B., Hessl, D., Zhang, L., Ono, M.Y., Tassone, F., Farzin, F., Brunberg, J.A., Grigsby, J. & Hagerman, R.J. (2007) Cognitive, anxiety and mood disorders in the fragile X-associated tremor/ataxia syndrome. *General Hospital Psychiatry* **29**, 4, 349-58.

Brega, A.G., Goodrich, G. Bennett, R.E., Hessl, D., Engle, K., Leehey, M.A., Bounds, L.S. , Paulich, M.J., Hagerman, R.J., Hagerman, P.J., Cogswell, J.B. Tassone, F., Reynolds, A., Kooken, R., Kenny, M. & Grigsby, J. (2008) The primary cognitive deficit among males with fragile X-associated tremor/ataxia syndrome (FXTAS) is a dysexecutive syndrome. *Journal of Clinical and Experimental Neuropsychology* **30**, 8, 853–869.

Burgess P. W. (1997) Theory and methodology in executive function research. In: *Methodology of Frontal and Executive Function* (ed. P. Rabbitt), pp. 81-116. Psychology Press, Hove, East Sussex.

Carlson, S.M. (2005) Developmentally sensitive measures of executive functioning in preschool children. *Developmental Neuropsychology* **28**, 2, 595-616.

Cassidy, S.B. (1997) Prader-Willi syndrome. *Journal of Medical Genetics* **34**,11, 917–23.

Clark, D.J., Boer, H., & Webb, T. (1995) General and behavioural aspects of PWS: a review. *Mental Health Research* **8**, 195, 38–49.

Corbett, B.A., Constantine, L.J., Hendren, R., Rocke, D. & Ozonoff, S. (2009) Examining executive functioning in children with autism spectrum disorder, attention deficit hyperactivity disorder and typical development. *Psychiatry Research* **166**, 210-22.

Cornish, K. M., Munir, F., & Cross, G. (2001) Differential impact of the FMR-1 full mutation on memory and attention functioning: A neuropsychological perspective. *Journal of Cognitive Neuroscience* **13**, 144–50.

Cornish, K. M., Sudhalter, V., & Turk, J. (2004) Attention and language in fragile-X syndrome. *Mental Retardation and Developmental Disabilities* **10**, 11–16.

Cornish, K., Swainson, R., Cunnington, R., Wilding, J., Morris, P., & Jackson, G. (2004) Do women with fragile X syndrome have problems in switching attention: Preliminary findings from ERP and fMRI. *Brain and Cognition* **54**, 235–39.

Curfs, L.M., Fryns, J.P. (1992) Prader-Willi syndrome: a review with special attention to the cognitive and behavioral profile. *Birth Defects* **28**, 1, 99–104.

Curfs L. M. G., Wiegers A. M., Sommers J. R. M. Borghgraef M. & Fryns J. P. (1991) Strengths and weaknesses in the cognitive profile of youngsters with Prader–Willi syndrome. *Clinical Genetics* **40**, 430-34.

De Luca, C.R. & Leventer, R.J. (2008) Developmental trajectories of executive functions across the lifespan. In: *Executive functions and the frontal lobes: A lifespan perspective* (eds V. Anderson, R. Jacobs, & P.J. Anderson), pp. 23-55. Taylor & Francis Group, Hove.

Don, A. J., Schellenberg, E. G.,& Rourke, B. P. (1999) Music and language skills of children with Williams syndrome. *Child Neuropsychology*, **5**, 154–70.

Duncan, J., Burgess, P. & Emslie, H. (1995) Fluid intelligence after frontal lobe lesions. Neuropsychologia **33**, 261-68.

Dykens, E. M. (2004) Maladaptive and compulsive behavior in Prader–Willi syndrome: New insights from older adults. *American Journal on Mental Retardation* **109**, 142–53.

Dykens, E. M., Hodapp, R. M. & Finucane, B. M. (2000) Genetics and Mental Retardation Syndromes: A New Look at Behavior and Interventions. Brookes, Baltimore.

Dykens, E. M. & Shah, B. (2003) Psychiatric disorders in Prader-Willi syndrome: epidemiology and management. *CNS Drugs* **17**, 167-78.

Friedman, N.P., Miyake, A., Corley, R.P., Young, S.E., DeFries, J.C. & Hewitt, J.K. (2006) Not all executive functions are related to intelligence. *Psychological Science* **17**, 2, 172-79.

Fuster, J.M. (1989) The prefrontal cortex. Raven Press, New York.

Garner, C., Callias, M. & Turk, J. (1999) Executive function and theory of mind performance in boys with fragile-x syndrome. *Journal of Intellectual Disability Research* **43**, 6, 466-74.

Gioia, G.A., Isquith, P.K. & Guy, S.C. (2001) Assessment of executive functions in children with neurological impairment. In: *Psychological and developmental assessment: Children with disabilities and chronic conditions* (eds R.J. Simeonsson & L. Rosenthal), pp. 317-56. Guildford Press, New York.

Gioia, G.A., Isquith, P.K., Guy, S.C. & Kenworthy, L. (2000) Behavior Rating Inventory of Executive Function. Psychological Assessment Resources, Odessa, FL.

Gioia, G.A., Isquith, P.K., Kenworthy, L. & Barton, R.M. (2002) Profiles of everyday executive function in acquired and developmental disorders. *Child Neuropsychology* **8**, 2, 121-37.

Goldman-Rakic, P. & Leung, H. (2002) Functional architecture of the dorsolateral prefrontal cortex in monkeys and humans. In: *Principles of frontal lobe function* (eds D. Struss & R. Knight.), pp. 85-95. OUP, New York.

Goldstein, S. & Reynolds, C.R. (1999) Handbook of neurodevelopmental and genetic disorders in children. Guilford Press, New York.

Gothelf, D., Furfaro, J.A., Penniman, L.C., Glover, A.H. & Reiss, A.L. (2005) The contribution of novel brain imaging techniques to understanding the neurobiology of mental retardation and developmental disabilities. *Mental Retardation and Developmental Disabilities Research Reviews* **11**, 331-39.

Grigsby, J., Brega, A. G., Leehey, M. A., Goodrich, G. K., Jacquemont, S., Loesch, D. Z., et al. (2007b) Impairment of executive cognitive functioning in males with fragile X-associated tremor/ataxia syndrome (FXTAS). *Movement Disorders* **248**, 227-33.

Hagerman, R. J. (1999) Neurodevelopmental Disorders. Oxford University Press, Oxford.

Happé, F., Booth, R, Charlton, R, & Hughes, C. (2006). Executive function deficits in autistic spectrum disorders and attention-deficit/hyperactivity disorder: Examining profiles across domains and age. *Brain and Cognition* **61**, 25-39.

Hiraiwa, R., Maegaki, Y., Oka, A. & Ohno, K. (2007) Behavioral and psychiatric disorders in Prader-Willi syndrome: A population study in Japan. *Brain and Development* **29**, 9, 535-42.

Holm, V.A., Cassidy, S.B., Butler, M.G., Hanchett, J.M., Greenswag, L.R., Whitman, B.Y., Greenberg, F. (1993) Prader-Willi syndrome: consensus diagnostic criteria. *Pediatrics* **91**, 2, 398–402.

Holsen, L.M., Dalton, K.M., Johnstone, T. & Davidson, R.J. (2008) Prefrontal social cognition network dysfunction underlying face encoding and social anxiety in fragile X syndrome. *NeuroImage* **43**, 592-604.

Hongwanishkul, D., Happaney, K.R., Lee, W.S.C. & Zelazo, P.D. (2005) Assessment of Hot and Cool Executive Function in Young Children: Age-Related Changes and Individual Differences. *Developmental Neuropsychology* **28**, 2, 617-44.

Hooper, S.R., Hatton, D., Sideris, J., Sullivan, K., Hammer, J., Schaaf, J., Mirrett, P. & Ornstein, P.A. (2008) Executive functions in young males with fragile X syndrome in comparison to mental age-matched controls: Baseline findings from a longitudinal study. *Neuropsychology* **22**, 1, 36-47.

Järvinen-Pasley, A., Bellugi, U., Reilly, J., Mills, D.L., Galaburda, A., Reiss, A.L. & Korenberg, J.R. (2008) Defining the social phenotype in Williams syndrome: A model for linking gene, the brain, and behavior. *Development and Psychopathology* **20**, 1–35.

Jauregi, J., Arias, C., Vegas, O., Alén, F., Martinez, S., Copet, P & Thuilleaux, D. (2007) A neuropsychological assessment of frontal cognitive functions in Prader-Willi syndrome. *Journal of Intellectual Disability Research* **51**, 5, 350-65.

Jones, W., Bellugi, U., Lai, Z., Chiles, M., Reilly, J., Lincoln, A. & Adolphs, R. (2000) Hypersociability in Williams syndrome. In: *Linking cognitive neuroscience and molecular genetics: new perspectives from Williams syndrome* (eds U. Bellugi & M. St. George), *Journal of Cognitive Neuroscience* **12**, supplement, 31-46.

Karmiloff-Smith, A., Grant, J., Ewing, S., Carette, M. J., Metcalfe, K., Donnai, D., et al. (2003) Using case study comparisons to explore genotype-phenotype correlations in Williams-Beuren syndrome. *Journal of Medical Genetics* **40**, 136–41.

Killeen, A. A. (2004). Principles of Molecular Pathology. Humana Press, New Jersey.

Kirk, J.W., Mazzocco, M.M.M. & Kover, S.T. (2005) Assessing executive dysfunction in girls with Fragile X or Turner Syndrome using the Contingency Naming Test (CNT). *Developmental Neuropsychology* **28**, 3, 755-77.

Korenberg, J.R., Chen, X, Hirota, H., Lai, Z., Bellugi, U., Burian, D., Roe, B. & Matsuoka, R. (2000) Genome structure and cognitive map of Williams syndrome. In: *Linking cognitive neuroscience and molecular genetics: new perspectives from Williams syndrome* (eds U. Bellugi & M. St. George), *Journal of Cognitive Neuroscience* **12**, supplement, 89-107.

Kuan, C.Y., Roth, K.A., Flavell, R.A. & Rakic, P. (2000) Mechanisms of programmed cell death in the developing brain. *Trends in Neuroscience* **23**, 7, 291-97.

Lezak, M.D. (1995) Neuropsychological assessment. OUP, New York.

Lightbody, A.A., Hall, S.S. & Reiss, A.L. (2006) Chronological age, but not FMRP levels predicts neuropsychological performance in girls with Fragile X syndrome. *American Journal of Medical Genetics*, **141B**, 468-72.

Liss, M., Harel, B., Fein, D., Allen, D., Dunn, M., Feinstein, C., Morris, R., Waterhouse, L. & Rapin, I. (2001) Predictors and correlates of adaptive functioning in children with developmental disorders. *Journal of Autism and Developmental Disorders* **31**,219-30.

Lopez, B.R., Lincoln, A.J., Ozonoff, S., & Lai, Z. (2005) Examining the relationship between executive functions and restricted, repetitive symptoms of autistic disorder. *Journal of Autism and Developmental Disorders* **35**, 4, 445-460.

Luna, B., Minshew, N.J., Garver, K.E., Lazar, N.A., Thulborn, K.R., Eddy, W.F., & Sweeney, J.A. (2002). Neocortical system abnormalities in autism: An fMRI study of spatial working memory. *Neurology* **59**, 834-40.

Manly, T., Robertson, I.H., Anderson, V. & Nimmo Smith, I. (1999) TEA-Ch: The Test of Everyday Attention for Children Manual. Thames Valley Test Company Limited, Bury St Edmunds, England.

Martens, M.A., Wilson, S.J., Reutens, D.C. (2008) Research Review: Williams syndrome: a critical review of the cognitive, behavioral, and neuroanatomical phenotype. *Journal of Child Psychology and Psychiatry* **49**, 6, 576–608.

Mazzocco, M. M., & Klover, S. T. (2005) Assessing executive dysfunction in girls with fragile X or turner syndrome using the Contingency Naming Test. *Developmental Neuropsychology* **28**, 3, 755-77.

Mazzocco, Pennington & Hagerman, R.J. (1993) Neurocognitive phenotype of female carriers of Fragile X: Additional evidence for specificity. *Developmental and Behavioral Pediatrics* **14**, 5, 328-35.

Menon, V., Leroux, J., White, C.D. & Reiss, A.L. (2004) Frontal striatal deficits in fragile X syndrome: Relation to FMR1 gene expression. *Proceeding of the National Academy of Science* **10**, 3615-20.

Mervis, C. B., Robinson, B. F., Bertrand, J., & Morris, C. A. (2000). TheWilliams syndrome cognitive profile. Brain and Cognition, 44, 604–628.

Namihira, T., Hirayasu, Y. & Koga, Y. (2003) The assessment of cognitive function in a Williams syndrome patient: A case report. *Psychiatry and Clinical Neurosciences* **58**, 99.

Oliver, C., Horsler, K., Berg, K., Bellamy, G., Dick, K. & Griffiths, E. (2007) Genomic imprinting and the expression of affect in Angelman syndrome. What's in the smile? *Journal of Child Psychology and Psychiatry* **48**, 571-79.

Ozonoff, S. & Jensen, J. (1999) Brief Report: Specific Executive Function Profiles in Three Neurodevelopmental Disorders. *Journal of Autism and Developmental Disorders* **29**, 2, 171-77.

Ozonoff, S., Pennington, B.F., & Rogers, S.J. (1991) Executive function deficits in high-functioning autistic individuals: Relationship to theory of mind. *Journal of Child Psychology and Psychiatry* **32**, 7, 1081-1105.

Pennington, B.F. (1997) Dimensions of executive function in normal and abnormal development. In: *Development of the prefrontal cortex: Evolution, neurobiology and*

behavior (eds N.A. Krasnegor, G.R. Lyons & P.S. Goldman-Rakic), pp.265-281. Brookes, Baltimore.

Phillips, L.H. & Henry, J.D. (2008) Adult aging and executive functioning. In: *Executive functions and the frontal lobes*: A lifespan perspective.(eds V. Anderson, R. Jacobs, & P.J. Anderson), pp. 57-79. Taylor & Francis Group, Hove.

Porter, M.A. (2005) Cognitive Heterogeneity in Williams syndrome. *Developmental Neuropsychology* **27**, 2, 275-306.

Reiss, A.L., Eliez, S., Schmitt, E., Straus, E., Lai, Z., Jones, W. & Bellugi, U. (2000) Neuroanatomy of Williams syndrome: A high-resolution MRI study. In: *Linking cognitive neuroscience and molecular genetics: new perspectives from Williams syndrome* (eds U. Bellugi & M. St. George), *Journal of Cognitive Neuroscience* **12** supplement, 65-73.

Russell, H. & Oliver, C. (2003) The assessment of food related problems in individuals with Prader-Willi syndrome. *British Journal of Clinical Psychology* **42**, 379-92.

Scerif, G., Cornish, K., Wilding, J., Driver, J. & Karmiloff-Smith, A. (2004) Visual search in typically developing toddlers and toddlers with Fragile X or Williams syndrome. *Developmental Science* **7**, 116-30.

Shallice, T. (1990) From neuropsychology to mental structure. OUP, New York.

Stauder, J.E.A., Boer, H., Gerits, R.H.A., Tummers, A., Whittington, J., & Curfs, L.M.G. (2005) Differences in behavioural phenotype between parental deletion and maternal uniparental disomy in Prader–Willi syndrome: An ERP study. *Clinical Neurophysiology* **116**, 1464–470.

Steinberg, L. (2005) Cognitive and affective development in adolescence. *Trends in Cognitive Sciences* **9**, 2, 69-74.

Stuss, D.T. & Alexander, M.P. (2000) Executive functions and the frontal lobes: A conceptual view. *Psychological Research* **63**, 289-98.

Turner, M. (1997) Toward an executive dysfunction account of repetitive behaviour. In: *Autism as an Executive Disorder* (ed J. Russell), pp. 57-100. Oxford University Press, Oxford.

Udwin, O.,&Yule, W. (1991). A cognitive and behavioral phenotype inWilliams syndrome. *Journal of Clinical and Experimental Neuropsychology* **13**, 232–44.

Walley, R.M. & Donaldson, M.D.C. (2005) An investigation of executive functioning abilities in adults with Prader-Willi syndrome. *Journal of Intellectual Disability Research* **49**, 8, 613-25.

Waters, J. (1999) Prader–Willi syndrome. A Practical Guide. Fulton, London.

Wigren, M. & Hansen, S. (2005) ADHD symptoms and insistence on sameness in Prader-Willi syndrome. *Journal of Intellectual Disability Research* **49**, 6, 449-56.

Wilding, J., Cornish, K., & Munir, F. (2002) Further delineation of the executive deficit in males with fragile-X syndrome. *Neuropsychologia* **40**,1343–49.

Woodcock, K. A., Oliver, C., & Humphreys, G, W. (2009a) Hypothesis: A specific pathway can be identified between genetic characteristics and behaviour profiles in Prader-Willi syndrome via cognitive, environmental and physiological mechanisms. *Journal of Intellectual Disability Research* **53**, 493-500.

Woodcock, K.A., Oliver, C. & Humphreys, G.W. (2009b) Task-switching deficits and repetitive behaviour in genetic neurodevelopmental disorders: Data from children with Prader-Willi chromosome 15 q11-q13 deletion and boys with Fragile-X syndrome. *Cognitive Neuropsychology* **26**, 2, 172-94.

Yamada, K., Matsuzawa, H., Uchiyama, M, Kwee, I.L., & Nakada, T. (2006). Brain developmental abnormalities in Prader-Willi syndrome detected by diffusion tensor imaging. *Pediatrics* **118**, 2, e442-e448.

Zelazo, P.D. (2010). Executive function. [Online] Available at: www.Aboutkidshealth.ca [accessed January 2010].

Zelazo, P. D., & Müller, U. (2002) Executive function in typical and atypical development. In: *Handbook of childhood cognitive development* (ed U. Goswami), pp. 445–69. Blackwell, Oxford.

Zelazo, P.D., Qu, L. & Muller, U. (2004). Hot and cool aspects of executive function: Relations in early development. In: Young children's cognitive development: Interrelationships among executive functioning, working memory, verbal ability and theory of mind (eds W. Schneider, R. Schumann-Hengsteler & B. Sodian), pp. 71-93. LEA, New Jersey.

Zheng-Yan Zha, Z. Shaoa, J., Xiea, C., Wanga, Y., Qina,,Y, Cornish, K. & Karmiloff-Smith, A. (2008) Visual search, attention and executive function in Chinese children with Williams syndrome. *Paediatrics* **141**, 2, s148.

Appendix A. Brain and Executive Functioning Development over childhood and adolescence. Sourced from De Luca and Leventer, (2008).

Age	*Brain Development*	*Cold EF*	*Hot EF*
Prenatal	CNS development begins at 18 days gestation 6 weeks neuroblasts for frontal regions develop 24 weeks migration complete 24+ cortical organisation		
Birth	Gyri formed Neurons wired into networks Brain largely unmyelinated		
12 weeks		Able to detect goal structure of events	
7-8 months	Synaptogenesis Myelination	First signs of working memory and inhibition systems	Able to distinguish animate and inanimate objects
12 months	Synaptogenesis Myelination		Joint attention

14 months	Synaptogenesis Myelination		Social Referencing
2 years	Brain 80% weight of adult Brain	Improvements in inhibition and working memory	Understanding of pretense
3 years	Increased gray and white matter volumes Increased metabolism	Improvement in inhibitory control and sustained attention until age 5	Improvement in affective decision making over this year
4 years	Increased gray and white matter volumes Increased metabolism	Improved cognitive flexibility	Success at false belief tasks
5 years	Increased gray and white matter volumes Increased metabolism	Gains in working memory and strategy formation	Awareness that a belief can be held about another's beliefs
6 years	Increased metabolism	Beginnings of planning and goal-directed behaviour	Sophisticated adult-like theory of mind
7 years	Increased metabolism		Understanding of conflicting mental states

8 years	Increased white matter in frontal areas	Mature cognitive flexibility skills Improvements in inhibition, vigilance and sustained attention seen until 11	Understanding of metaphors and social deception
9 years	Increased white matter in frontal areas	Gains in working memory and strategic planning	Understanding of faux pas develops until 11
10 years	Increased white matter in frontal areas		
11 years	Second wave of cortical development seen for girls		
12 years	Second wave of cortical development seen for boys	Spurt in goal-directed behaviour	
13 years	Increased white matter in frontal areas		
14 years	Increased white matter in frontal areas Decreased gray matter seen-reduced synaptic density		Improvements in affective decision making until 17

15 years	Increased white matter in frontal areas Decreased gray matter seen-reduced synaptic density	Improved attentional control Increased processing speed Mature inhibition	
16-19 years	Increased white matter in frontal areas Decreased gray matter seen-reduced synaptic density	Gains in working memory, strategic planning, and problem solving until 19	
20-29 years	Completion of myelination	Mature working memory, strategic planning	Mature affective decision making ToM deficits still evident under specific circumstances
30-49 years	Brain weight begins to decline, drops by 10% to age 90		

50-64 years	Preferential white matter loss in prefrontal cortex	Sees the beginning of decreased concept generation, organization, planning, set-shifting, working memory, and goal setting Slowed processing Speed	
65-74 years	Senile plaques and neurofibrillary tangles Decreased cerebral blood flow		Reduced performance in affective decision making
75+ years	Senile plaques and neurofibrillary tangles Decreased cerebral blood Flow		Theory of mind deficits become evident

Appendix B. Glossary

ADHD Attention deficit hyperactivity disorder

EF Executive Function

fMRI Functional Magnetic Resonance Imaging

FXS Fragile X syndrome

MRI Magnetic Resonance Imaging

PWS Prader Willi syndrome

WS Williams syndrome

Appendix C. Literature Review Method

Firstly the overall aim of the literature review was identified. This was to look at what research had been carried out regarding executive functioning in children with three developmental disorders: Fragile X, Williams and Prader Willi.

The statement of intent was to find studies that had examined executive functioning in these developmental disorders, in order to see what measures had been used, and the key results that were being found regarding executive functioning and the implications for the groups studied as well as for the development of executive functioning normal population.

The electronic databases that were searched as they seemed most appropriate for this area of questioning were

Psychlit

Psychinfo

BIDS

Biological Abstracts

Web of Knowledge

The keywords used were 'Executive Function*and (development* disabilit* or genetic syndrome* or autis* or Fragile x or Prader Willi or Williams)

The number of references that were identified was 50 for executive functioning and the three genetic syndromes, and 57 for executive functioning and autism spectrum disorder.

Other references were gathered using the reference lists from the identified papers.

2. Empirical Paper

Executive Functioning in Cornelia de Lange Syndrome (CdLS)

CONTENTS

TABLES

FIGURES

APPENDICES

Abstract

Introduction: Cornelia de Lange Syndrome (CdLS) is a genetic disorder caused by mutations to Chromosomes 5, 10 or X. In addition to mild to profound intellectual disability and the distinctive physical phenotype, emerging evidence has suggested that there are a number of age-related changes in behaviour occurring during adolescence and early adulthood, including an increase in preference for routine, difficulty coping with change, repetitive behaviours, and selective mutism. Research into executive functioning and behaviour in other neurodevelopmental disorders, suggests that behaviours that are phenotypic of a syndrome are underpinned by specific executive functioning impairments. Given this evidence, it seems likely that the emotional and behavioural difficulties reported in adolescents and adults with CdLS may be underpinned by specific executive functioning impairments. This study aims to examine the main areas of executive functioning in adolescents and adults with CdLS and identify whether there is a profile of executive functioning specific to these individuals. *Method:* Twenty-four participants with Cornelia de Lange Syndrome (14 females and 10 males) aged 13-42 years (M = 22), and a comparable contrast group of 21 individuals with Down syndrome (13 females and eight males) aged 15-33 years (M = 24), participated in the study. A range of measures were selected to test verbal and visual fluency, inhibition, perseverance/flexibility, and working memory. Measures consisted of both questionnaire and performance tests. *Results:* The group of participants with CdLS showed significantly more impairment on tasks requiring generativity (verbal fluency), flexibility and inhibition (rule switch), despite there being no significant differences in working memory. These impairments were also reported in the parent/carer-rated questionnaire measures. There was also anecdotal evidence suggesting that there may be difficulties with initiation in the CdLS group, explaining their difficulties starting and or/completing some of the tasks. *Conclusions:* The relative deficits in executive functioning task performance may be important in understanding the behavioural phenotype of CdLS. Further longitudinal research of participants with CdLS from early childhood onwards is needed to examine how changes in executive functioning map onto changes in behaviour in CdLS. Limitations and future directions for research are discussed.

1.0. INTRODUCTION

Cornelia de Lange Syndrome (CdLS)[1] is a genetic disorder that has an estimated prevalence of 1 in 30,000 live births (Beck, 1976; Beck & Fenger, 1985). Mutations of the NIPBL gene on chromosome 5 have been found to cause CdLS in approximately 20 to 50% of individuals with the syndrome (Krantz *et al.*, 2004; Tonkin, Wang, Lisgo, Bamshad & Strachan, 2004; Miyake *et al*, 2005) and mutations of SMCIA on the X chromosome and SMC3 on chromosome 10 are also implicated in the disorder. It is probable that unidentified mutations of other genes account for other individuals with the syndrome (DeScipio *et al.*, 2005).

The physical phenotype of CdLS has been well documented. Low birth weight, small stature, limb abnormalities and distinctive facial features, such as synophrys, a long philtrum, thin lips and a crescent shaped mouth, are common features (Jackson *et al*., 1993). CdLS is also associated with health problems, such as hearing and eye abnormalities, and cardiac, genito-urinary and gastro-intestinal disorders (Hall *et al.,* 2008; Jackson *et al.*, 1993; Luzzani *et al.*, 2003). Degree of intellectual disability is variable but most individuals show a severe (30%) to profound (45%) intellectual disability with notably poor expressive communication (limited or absent speech) in relation to receptive language skills (Goodban, 1993; Sarimski, 1997; Berney, Ireland & Burn, 1999; Oliver *et al*., 2008). The average reported IQ is 53 (range 30-86) (Kline *et al*., 1993).

In comparison to the literature on physical characteristics in Cornelia de Lange syndrome, less research has been published on the behavioural and cognitive phenotype of CdLS. Behavioural research has focused predominantly on self-injurious behaviour, although a

[1] CdLS is sometimes referred to as Brachmann de Lange syndrome

number of studies have also been published on autism spectrum disorder in CdLS (e.g. Berney, Ireland & Burn, 1999; Oliver *et al*., 2008; Moss *et al*., 2009). The reported prevalence rate of autism spectrum disorder in CdLS ranges between 32.1% (Oliver *et al*., 2008) and 66.6% (Bhyuian *et al*., 2006). This rate is higher than that for comparable individuals without the syndrome. For example, Moss *et al.* (2008) found that 61.8% of participants with CdLS (n =34) scored above the cut-off for Autism on the Autism Diagnostic Observation Schedule, compared to only 39.2% in a contrast group. The profile of autism spectrum impairments in CdLS is reported to be atypical to that of idiopathic autism (Moss *et al*., 2009) and is not solely accounted for by degree of intellectual disability (Oliver *et al*., 2008). Individuals with CdLS show impairments in communication and demonstrate the presence of repetitive behaviour but show less impairments in social interaction than would typically be expected in individuals with autism spectrum disorder (Moss *et al.*, 2008). Moss *et al.* (2008) reported anecdotally that there were social impairments observed in several participants with CdLS (including, extreme shyness, social anxiety and selective mutism) but these were different to those reported in idiopathic autism.

There is little known about the developmental trajectory of the behavioural phenotype in CdLS. Emerging evidence has suggested that there are a number of age-related changes in behaviour. A pilot study, involving open-ended interviews, with nine parents of adolescents and adults with CdLS indicated changes in behaviour indicative of low mood and social anxiety with age (Collis, Oliver & Moss, 2006). The most commonly reported behaviours related to a change in mood, were tearfulness, loss of interest in activities previously enjoyed and feeling "unwell". Commonly reported behaviours which may relate to social anxiety were a reluctance to speak to unfamiliar people, preferring to watch peers rather than join in with their activities, having one or two good friends rather than more friends, experiencing selective mutism, appearing very shy and being reluctant to speak in a group setting. All

participants were reported to have a strong preference for routine and experienced difficulty coping with change, perhaps indicating that these difficulties are related to impairments in executive functioning, e.g., mental flexibility. The evidence from this pilot study indicates that there may be behavioural and emotional age-related changes in Cornelia de Lange syndrome, occurring during adolescence and early adulthood.

Kline *et al*. (2007a; 2007b) have also reported both behavioural and emotional changes in approximately 80% of individuals with CdLS including increased levels of depression, self-injury, obsessive-compulsive behaviours, anxiety, aggression and hyperactivity. Blagowidow, Kline & Audette (2004) found that carers reported these behavioural issues as worsening with the onset of puberty. In further support of these findings, Basile *et al.* (2007) found a significant relationship between chronological age and a range of behavioural issues (including communication disturbances and anxiety) in a group of 56 individuals with CdLS aged 11 to 31 years, with significantly more behavioural problems being associated with older individuals. Furthermore, Sarimski (1997) compared behaviour in older (above 6 years) and younger children (below 6 years) with CdLS and found that older children experienced significantly more social isolation and anxiety.

Oliver, Berg, Moss *et al*. (in submission) conducted a questionnaire study to examine mood, interest and pleasure across several syndrome groups, including individuals with CdLS. Amongst their results they found that adults (over the age of 18) with CdLS were more likely to experience high levels of negative affect (13%) compared to younger individuals (3%) with the syndrome. This profile of behaviour was not reported in any of the other six syndrome groups assessed, indicating there may be an atypical trajectory of mood, interest and pleasure, in Cornelia de Lange syndrome. Therefore, the research to date on age-related changes in CdLS suggests that there are a number of behavioural and emotional changes occurring with age in the syndrome.

The behavioural changes reported to occur with age in CdLS include, increased levels of depression, self-injury, obsessive-compulsive behaviours, anxiety, aggression, hyperactivity, communication disturbances, social anxiety and selective mutism. The suggested high prevalence of age-related changes in CdLS indicates that this trajectory of behavioural change is likely to be characteristic of individuals with CdLS. The use of contrast groups in some of the previous studies, such as Oliver *et al.'s* (in submission) study, also indicates that the developmental trajectory of these behaviours may be atypical in relation to other comparable syndrome groups. This is also supported by literature published on age-related changes in other neurodevelopmental disorders, such as autism spectrum disorder, where it is recognized that most symptoms are established by three years old (Rogers, 2009). Given that there appears to be a number of syndrome-specific, age-related, behavioural changes in CdLS, which are atypical in relation to other groups of individuals with neurodevelopmental disorders, this indicates that these behavioural changes appear to be unaccounted for by degree of disability and the association with autism spectrum disorder. It is therefore likely that there are syndrome-specific changes at a biological and thus a cognitive level, which account for the number of behavioural and emotional age-related changes in the syndrome.

In contrast to what is known about the behavioural phenotype of CdLS, comparatively less research has been published on cognition in CdLS. This research aims to address this paucity of knowledge and examine whether there are cognitive impairments that may help explain these behavioural changes. The area of cognition of key interest is executive functioning. Executive functioning refers to a set of cognitive abilities that control and regulate other abilities and behaviours. Executive functions are necessary for goal-directed behaviour. They include the ability to initiate and stop actions, to monitor and change behaviour as needed, and to plan future behaviour when faced with novel tasks and situations. Executive functions allow individuals to anticipate outcomes and adapt to changing situations. The ability to form

concepts and think abstractly, are often considered components of executive function (Hill, 2004).

The frontal lobes are postulated to play a major role in executive functioning (Anderson, Jacobs & Anderson, 2008). Research examining the impact of frontal lobe injuries has shown that affected individuals have executive functioning difficulties. The frontal lobes are the last part of the brain to fully develop, and as such, many executive functions do not fully develop until the late 20's (Barry, 2010; Zelazo, 2008). It may be postulated therefore that age-related changes, particularly around adolescence and early adulthood, may be tied to frontal lobe development. It may also be postulated that if executive functioning resides in the frontal lobes, then deficits in this area resulting from a developmental disorder may result in executive dysfunction. Indeed, neurological studies of Prader Willi, Fragile X and Williams syndrome have revealed abnormalities in the frontal region that may be related to the profiles of executive functioning associated with each syndrome (see Literature Review, this volume). For example, fMRI scanning of individuals with Fragile X has showed reduced activation in the prefrontal cortex (Holsen *et al*., 2008). This syndrome group has been associated with executive functioning difficulties with inhibition and visual attention switching (Cornish, Munir, & Cross, 2001; Wilding, Cornish, & Munir, 2002).

Brain imaging studies of CdLS are lacking, however the few autopsies that have been documented have revealed frontal lobe hypoplasia in CdLS, indicating that there may be difficulties with axonal growth, neural priming and neuron cell repair (Vuilleumier *et al*, 2002). Therefore it may be tentatively postulated that impaired growth of the frontal lobes may influence some of the behaviours seen in CdLS, especially those that are occurring during adolescence and adulthood, where research has shown not only that the frontal lobe growth is at an important developmental point, but that executive functioning development is crucial for social, emotional and moral development (Zelazo, 2008).

Problems in executive functioning may impact on social functioning in different ways. For example, individuals may have attentional difficulties, which could mean that they find it difficult to attend to, and thus maintain, a conversation; or people may have problems with inhibition and/or perseveration, leading them to say inappropriate things or become 'stuck' on the same activities. These are examples which highlight how impairments in certain areas of executive functioning can impact on social relationships with others (Anderson, 2008). Impairments in the ability to regulate, control and generate behaviour account for some of the social deficits in autism (e.g. Happé, Booth, Charlton, & Hughes, 2006). Additionally, such deficits are also thought to account for the social difficulties experienced by individuals with ADHD (e.g. Scheres *et al*., 2004). To date there has been no published literature that has examined executive functioning in people with CdLS. However, in other populations, including individuals with autism and individuals with specific genetic syndromes, such as Fragile X syndrome, assessments of executive functioning have been well documented (e.g. Rowe, Lavender & Turk, 2006; Wilding, Cornish & Munir, 2002; Jarrold *et al*., 1999; See Literature Review, this volume).

Specific deficits in executive functioning in these groups have been used to account for behavioural problems seen in these individuals. For example, Moss *et al.* (2008) report that research into Prader Willi syndrome has found evidence of a short-term memory deficit and limited attention-switching capacity (Dykens, Hodapp & Finucane, 2000) which they tentatively suggest may help explain the high preference for routine and repetitive questioning that is common within the syndrome (Dykens, Leckman & Cassidy, 1996). Woodcock, Oliver & Humphreys (2009) have reported that boys with Fragile X syndrome showed an impairment in inhibition and this was related to a measure of repetitive behaviour (adherence to routine), providing evidence for an executive functioning-behaviour link. The evidence published to date on executive functioning and behaviour in other

neurodevelopmental disorders suggests that behaviours that are phenotypic of a syndrome may be underpinned by specific executive functioning impairments. Given this evidence, it seems likely that the emotional and behavioural difficulties reported in adolescents and adults with CdLS, are underpinned by specific executive functioning impairments. A study examining executive functioning in adolescents and adults with CdLS, is therefore essential to understand the cause of the behavioural change with age reported in the syndrome. The behavioural changes that have been reported in CdLS are around the age of adolescence/early adulthood. For this reason, the current study will assess executive function in adolescent and adult participants with CdLS in order to enhance understanding of the possible causes of behavioural and emotional changes reported in the syndrome and provide information about the possible aetiological pathways underpinning these difficulties.

A comparable contrast group was needed for the current study because the tests of executive functioning used were not developed or normed for populations with neurodevelopmental disabilities. A comparable contrast group of individuals with Down syndrome, matched for age, gender, mobility, level of adaptive behaviour and receptive language (a domain not thought to tap into executive functioning; Joseph, McGrath & Tager-Flusberg, 2005), were included in the current study. Down syndrome has a natural prevalence of 1 in 600 live births. The syndrome is caused by an extra 21st chromosome in 95% of people affected (Selikowitz, 2008). The physical phenotype of Down syndrome includes epicanthic folds, protruding tongue, flat nasal bridge, brachcephaly, broad hands, brachydactyly, and lax ligaments (Henderson, 2005). There is also developmental delay. At age 21, mean IQ is 42 (range 8-67) (Henderson, 2005). According to recent studies (e.g. Fidler, 2005), the behavioural and cognitive phenotype for Down syndrome includes relative strengths in elements of visuospatial processing (Jarrold, Baddeley, & Hewes, 1999; Klein & Mervis, 1999), and social functioning (Rodgers, 1987; Wishart & Johnston, 1990), alongside relative

deficits in language (Sigman & Ruskin, 1999), verbal processing (Byrne, Buckley, MacDonald, & Bird, 1995; Jarrold *et al*., 1999). Down syndrome (DS) is often used as a contrast group when investigating cognitive and behavioural profiles of other developmental disorders (Seltzer *et al*., 2004).

It was decided to choose a homogenous group of people with DS rather than a heterogeneous group of mixed learning disabilities as more is known about this group than any other, and due to the relatively small sample sizes, a homogenous group would add more power to the results than a heterogeneous group. Also, a group that was heterogeneous may include individuals who are not yet diagnosed, and it could also be that their disabilities are acquired as opposed to developmental, both of which could add noise to the data.

This study aims to examine the main areas of executive functioning (i.e. mental flexibility, inhibition, fluency and working memory) in adolescents and adults with CdLS and identify whether there is a profile of executive functioning deficits. In addition, the data may indicate whether impairments of executive functioning are related to age and whether these changes are associated with repetitive behaviour.

2.0. METHOD

2.1. Participants

Twenty-four participants with Cornelia de Lange Syndrome (14 females and 10 males) aged 13-42 (M = 22), and 21 participants with Down syndrome (13 females and eight males) aged 15-33 (M = 24) years participated. One participant with CdLS did not complete any of the tests of executive functioning. Comparisons between those participants who completed the executive functioning tasks and those who did not revealed that there were no

significant differences in age, gender BPVS scores or VABS scores (see Appendix A). There are five missing VABS for the Down syndrome group due to failure to be able to contact the caregivers in the month following the visit.

Participants with CdLS were recruited directly through a research database of individuals with neurodevelopmental disorders who have participated in research and consented to being contacted again. Participants with CdLS were also recruited indirectly, through the Cornelia de Lange Syndrome Foundation (UK and Ireland). Participants with Down syndrome were recruited directly through the research database.

Inclusion criteria comprised: individuals having the relevant diagnosis from an appropriate professional, aged 12 or over, able to speak at least 30 words, having a self-help score indicating they were at least partly able in self-help skills (indicated by scores on the Wessex Scale (Kushlick, Blunden & Cox, 1973) of seven or more out of nine), a receptive vocabulary age equivalent score of at least 40 months on the Vineland Adaptive Behavior Scale (VABS; Sparrow, Balla & Cicchetti, 1984) and being mobile. For practical reasons, participants were required to live within 200 miles of the research base.

Thirty-five individuals on the CdLS database met these criteria and were invited to participate. Twenty-three expressed interest and were sent questionnaire packs. Three of these participants did not take part in the research visits; one person was living too far from the research base, another was demonstrating signs of severe anxiety (e.g. difficulties eating and sleeping) related to the proposed visits and the final potential participant's family had noted that her behaviour had significantly deteriorated during the recruitment phase and hence thought she would no longer be able to take part. Executive functioning data were not collected for one of the remaining 20 participants as they were unable to sit for long enough to complete the tasks.

A call for participation in the study was made through the Cornelia de Lange Foundation (UK and Ireland) by placing an advert in the magazine produced by the parent support group. Additionally flyers were sent to the 325 families the Foundation had contact details for who were not on the university research database. Families who responded to the flyer or the advert in the magazine were screened to ensure participants were able enough to take part.

Eleven families responded to the advert or flyer. Four of these withdrew: one did not meet the inclusion criteria, two were ill at the time the research was taking place, and one felt too anxious about the visit. The remaining seven individuals were visited, one of whom would not sit for long enough to complete any of the assessments, consequently data were collected for six participants. In total, 25 participants with Cornelia de Lange syndrome took part.

In the Down syndrome group, 48 individuals in the database were identified as being appropriate for the study. Of these 48 families, 24 showed interest in taking part in the study. Three did not take part for various reasons; one had moved to another country, one was on holiday and one could not be contacted. In total, 21 individuals with Down syndrome took part. Table 3.1 shows the demographic information of both groups.

2.2. Measures

2.2.1. Demographic Questionnaire

The Demographic Questionnaire was used to obtain background information regarding age, gender and diagnostic status (i.e. whether a diagnosis had been made and by whom the diagnosis was made by). This can be found in Appendix B.

2.2.2. The British Picture Vocabulary Scale – Second Edition (BPVS II; Dunn et al., 1997)

The BPVS II is designed to serve as a "norm referenced wide-range test of hearing vocabulary for Standard English" (Dunn *et al*., 1997). It is used to assess receptive vocabulary in typically developing children aged between three and 15 years. The assessment comprises 168 items, presented as fourteen sets of twelve items. For each item, the examiner orally presents a word to the individual and the person is asked to select the picture which most accurately represents the meaning from four alternative pictures in a stimulus book. The test has been standardised on individuals who are typically developing and it has been reported to be psychometrically robust with good validity and reliability (Dunn *et al*., 1997). Age equivalence can be calculated.

2.2.3. The Vineland Adaptive Behavior Scale (VABS-II; Sparrow, Balla & Cicchetti, 1984)

The VABS is a leading assessment of adaptive behaviour (an individual's personal and social skills as s/he interacts with her/his environment), widely used for supporting the diagnosis of intellectual and developmental disabilities (Sparrow, Balla & Cicchetti, 1984). It is administered in a semi-structured survey format to the parents or caregivers of the individual being assessed. The test measures four main domains: Communication', 'Daily Living Skills', 'Socialization', and 'Motor Skills'. The VABS was conducted face-to-face or via the telephone with the participant's parent/carer.

2.2.4. The Repetitive Behaviour Questionnaire (RBQ) (Moss & Oliver, 2008)

Deficits in executive functioning have been proposed to account for repetitive behaviours in some syndrome groups (Turner, 1997). As such it was decided to measure repetitive behaviour in the two groups to see whether or not executive functioning correlated

with observations of repetitive behaviour. The Repetitive Behaviour Questionnaire (RBQ) was used for this purpose (Moss & Oliver, 2008).

The RBQ is an informant report questionnaire to rate the frequency of occurrence of nineteen observable, operationally defined repetitive behaviours over the last month (See Appendix C). A five-point Likert scale is used ('Never', 'Once a month', 'Once a week', 'Once a day', 'More than once a day'). The items make up five subscales: stereotyped behaviour, compulsive behaviour, insistence on sameness, restricted preferences and repetitive speech.

Previous studies have shown strong inter-rater reliability across individuals with heterogeneous causes of intellectual disability, high test- retest reliability and strong concurrent validity e.g. there is a strong association between pairs of scores referring to the same behaviour on the RBQ and the Repetitive Behaviour subscale of the Autism Screening Questionnaire (Moss *et al*., 2009).

2.3. Measures of Executive Functioning

To assess executive functioning abilities a number of assessments were used. To get a general overview, a well used parent/carer rated questionnaires of executive functioning was used- the BRIEF-P (Gioia *et al.*, 2000).

Working memory consists of verbal and visuospatial subsystems (Baddeley & Hitch, 1974). Participants working memory capacity will be examined using two tests designed to tap into each of these subsystems separately- the Digit Span and Corsi Span tests. The Corsi Block-Tapping Task measures visuospatial short-term and working memory and is, arguably, the 'single most important nonverbal task in neuropsychological research' (Berch, Krikorian &

Huha, 1998). The Corsi blocks task was developed in the early 1970s as a visuospatial counterpart to the verbal-memory span task (Milner, 1971).

One of the most often cited tests of executive functioning is verbal fluency (Rabbitt, 1997). This is reported to be a test that is easy to administer, reliable and with good discriminatory power (Denckla, 1994). Also a visual-spatial test of fluency- design fluency (from the NEPSY, Korkman *et al.*, 1998) was used.

Flexibility and inhibition were assessed using the Dimensional Card Change Sorting task (DCCS; Frye *et al.*, 1995). The DCCS task is a widely used measure of executive functioning suitable for use with participants across a wide range of ages (Zelazo, 2006). The majority of three years old successfully sort the cards on the first dimension, but demonstrate perseveration during the post-switch phase, exhibiting inflexibility (Zelazo, 2006). By five years old, most children switch when instructed to do so. An additional challenge can be added for those participants who successfully switch to the new rule. They are given a 'border' version, whereby if a card has a border around it they are to sort by colour, if there is no border then they are to sort by shape.

A more in depth description of each of the measures used is given below. Record sheets for the performance measures, with their instructions are given in Appendix D.

2.3.1. Global Measure of Executive Function

Behaviour Rating Inventory of Executive Function-Parent Form (BRIEF-P; Gioia, et al., 2000).

The BRIEF-P (Appendix E) is an informant-based questionnaire designed to examine deficits in several areas of executive function. The 63-item questionnaire, for use with

children with neurological and developmental disorders/autism, is completed by a parent/carer who rates the person's executive functioning within the context of everyday environments. It is reported to be an ecologically valid and efficient tool for screening, assessing, and monitoring executive functioning. Ratings are made on a three-point Likert scale ("Never", "Sometimes", and "Always") whether a specific behaviour has been a problem for their child over the last six months.

The five non-overlapping scales of the BRIEF-P are Inhibit, Shift, Emotional Control, Working Memory, and Plan/Organize. These clinical scales form three indices : Inhibitory Self Control (Inhibition + Emotional control), Flexibility (Shift + Emotional Control) and Emergent Meta Cognition (Working memory + Plan/Organise) and one composite score (Global Executive Composite). The authors report high internal consistency reliability (.80-.95) and test-retest reliability (.78-.90). Higher scores indicate greater deficit.

2.3.2. Working Memory: Phonological Loop

2.3.2.1 Digits Forward from the Wechsler Intelligence Scale for Children – Third Edition UK (WISC-III; Wechsler, 1992)

The Digits Forward test compromises the first half of the Digits Span test, developed to measure working memory in typically developing children aged between six and sixteen years. This test consists of eight items, each containing two trials. During the test, the examiner reads out a series of numbers ranging from one to nine. After listening to the numbers, the participant is asked to immediately recall them in the same order. The test becomes increasingly difficult so that on the first item the participant hears a sequence of two numbers, on the second item the participant hears a sequence of three numbers etc. until item eight when a participant is presented with a sequence of nine numbers. The test is

discontinued if the participant fails both trials on any item. The dependent variable for the analysis was number of trials correct. A participant's score on the Digit span task is the number of strings of digits they correctly recalled. The maximum length of the digit string correctly recalled was also recorded.

2.3.2.2. Digits Backward from the Wechsler Intelligence Scale for Children – Third Edition UK (WISC-III; Wechsler, 1992)

The Digits Backward test comprises the second half of the Digits Span test. This test consists of eight items (ranging from two to nine digits), each containing two trials. The test is administered in the same way as the Digits Forward test. However, after the numbers have been presented, the participant is expected to recall them in the reverse order to which they were heard. The participant obtains a score of one for each correct answer so the maximum possible score is fourteen. The test is discontinued if the participant fails both trials on any item. The reliability and validity of this test has been reported to be good (Weschler, 1992). The score is the total number of trials correct.

2.3.3. Working Memory: Visuospatial

2.3.3.1. Corsi Span Forward: The Corsi Block-Tapping Test (*From the NEPSY; Korkman et al., 1998)*

This test consists of eight items, each with two trials. Item one consists of two blocks to be tapped, and the number increases by one for each trial. If participants do not get the practice item correct, they are given the demonstration again. If they still get it incorrect then the test is discontinued. For those that pass the practice, the test is discontinued when the

participant gets both trials on an item incorrect. A participant's score on the Corsi span task was determined by the number of trials they got correct. The maximum length of the string of block-taps they correctly recalled was also recorded.

2.3.3.2. Corsi Span Backward: The Corsi Block-Tapping Test (From the NEPSY; Korkman *et al.*, 1998)

The Corsi Span backward immediately follows the forward version of the task. It follows the same format as the forwards version. The score for a participant is the number of items correct. The maximum length of the string of block-taps they correctly recalled was also recorded.

2.3.4. Fluency

2.3.4.1. Verbal Fluency from the NEPSY (Korkman et al., 1998)

This test assesses the ability to generate words quickly, according to semantic and phonemic categories. The Verbal Fluency test has been designed to assess fluency / generativity in typically developing children aged between three and twelve years old. The test is comprised of two parts: *Semantic Fluency* (listing as many words as possible in 60 seconds that are animals in trial 1 and food & drink in trial 2) and *Phonemic Fluency* (listing as many words in 60 seconds, excluding names of places and people, beginning with 'S' in trial 1 and 'F' in trial 2). The total raw score is calculated by summing up the number of correct words produced in each part of the test. The psychometric properties appear robust for this measure (Rabbitt, 1997).

Scores on the Verbal fluency tasks were determined by the number of novel words relating to a category that were generated in the 60 second time period.

2.3.4.2. Design Fluency from the NEPSY (Korkman et al., 1998)

Design fluency is a measure of non-verbal fluency. The test assesses the individual's ability to generate novel designs as quickly as they can in a limited time period (60 seconds). It utilises executive functioning as participants need to plan and monitor their designs throughout the tasks, keeping the goal in mind. There are two tasks: participants are asked to connect two or more dots using straight lines to make a design on a structured array of dots, each contained in a separate box; and then do the same on an unstructured array of dots each contained in a separate box (See Appendix F). Each design has to be different from the others.

The unstructured array increases executive load (Rabbitt 1997). The total score is the number of novel designs generated. The number of repeated designs will also be examined to see whether there is more perseveration demonstrated within either of the groups.

2.3.5. Mental Flexibility & Inhibition

2.3.5.1. Dimensional Change Card Sorting Task (DCCS; Frye *et al.*, 1995)

In the DCCS task, participants are required to sort a series of bivalent cards, first according to one dimension (colour; red or blue), and then according to the other (shape; boat or rabbit). Appendix G shows a visual example of the cards used. Performance on the task reflects executive functioning development in flexibility and inhibition. There were three

elements on the DCCS task, which produced three sets of scores. Firstly the number of correct card sorts (out of six) to colour. Secondly the number of correct card sorts (out of six) to shape. Finally the number of correct card sorts to shape/colour dependent on border (out of 12). The types of errors that are made in the border version of the task (i.e. colour as shape or shape as colour were also recorded. As was the case for the standard version, no feedback was provided at any point.

2.4. Procedure

Ethical approval was obtained from the School of Psychology Ethical Review Board at the University of Birmingham. Participants were assessed in their homes. They were told that if at any point they appeared or stated that they did not want to take part in the study, it would have been assumed that they wanted to withdraw and the study would be terminated.

On confirmation of the research visit, the participant's parent/carer(s) were sent a questionnaire pack (which included those presented in Appendix B-D) to complete. The questionnaires were picked up when the researcher conducted the visit.

On the day of the visit, the first 20 minutes were spent building rapport and answering any questions that participants or their families may have had. The rest of the day consisted of administering the battery of tests[2]. Participants were given regular breaks throughout the testing, as and when needed. On completion of the test battery, participants and their families were given further opportunity to ask any questions, and debriefed. Participants were told

[2] As this study is part of a larger study, there are tests in the larger battery (examining sociability and theory of mind) that will not be discussed here but will be written up in a separate thesis by Lisa Collis.

they would receive a certificate for taking part and that the family would receive a copy of the study once it was written up along with an individual performance report.

2.5. Data Analysis

To examine differences in the dependent variables investigated independent samples *t*- tests were used to compare the two groups. Data were checked to make sure they were normally distributed and although there were some variables that were skewed (Number of correct items in DCCS shape and border version) they followed the same pattern in both groups. Levene's test of homogeneity of variance was employed to address the assumption of equal variance. For those variables where equal variance could not be assumed, the more stringent value of *t* provided in the SPSS output was used. To control for family-wise error, the two-tailed Bonferroni *t* test (Dunn, 1961) were used.

3.0. RESULTS

3.1. Demographics

A comparison of the group demographics, demonstrated that the two groups did not differ in relation to age, gender, receptive language and adaptive behaviour (see Table 3.1.). The age of participants with CdLS ranged from 13 to 52 years old, and participants with DS ranged from 15 to 33.

Table 3.1. *A comparison of demographic information between the CdLS (N = 24) and DS (N = 21) groups*

			CdLS	*DS*	t / χ^2	*p*
Age (years)		*M* *SD*	22.29 *8.98*	24.38 *5.82*	-.91	n.s.
Gender	% Female	*%* *df*	58.3 (1,45)	61.9	.06	n.s.
BPVS	Raw Score	*M* *SD*	66.63 *20.23*	67.19 *23.70*	- .09	n.s.
	Age Equivalence (years)	*M* *SD*	6.12 *2.15*	6.29 *2.72*	- .22	n.s.
VABS	Communication Domain (standard score)	*M* *SD*	49.17 *16.74*	48.94 *24.36*	.04	n.s.
	Daily Living Skills (standard score)	*M* *SD*	55.96 *14.16*	56.0 *11.10*	-.01	n.s.
	Socialization	*M* *SD*	56.87 *18.09*	52.56 *24.97*	.63	n.s.

3.2. RBQ

The results of the Repetitive Behaviour Questionniare questionnaire, to investigate repetitive behaviour in the groups, are presented in Table 3.2. As can be seen from the table, two of the five subscales of the RBQ evidenced a significant difference between the CdLS and DS groups; 'Restricted preferences' (t (40) = 2.06, $p < .05$) and 'Repetitive use of language' (t (40) = 2.97, $p < .01$). The participants with CdLS were more likely to demonstrate restricted preferences and repetitive use of language than participants with DS.

Table 3.2. *Scores for subdomains of the RBQ for participants with CdLS (n = 23) and DS (n = 19).*

RBQ Subscale		CdLS	DS	*t (40)*	η^2	*p*
Stereotyped behaviour	*M*	2.09	2.21	-.12	.00	n.s.
	SD	*2.97*	*3.47*			
Compulsive behaviour	*M*	4.65	6.05	-.76	.01	n.s.
	SD	*4.90*	*6.94*			
Restricted preferences	*M*	4.22	2.32	2.06*	.096	<.05
	SD	*3.22*	*2.65*			
Insistence on sameness	*M*	3.00	3.17	-.19	.001	n.s.
	SD	*2.66*	*2.96*			
Repetitive use of language	*M*	3.76	1.11	2.97[a]**	.166	<.01
	SD	*3.64*	*2.05*			
Total Score	*M*	17.38	14.96	.59	.009	n.s.
	SD	*12.04*	*13.86*			

The individual items that showed significant differences between the two groups included item 9, *Asking specific questions* (t (40) = 2.40, p = .02; η = .12), and item 14, *Echolalia:* (t (40) = 2.40, p = .04; η = .10). Participants with CdLS were reported by their caregivers as asking more repetitive questions (M = 1.87, SD = 1.82) than participants with DS (M = .68, SD = 1.38) and as having more echolalia in their speech (M= .91, SD = 1.47; M = .16, SD = .50, for CdLS and DS respectively). There were no other significant differences.

3.3. Executive Functioning Measures

3.3.1. BRIEF-P

Table 3.3. shows the mean score on each subscale and index of the BRIEF-P for each group. Analysis of the results of the BRIEF-P, showed significant differences on the Shift (t

Table 3.3. *Descriptives of the Subscales & Indices of the BRIEF-P.*

BRIEF-P Index		CdLS (n = 22)	DS (n = 19)	t (39)	η^2	p
Inhibition	*M*	26.91	24.37	1.54	.06	n.s.
	SD	*5.59*	*4.87*			
Shift	*M*	19.95	17.10	2.24*	.11	<.05
	SD	*3.90*	*4.25*			
Emotional Control	*M*	18.34	15.42	2.22*	.11	<.05
	SD	*4.37*	*4.00*			
Working Memory	*M*	30.23	27.44	1.35	.05	n.s.
	SD	*6.74*	*6.12*			
Plan/Organise	*M*	17.50	16.16	1.27	.04	n.s.
	SD	*3.32*	*3.42*			
Indices						
Inhibitory self control	*M*	45.3	39.8	2.16*	.11	<.05
	SD	*9.20*	*6.55*			
Flexibility	*M*	38.3	32.5	2.60*	.15	<.05
	SD	*6.99*	*7.21*			
Emergent Meta cognition	*M*	44.7	43.8	1.34	.05	n.s.
	SD	*9.61*	*8.92*			

(39) = 2.24; $p < .05$) and Emotional Control (t (39) = 2.22; $p < .05$) subscales. There was no evidence of significant differences on the Inhibition, Working Memory and Plan/Organise subscales ($p > .05$). The CdLS group scored higher on the Shift and Emotional Control subscales than the DS group, indicating they are more impaired on these areas.

In relation to the indices, as can be seen from the table, the CdLS group were significantly more impaired on the Inhibitory Self-Control and Flexibility Indices.

3.3.1.1. Correlations BRIEF-P and Performance on Executive Functioning Tasks

To evaluate concurrent validity of the BRIEF-P the five subscales, three indices and the composite score were correlated with the performance outcome measures across both groups combined. The results are given in Appendix H. The correlations demonstrate the BRIEF-P is a valid measure for the CdLS and DS populations studied here and that the links between the questionnaire and the practical measures of executive functioning appear to be triangulated (e.g.. the inhibition subscale of the BRIEF-P correlates with the inhibition task of the DCCS). The majority of the correlations are highly significant ($p < .01$).

3.3.2. Digit Span

On the digit span forward task, 18 of the 24 participants with CdLS and all 21 of the DS group completed the task. Four participants with CdLS demonstrated selective mutism on verbal tasks, and two were hard to engage. Appendix I shows the results. There were no significant difference between the groups on the length of sequence they recalled either on the forward or backward versions of the task. Both the CdLS (*SD* = 2.81) and DS (*SD* = 2.21) groups recalled a maximum of between three and four digits correctly.

Seventeen participants with CdLS (*SD* = 1.90) and all participants with DS (*SD* = *2*.16) completed the backwards version of the task, recalling, on average, a maximum of two digits correctly. There were no significant differences in number of items correct, with both groups scoring around two items (CdLS: *M* = 2.4, *SD* = 1.9; DS: *M* =2.5, *SD* = 2.2). This suggests there is little difference in phonological working memory between the two groups.

3.3.3. Corsi Block-Tapping test

Twenty-one of the 24 in the CdLS group and all 21 of the DS group completed the Corsi span forward and backward tasks. Table 3.4. shows these results.

Table 3.4. *Results on the Corsi span tests.*

Corsi Span Test			CdLS	DS	*t(40)*	η^2	*p*
Forward	Number correct	*M*	4.52	7.05	-2.49*	.14	<.05
		SD	*3.27*	*3.29*			
	Maximum length	*M*	2.90	4.00	-2.55*	.14	<.05
		SD	*1.51*	*1.26*			
Backward	Number correct	*M*	3.53	3.16	.41	.00	n.s.
		SD	*3.20*	*2.04*			
	Maximum length	*M*	2.33	2.29	.10	.00	n.s.
		SD	*1.85*	*1.35*			

The CdLS group recalled an average of 5 sequences correctly compared to 7 for the DS group. This difference is significant. The CdLS group recalled a mean sequence length of 2.9 taps correctly, and the DS group recalled a mean sequence length of 4 taps correctly on the Forward version. This difference is significant ($p = .01$, $\eta^2 = .14$). On the Backwards version, both groups recalled a maximum of around two taps ($p = .69$).

3.3.4. Verbal Fluency

Comparisons between the two groups on the verbal fluency task are shown in Table 3.5 As can be seen, there is one significant difference between the two groups on Food and Drink. The DS group generated significantly more words ($M = 10.86$ words) on this category

than the CdLS group (*M* = 6.85 words). Both groups showed difficulty on the phonemic task, recalling 2-3 words in each category in the 60 seconds

Table 3.5. *Comparisons of CdLS (n = 20) and DS (n = 21) groups on Verbal Fluency task.*

Verbal Fluency Task		CdLS	DS	*t* (39)	η^2	*p*
Animals	*M*	7.35	8.14	-.47	.006	n.s.
	SD	*6.03*	*4.67*			
Food & Drink	*M*	6.85	10.86	-2.32*	.12	<.05
	SD	*6.00*	*5.02*			
Semantic total	*M*	13.52	19.00	-1.72	.07	n.s.
	SD	*11.61*	*8.89*			
'S' words	*M*	2.45	3.05	-.71[a.]	.01	n.s.
	SD	*3.17*	*2.09*			
'F' words	*M*	2.50	2.38	.15	.001	n.s.
	SD	*3.02*	*1.86*			
Phonemic total	*M*	4.71	5.43	-1.72	.006	n.s.
	SD	*5.91*	*3.66*			

[a] : Levene's significant, stringent *t* value used.

Table 3.5. shows the overall mean semantic and phonemic scores. Although there is a difference between the CdLS and DS groups on the semantic total scores, this difference is not significant.

3.3.5. Design Fluency

On this task participants with DS generated slightly more novel designs than participants with CdLS. The mean number of novel designs generated by the CdLS group

was 4.70 (*SD* = 3.18) in the structured array and 5.09 (*SD* = 3.50) in the random array. The DS group generated a mean of 6.10 (*SD* = 3.03) novel designs in the structured array and 6.19 (*SD* = 3.48) in the random array. There was no evidence of significant differences in either the structured or random array elements of the design fluency task ($p > .05$).

In relation to planning and self monitoring, both groups showed deficits. The CdLS group had a mean of 3.26 (*SD* = 5.22) designs that were repeats of the other designs in the structured array and the DS group had 3.76 (*SD* = 5.05), over half of the number of correct designs. The same was true for the random array; CdLS (*M* = 3.44, *SD* = 4.05) and DS (*M* = 4.52, *SD* = 5.06). There were no significant differences between groups. This suggests both individuals with CdLS and DS have difficulty planning and monitoring their goals.

3.3.6. DCCS

The results of the DCCS are shown in Figure 3.1. Analysis of the Dimensional Card Sort revealed significant differences on the second and third elements of the task. Both participants with CdLS (*n* = 23) and DS (*n* = 21) were able to correctly sort the six cards according to colour in the first part of the task. When the rule was changed to sort for shape, the participants with Down Syndrome sorted significantly less cards according to this rule, continuing to sort by colour for some of the cards. Participants with DS correctly sorted more cards (*M* = 5.43, *SD* = 2.63) than those with CdLS (*M* = 3.52, *SD* = 1.80; t (39) = -2.83, $p < .01$, $\eta^2 = .16$). The final part of the task required participants to sort by colour if the picture was surrounded by a border, and shape if there was no border. Only participants who had correctly sorted two of the six in the previous element of the task participated in this final part (*n* = 19 for DS; *n* = 13 for CdLS) Again, the DS group (*M* = 8.48, *SD* = 3.46) performed

much better than the CdLS group (M = 4.05, SD = 3.70; t (41) = -3.97, p < .01, η^2 = .28) suggesting that the CdLS group have difficulty in flexibility and inhibition.

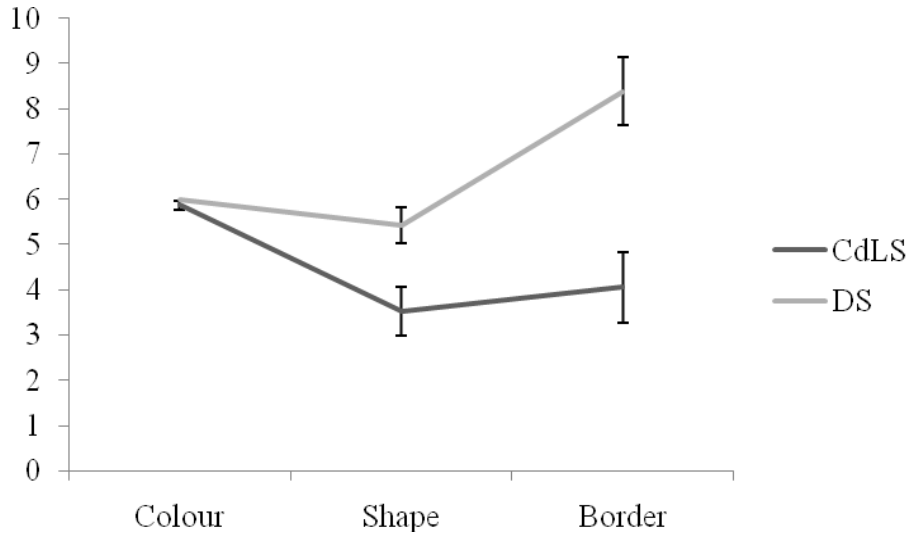


Figure 3.1. Number of cards correctly sorted for the colour, shape and border elements of the DCCS task. Number of cards in each element (colour, shape and border) was 6, 6 and 12 respectively.

On closer analysis of the data, there was a significant difference between the groups on the border version of the task in the errors that were being made. The CdLS group were mainly making the error of sorting shape cards by colour (M = 2.47, SD = 1.51; t (30) = 2.76, p < .05, η^2 = .20),the original rule, again providing support for the CdLS group being stuck in set.

3.4. Relationship between Age and Executive functioning

3.4.1. Chronological Age[3]

Correlations between chronological age (CA) and measures of executive functioning were examined. These can be found in Appendix J. For the CdLS group, age was negatively correlated with maximum span on the Digit Span Backwards task (r (17) = -.50, p = .04), and positively correlated with the number of verbal fluency 's' repeats (r (20) = .65, p = < .01) and the number of verbal fluency 'f' repeats (r (20) = .47, p = .04). This suggests that older participants with CdLS have poorer verbal working memory and are more verbally repetitive, then younger participants with CdLS.

The Down syndrome group showed significant positive correlations of age with the number of items correct on the border version of the DCCS (r (21) = 51, p = .02) and with the number of items on the task that were sorted (incorrectly) according to the original rule (r (19) = -.59, p < .01). This suggests that as people with Down Syndrome get older their rule switching abilities improve. No other correlations were significant[4].

[3] Developmental Trajectories: The next step in analysis would ideally have been to calculate developmental trajectories for performance on all the executive functioning tasks using the methodology detailed in depth by Thomas (2009). However due to the small *n*, and the range of chronological ages, it proved very difficult to fit regression lines to the data. Comparing non-overlapping trajectories would necessitate extrapolating a prediction of task performance for one of the groups outside of the age or ability range over which performance has been measured (Thomas *et al*., 2009). Tentative lines of fit are shown in Appendix L. The natural follow up from this study would be to gather more data in order to examine the question of whether, and how, the two groups differ in their developmental trajectories, and to triangulate this with brain imaging studies.

[4] Mental age correlations, based on the BPVS age scores, are given in Appendix K. These correlations are not as insightful as mental age is obviously related to executive functioning development.

3.5. Relationship between Repetitive Behaviour and Executive Functioning Measures

We also examined the relationship between executive function deficits in the participants and repetitive behaviours. Pearson's partial correlation coefficients were calculated between performances on the executive function tasks and the five subscales of the RBQ for both groups combined. Age and receptive vocabulary scores were used as covariates. Due to the large number of correlations, significance levels were set to the more stringent level of $p < .01$. (see Appendix M).

The Restricted Preferences subscale correlated negatively with Digit Span backwards (r = -.45, p <.01, df = 29) and Corsi Span backwards r = -.51, p < .01, df = 29. These tasks tap into the central executive component of working memory, postulated by Baddeley (1986) to be responsible for the selection, initiation, and termination of processing routines (encoding, storing, and retrieval).

Repetitive Language negatively correlated with the results on the DCCS border task (r = -.54, p <.01, n = 29). Therefore greater impairments in task switching/inhibition were associated with more repetitive language.

There were no significant correlations between executive functioning tasks and Stereotyped Behaviour, Compulsive Behaviour and Insistence on Sameness subscales.

4.0. DISCUSSION

This study details the results of the first assessment of the executive functioning profile in adolescents and adults with Cornelia de Lange syndrome. Participants with CdLS were compared to participants with Down syndrome, using several measures of executive

functioning. Initial comparisons indicated that the two participant groups did not differ with regard to gender, age, and receptive language age equivalence scores.

Strengths of the study included using a range of well-established executive functioning measures, having matched groups, and using a homogenous syndrome group as a comparison. By comparing the results to a group with Down syndrome, syndrome-related impairments of executive functioning can be addressed (Dykens, Hodapp & Finucane, 2000). It is important to look at syndrome related behaviour in order to help understand the role of genes that underlie the syndrome (Hodapp & Dykens, 1994). Also, the development of an executive functioning profile for CdLS, and indeed other syndromes, will aid clinicians in their diagnosis and interventions for the disorder.

Comparisons between syndromes in the literature have been rare (Hodapp & Dykens, 1994), however such comparisons are needed in order to identify gene-behaviour links, to identify deficits that are syndrome specific rather than being shared by other conditions associated with intellectual disabilities. The results demonstrated that despite having two groups matched on receptive vocabulary, with no significant differences in age or adaptive behaviour, there were differences in executive functioning abilities.

The carer rated BRIEF-P revealed several differences between the groups. These included significant differences on the Shift and Emotional control subscales with individuals with CdLS rated as having more difficulties shifting between tasks and controlling their emotions. Indices of the BRIEP-P showed that the CdLS group were more impaired in inhibition and flexibility. The scores for the overall Global Executive Composite showed that participants with CdLS were significantly more impaired in their overall executive functioning abilities than participants with DS.

On the tasks measuring the different aspects of executive functioning, there were a number of differences. The group with DS performed better than the group with CdLS on all measures that were significant. Verbal fluency was better in the DS group, especially on one element of semantic fluency (food and drink), than the CdLS group. Both groups had difficulty with the more complex fluency tasks. The semantic tests are easier for participants, but the phonemic tests are considerably harder, requiring a greater capacity of executive functioning as they require participants to organize concepts in a novel way (Anderson *et al*., 2001).The differences in verbal fluency are particularly salient as there were no significant differences between the groups on the BPVS i.e. differences were not due to a lower vocabulary in participants with CdLS. This suggests the differences lay in the cognitive process of fluency/generativity.

Results of the design fluency task revealed that there was little difference between the two groups. Both showed difficulties in monitoring their drawings, with many repeated designs being drawn. This difficulty in planning and monitoring shows an impairment in these executive functioning abilities. There were significant differences in visual-spatial working memory, with individuals with DS having a greater capacity than those with CdLS, however this seemed to have little impact on performance on this task.

On the DCCS task, participants with CdLS demonstrated difficulty in rule shifting, sorting cards by the original rule rather than the new rule. Of the 23 CdLS participants who started the task, five did not get more than two of the six items in the second rule correct. In the final part of the DCCS task the remaining participants were asked to sort to colour or shape depending on whether a border was present on the cards. The CdLS group had more difficulty on this task, correctly sorting half of the amount of the group with DS. There were no significant differences in phonological working memory between the two groups, which would suggest there should not be differences in being able to keep a rule in mind. However

there were significant differences on the DCCS task suggesting the problem was not in learning a rule but in perseveration and inflexibility. This is further supported by differences reported on the BRIEF-P Shift and Flexibility subscales.

In relation to repetitive behaviour, measured by the RBQ, the CdLS group demonstrated greater restricted preferences and repetitive use of language than the DS group. Correlations between measures of executive functioning and the RBQ subscales revealed these two subscales showed several significant negative correlations. A greater demonstration of restrictive preferences was associated with deficits of the central executive of working memory (Digit and Corsi span backwards). This may be expected given that the central executive is implicated in trouble shooting, decision making and overcoming habitual responses.

The RBQ subscale of repetitive language negatively correlated with the results on the DCCS border task. Therefore greater impairments in task switching/flexibility were associated with more repetitive language. As the CdLS and DS groups were significantly different on this measure of executive functioning, it may be postulated that deficits in task switching may account for one aspect of the behavioural phenotype of CdLS- repetitive language.

Some of the CdLS participants failed to complete all of the tasks. Those who did not complete were not significantly different to those that did complete in relation to their background characteristics. As discussed earlier, there were no significant differences in phonological working memory as reported by caregivers and on testing using the Digit span test. In typically-developing populations, digit spans typically increase from a digit span of three at four to five years of age to a digit span of seven to eight at 16 years (Chi, 1977). So both groups are limited in the capacity expected given their chronological ages (both having digit spans of three). Impairments in capacity of the phonological loop impact on speech and

language development (Buckley & Bird, 2001), which is consistent with the developmental profile of these groups.

However the fact that there were still differences between the groups on the other measures indicates that differences in starting the tasks is not due to weaknesses in keeping the instructions in mind. It is tentatively suggested that problems with initiation may account for the difficulties some participants with CdLS have in starting the tasks. This is supported by the author's clinical observations and research observations (Collis, 2010) that individuals with CdLS have difficulty with initiating a task. It needs to be determined whether this is due to social/performance anxiety or whether there are specific executive functioning difficulties that are occurring.

These differences in executive functioning are supported by observations of the behaviour of individuals with CdLS. Parents, carers and researchers have reported an increase in repetitive behaviours, reluctance to try new things, obsessions, tidying up and lining up behaviours as individuals with CdLS age (Moss *et al.*, 2009). These behaviours may all be explained by these differences in executive functioning. There were significant correlations found between age and some measures of executive abilities suggesting that older participants with CdLS have poorer working memory and are more verbally repetitive, then younger participants with CdLS. A larger sample with a wider age range is needed to examine the correlation between age and executive functioning in more depth as it may be that individuals in the sample used were already experiencing some age-related changes so correlations may have been weaker as a result.

4.1. Conclusions

This research has addressed questions about the domain asynchrony and syndrome specificity of executive functioning in CdLS and Down syndrome. Three dimensions of executive functioning- flexibility/task-switching, inhibition and fluency have been found to be significantly different between the two groups and may be important in understanding the behavioural phenotype of the syndromes. The need to examine the links between specific executive functioning deficits and behaviour has started to be addressed by other researchers (see literature review, this volume for a detailed overview). Woodcock, Oliver & Humphreys (2009) examined the link between switching and repetitive behaviours in Prader Willi syndrome and boys with Fragile X syndrome, finding that difficulties in task switching were associated with specific types of repetitive behaviour. Lopez, Lincoln, Ozonoff & Lai (2005) examined a broad range of executive functions and their relationship to repetitive, restrictive behaviour demonstrated in autism spectrum disorder, and found that cognitive flexibility, working memory, and response inhibition were highly related to these behaviours. For the CdLS group in the current study, the difficulties with task switching and flexibility was significantly correlated with reports of repetitive language. It may be conceived that a combination of switching capacity, flexibility and fluency may help explain their repetitive behaviours (Collis, 2010). It was also suggested in this study that there may be difficulties with initiation in the CdLS group, explaining their difficulties starting and or/completing some of the tasks. A more vigorous exploration of behaviours associated with CdLS is clearly warranted in order to associate behaviour with executive function deficits.

As regards syndrome specificity, it is important to note that the present data are limited because they only reflect comparisons with Down syndrome. Although our results suggest that Down syndrome provides a useful comparison for CdLS, with the results showing that on these areas of executive functioning the CdLS group are significantly more compromised,

many other syndrome groups need to be examined in order to conclude as to whether the deficits discussed are syndrome specific.

The fact that differences occur in CdLS and DS shows that these differences are important. It is already known from literature that individuals with DS are significantly impaired in executive functioning and working memory abilities compared to typically developing children (Logie, 1996; Rowe, Lavender & Turk, 2006) so the fact that individuals with CdLS are even more impaired is an important finding and may help understand some of their behavioural phenotype.

As highlighted by Abbeduto *et al*. (2001), although research such as this helps address domain asynchrony and syndrome specificity, there is much to learn. As regards domain asynchrony, it is not yet clear how the impairments in all the elements of executive functioning combine to affect day-to-day behaviours in social situations. Triangulating the data with qualitative observations of the syndrome groups, can help to answer this question.

4.2. Limitations and Directions for Future Research

This study was designed to examine executive functioning in CdLS. The current study used a variety of tests to examine different aspects of executive functioning. As there are many elements to executive functioning, there are some that have not been addressed and as such will need to be looked at in future research to complete the picture of executive functioning in these groups.

There was no formal measure of planning in the current study, although the design fluency required a degree of planning to carry out the task correctly. Future research could use the Zoo Map or Key Search tasks from the Behavioral Assessment of Dysexecutive Syndrome

(BADS; Wilson *et al*., 1996) to examine this element of executive functioning. There was also no measure of motor abilities in the current study. This would be a useful measure to use in future research so as to rule out difficulties in motor skills as explaining difficulties with tasks requiring the participants to draw or write, for example Design Fluency.

It was noted in the current study that both the DS and CdLS groups had difficulty grasping the concept of 'backwards' in the backwards versions of the Digit and Corsi Blocks Span tasks. This highlights a general limitation of all the tests used to assess executive functioning. They have all been designed for use on a typically developing population- as such the terms used can be too advanced for some populations.

It needs to be highlighted that the CdLS participants in the current study are among the most able in the UK. As such, care needs to be taken in generalising these results to all individuals with CdLS. Ideally all adolescents and young adults with CdLS would have been sampled, however research is limited by the lack of measures sensitive to measuring executive functioning in individuals with learning disabilities.

The use of a group of participants with Down Syndrome warrants comment. One difficulty with using this group is related to their increased risk of dementia as they age. Alzheimer-related dementia in DS has a prevalence of 0-2% in individuals under 40 years old, to more than 40% in those over 60 years old (Holland *et al*., 2000). Later stages of dementia are well documented in the literature however research into the earlier cognitive and behavioural changes in the initial stages of dementia has only started to emerge in recent years (see Adams & Oliver, 2010). One early indicator identified through longitudinal studies is a decline in working memory (Oliver *et al.*, 1998).

The DS sample in the current study were all under 40, however it may be possible some of these individuals may have early stages of dementia that could then impact on their results.

As it happens, the group with CdLS performed significantly worse than the group with DS on many of the measures. If the result had been reversed it may have been concluded erroneously that the DS group were significantly more impaired on those measures, where in fact it may be that DS *with dementia* were significantly more impaired. Following the same argument, on measures where the CdLS and DS group failed to differ, for example on the Digit Span task, it may be that some members of the DS group are in the early stages of dementia, causing their scores to be lower. However, the age range of the DS participants (15-33 years) limits the likelihood of dementia given the 2% prevalence rate. The use of a longitudinal study would help rule out this alternative explanation. As research continues to progress into early indicators of dementia, this potential confound may be able to be tested in future studies.

The battery of tests presented to the participants was long, requiring a day to administer with the inclusion of several breaks. The tests were all presented in the same order so any carry over effects would apply to both groups. Ideally the tests would have been conducted over several sessions, however due to the logistics and time restraints this was not possible.

It is possible that the association between executive functioning deficits and behaviour demonstrated in CdLS may not be causal but correlational, with the possibility that the behaviours may cause the executive functioning deficits. It is also possible that another factor, not examined in this research, could underlie executive functioning and behaviour difficulties.

Future research should involve examining executive functioning across both children and adults with CdLS in order to understand whether there is a change in the trajectory of executive functioning with age. A longitudinal follow-up of executive functioning will help to determine whether there are changes in executive functioning with age without the

possibility of cohort effects. Also, it is important to conduct research examining the links between cognition and behaviour in adolescents and adults with CdLS so that we can identify whether there is a common causal pathway underpinning the number of behavioural changes reported with age in CdLS or whether there are specific pathways underpinning the different behavioural changes with age. A neuroimaging study of children and adults with CdLS will also be important in order to understand, at a biological level, the changes that may be occurring with age. A subsequent examination of the relationship between the results of the imaging study, with cognition, behaviour and age will go some way to aid understanding of the pathways from genes to behaviour via cognition, and how these pathways may change with age.

In relation to the sample of participants used, the numbers were quite small. Combined with the wide range of ability within groups, this will limit the power to find significant differences. Larger samples in future research are recommended. The fact that the current study compared individuals with CdLS with individuals with DS and found differences helps rule out the alternative explanation that any differences between normal developing children and those with CdLS were accounted for by a test that is biased towards the normal developing children. However, future studies would benefit from comparing the groups with a neurodevelopmental disorder to typically developing children to get a fuller picture of the impairments that are acquired.

It is not clear from the data whether all the individuals with CdLS are performing at a lower level as they age or only some of them, as attempts to unravel the results are further confounded by cohort effects, and absence of data on their previous levels of cognitive impairment. Due to variability within syndrome groups and the degree of original impairment, sequential assessments are needed. This would allow for testing of the

significance of decline of executive functioning in relation to a past performance, and chart the developmental course of executive functioning in the syndromes.

This study goes some way to support the need for neuroimaging in genetic syndromes which will allow for a more thorough exploration of the genetic links to executive functions. Greene, Braet and Bellgrove (2007) argue that using the more advanced recent techniques such as potential endophenotypes can help to discovering the genetic causes of executive function.

4.3. Implications

From a pedagogical perspective, this research can begin to give ideas to inform the design of more effective education and rehabilitation strategies that are tailored to the syndrome (Hodapp, 1998). For example, there may be strategies to help develop executive functioning in different areas or to help compensate for deficits, so optimising a person's potential. As is the case in typically developing individuals, those with a developmental disorder will demonstrate variable cognitive development between them. As it is not possible to accurately predict the cognitive capabilities of an individual from birth it is important to be mindful of development and to use intervention strategies where appropriate.

Ultimately, research looking at cognitive and behavioural phenotypes will help forge a greater understanding of neurodevelopmental disorders, and help parents, teachers and society understand the disorders much better, helping optimise the quality of life that the individuals with neurodevelopmental disorders may have.

5.0. REFERENCES

Abbeduto, L., Pavetto, M., Kesin, E., Weissman, M., Karadottir, S., O'Brien, A. & Cawthon, S. (2001) The linguistic and cognitive profile of Down syndrome: Evidence from a comparison with Fragile X syndrome. *Down syndrome Research and Practice* **7**, 1, 9-15.

Adams, D. & Oliver, C. (2010) The relationship between acquired impairments of executive function and behaviour change in adults with Down syndrome. *Journal of Intellectual Disability Research* **54**, 5, 393-405.

Anderson, V.A., Enderson, P., Northam, E., Jacobs, R. & Catroppa, C. (2001) Development of executive functions through late childhood and adolescence in an Australian sample. *Developmental Neuropsychology* **20**, 1, 385–406.

Anderson, V.A., Jacobs, R. & Anderson, P.J. (2008) Executive functions and the frontal lobes. Psychology Press, London.

Baddeley, A.D. (1986) Working memory. Clarendon Press, Oxford.

Baddeley, A.D., Hitch, G.J.L (1974) Working Memory. In: *The psychology of learning and motivation: advances in research and theory* (ed G.A. Bower), Vol. 8, pp. 47-89. Academic Press, New York.

Baron-Cohen, S, & Moriarty, J, (1995) Developmental Dysexecutive Syndrome: does it exist? A neuropsychological perspective. In: *Movement and allied disorders in childhood* (eds M. Robertson M. & V. Eapen). Wiley, London.

Barry, D. (2010) Executive Function. The Encyclopaedia of Mental Disorders. [Online]. Available at: http://www.minddisorders.com/Del-Fi/Executive-function.html [accessed February 2010].

Basile, E., Villa, L., Selicorni, A., & Molteni, M. (2007) The behavioural phenotype of Cornelia de Lange syndrome: A study of 56 individuals. *Journal of Intellectual Disability Research* **51**, 671–81.

Beck, B. (1976) Epidemiology of Cornelia de Lange's syndrome. *Acta Paediatrica Scandinavica* **65**, 5, 631-38.

Beck, B. & Fenger, K., (1985). Mortality, pathological findings and causes of death in the de Lange syndrome. *Acta Paediatrica Scandinavica* **74**, 765-69.

Berch, D.B., Krikorian, R. & Huha, E.M.(1998) The Corsi Block-Tapping Task: Methodological and Theoretical Considerations. *Brain and Cognition* **38**, 317-38.

Berney, T. P., Ireland, M., & Burn, J. (1999) Behavioural phenotype of Cornelia de Lange syndrome. *Archives of Disease in Childhood* **81**, 333–36.

Bhuiyan, Z. A., Klein, M., Hammond, P., van Haeringen, A., Mannens, M. A. M., Van Berckelaer-Onnes, I., & Hennekam, R. C. M. (2006) Genotype-phenotype correlations of 39 patients with Cornelia de Lange syndrome: The Dutch experience. *Journal of Medical Genetics* **46**, 568–75.

Blagowidow, N., Kline, A.D., & Audette, L. (2005) Puberty and adolescence in Cornelia de Lange Syndrome. *Proceedings of the Greenwood Genetic Center* **24**, 175-176.

Buckley, S.J., & Bird, G.(2001) Memory development for individuals with Down syndrome– An overview. Down Syndrome Issues and Information. [Online] Available at:

http://www.down-syndrome.org/information/memory/overview/?page=1 [accessed January 2010].

Byrne, A., Buckley, S., MacDonald, J., & Bird, G. (1995) Investigating the literacy, language, and memory skills of children with Down's syndrome. *Down's Syndrome: Research and Practice* **3**, 53–8.

Chi, M. (1977) Age differences in memory span. *Journal of Experimental Child Psychology* **23**. 226-81.

Collis, L. K. (2010) Doctoral dissertation in preparation. University of Birmingham, Birmingham, UK.

Collis, L.K., Oliver, C. & Moss, J. (2006) Poster 4: Low mood and social anxiety in Cornelia de Lange syndrome. *Journal of Intellectual Disability Research* **50**, 792.

Denckla, M.B. (1994) Measurement of executive functioning. In: *Frames of Reference for the Assessment of Learning Disabilities: New Views on Measurement Issues* (ed G.R. Lyon), pp117-42. Brookes, Baltimore.

Descipio, C., Schneider, L., Young, T.L., Wasserman, N., Yaeger, D., Lu, F., Wheeler, P.G., Williams, M.S., Bason, L., Jukofsky, L., Menon, A., Geschwindt, R., Chudley, A.E., Saraiva, J., Schinzel, A.A., Guichet, A., Dobyns, W.E., Toutain, A., Spinner, N.B. & Krantz, I.D. (2005) Subtelomeric deletions of chromosome 6p: molecular and cytogenetic characterization of three new cases with phenotypic overlap with Ritscher-Schinzel (3C) syndrome. *American Journal of Medical Genetics* **134**, 1, 3-11.

Dunn, L.M., Dunn, L.M., Whetton, C. and Burley, J.(1998) The British Picture Vocabulary Scales. 2nd edition. NFER Nelson, Windsor.

Dunn, O.J. (1961) Multiple comparisons among means. *Journal of the American Statistical Association* **56**, 54-64.

Dykens, E. M., Hodapp, R. M., & Finucane, B. M. (2000) Genetics and Mental Retardation Syndromes. Brookes, Baltimore.

Dykens, E. M., Leckman, J. F., & Cassidy, S. B. (1996) Obsessions and compulsions in Prader-Willi Syndrome. *Journal of Child Psychology and Psychiatry* **37**, 1003-1014.

Fein, D., Allen, D., Dunn, M., Feinstein, C., Morris, R., Waterhouse, L. & Rapin, I. (2001) Executive Functioning in High-functioning Children with Autism. *Journal of Child Psychology and Psychiatry* **42**, 2, 261-70.

Fidler, D.J. (2005) The emerging Down syndrome behavioural phenotype in early childhood: Implications for practice. *Infants and young Children* **18**, 2, 86-103.

Frye, D., Zelazo, P.D. & Palfas, T. (1995) Theory of mind and rule-based reasoning. *Cognitive Development* **10**, 483-527.

Gioia, G.A., Isquith, P.K., Guy, S. C., & Kenworthy, L. (2000) Behavior Rating Inventory of Executive Function: Professional Manual. Psychological Assessment, Lutz, FL.

Goodban, M. T. (1993) Survey of speech and language skills with prognostic indicators in 116 patients with Cornelia de Lange Syndrome. *American Journal of Medical Genetics* **47**, 1059-63.

Greene, C.M., Braet, W., Johnson, K.A., Bellgrove, M.A. (2007) Imaging the genetics of executive function. *Biological Psychology* **79**, 30.

Hall, S.S., Arron, K., Sloneem, J. & Oliver, C. (2008) Health and sleep problems in Cornelia de Lange Syndrome: A case control study. *Journal of Intellectual Disability Research* **52**, 5, 458-68.

Happé, F., Booth, R., Charlton, R., Hughes, C. (2006) Executive function deficits in autism spectrum disorders and attention-deficit/hyperactivity disorder: examining profiles across domains and ages. *Brain and Cognition* **61**, 1, 25-39.

Henderson, A. (2005) Down Syndrome. NHS evidence [Online]. Available at: http://www.library.nhs.uk/geneticconditions/viewresource.aspx?resID=88948 [Accessed January 2010]

Hill, E.L. (2004) Evaluating the theory of executive dysfunction in autism. *Developmental Review* **24**, 189–233.

Hodapp, R. M. (1998) Development and Disabilities: Intellectual, Sensory, and Motor Impairments. Cambridge University Press, Cambridge.

Hodapp, R. M., & Dykens, E. M. (1994). Mental retardation's two cultures of behavioral research. American Journal on Mental Retardation, 98, 675-687.

Holland , A.J., Hon, J., Huppert, F.A. & Stevens, F. (2000) Incidence and course of dementia in people with Down's syndrome: findings from a population-based study. *Journal of Intellectual Disability Research* **44**, 138-46.

Hyman, P., Oliver, C., & Hall, S. (2002) Self-Injurious Behavior, Self-Restraint, and Compulsive Behaviors in Cornelia de Lange Syndrome. *American Journal of Mental Deficiency* **107**, 146-54.

Jackson, L., Kline, A. D., Barr, M., & Koch, S. (1993) de Lange syndrome: A clinical review of 310 individuals. *American Journal of Medical Genetics* **47**, 940-46.

Jarrold, C., Baddeley, A. D. & Hewes, A. K. (1999) Genetically dissociated components of working memory: evidence from Down's and Williams syndrome. *Neuropsychologia* **37**, 637-51.

Jarrold, C., Baddeley, A.D. & Philips, C. (1999) Down syndrome and the phonological loop: Evidence for, and importance of, a specific verbal short term memory deficit. *Down Syndrome Research and Practice* **6**, 2, 61-75.

Joseph, R.M., McGrath, L.M. & Tager-Flusberg, H. (2005) Executive dysfunction and its relation to language ability in school-age children with autism. *Developmental Neuropsychology* **27**, 3, 361-78.

Klein, B. P., & Mervis, C. B. (1999) Contrasting patterns of cognitive abilities of 9- and 10-year-olds with Williams syndrome or Down syndrome. *Developmental Neuropsychology* **16**, 177–96.

Kline, A.D., Grados, M., Sponseller, P., Levy, H.P., Blagowidow, N., Schoedel, C., Rampolla, J., Clemens, D.K., Krantz, I., Kimball, A., Pichard, C., & Tuchman, D. (2007a) Natural History of Aging in Cornelia de Lange Syndrome. *American Journal of Medical Genetics* **Part C**, 145C, 248-60.

Kline, A.D., Krantz, I.D., Sommer, A., Kliewer, M., Jackson, L.G., FitzPatrick, D.R., Levin, A.V., & Selicorni, A. (2007b) Cornelia de Lange Syndrome: Clinical Review, Diagnostic and Scoring Systems, and Anticipatory Guidance. *American Journal of Medical Genetics* **Part A**, 143A, 1287-296.

Kline A.D., Stanley C, Belevich, J, Brodsky K, Barr M, Jackson LG.(1993) Developmental data on individuals with the Brachmann-de Lange syndrome. *American Journal of Medicine and Genetics* **47**, 1053–58.

Korkman, M. Kirk, U. & Kemp, S. (1998) NEPSY: A developmental neuropsychological assessment. The Psychological Corporation, Saint Antonio.

Krantz, I.D., McCallum, J., DeScipio, C., Kaur, M., Gillis, L.A., Yaeger, D., Jukofsky, L.,Wasserman, N., Bottani, A., Morris, C.A., Nowaczyk, M.J., Toriello, H., Bamshad, M.J.,Carey, J.C., Rappaport, E., Kawauchi, S., Lander, A.D., Calof, A.L., Li, H.H., Devoto, M. & Jackson, L.G. (2004) Cornelia de Lange syndrome is caused by mutations in NIPBL, the human homolog of Drosophila melanogaster Nipped-B. *Nature Genetics* **36**, 6, 631-35.

Kushlick, A., Blunden, R. & Cox, G. (1973) A method of rating behaviour characteristics for use in large scale surveys of mental handicap. *Psychological Medicine* **3**, 466-78.

Logie, R.H. (1996) The seven ages of working memory. In: *Working memory and human cognition* (ed J. Richards) pp. 31-65. Oxford University Press, New York.

Lopez, B.R., Lincoln, A.J., Ozonoff, S., & Lai, Z. (2005) Examining the relationship between executive functions and restricted, repetitive symptoms of autistic disorder. *Journal of Autism and Developmental Disorders* **35**, 4, 445-60.

Luzzani, S., Macchini, F., Valade, A., Milani, D., & Selicorni, A. (2003). Gastroesophageal reflux and Cornelia de Lange syndrome. *American Journal of Medical Genetics* **119**, 283-87.

Miclea, M., Benga, O. & Vis-petra, L. (2007). Dimensions of attention and executive functioning in 5 to 12 year old children. *Cognition, Brain & Behaviour* **3**, 585-608.

Milner, B. (1971) Interhemispheric differences in the localisation of psychological processes in man. *Cortex* **27**, 272–77.

Miyake, N., Tonoki, H., Gallego, M., Harada, N., Shimokawa, O., Yoshiura, K.I., Ohta, T.,Kishino, T., Niikawa, N. & Matsumoto, N. (2005) Phenotype-genotype correlation in two patients with 12q proximal deletion. *Journal of Human Genetics* **49**, 5, 282-84.

Moss, J., Oliver, C., Arron, K., Burbidge, C. & Berg, K. (2009). The Prevalence and Phenomenology of Repetitive Behavior in Genetic Syndromes. *Journal of Autism and Developmental Disorders* **39**, 4, 572-88.

Moss, J.F., Oliver, C., Berg, K., Kaur, G., Jephcott, L. & Cornish, K. (2008) Prevalence of autism spectrum phenomenology in Cornelia de Lange and Cri du Chat syndromes.. *American Journal of Mental Retardation* **113**, 4, 278-91.

Oliver, C., Arron, K., Sloneem, J. & Hall, S. (2008). Behavioural phenotype of Cornelia de Lange syndrome: case-control study. British Journal of Psychiatry, 193, 466-70.

Oliver, C., Berg, K., Moss, J., Arron, K., & Burbidge, C. (in submission) Delineation of behavioural phenotypes in genetic syndromes: 1. Autism Spectrum Disorder, Affect and Hyperactivity.

Oliver, C., Crayton, L., Holland, A., Hall, S., & Bradbury, J. (1998) A four year prospective study of age-related cognitive changes in adults with Down's syndrome. *Psychological medicine* **28**, 1365-377.

Petty, J. & Oliver, C. (2005) Self-injurious behaviour in individuals with severe intellectual disabilities. *Current Opinion in Psychiatry* **18**, 484-89.

Rabbitt, P. (1997) Methodology of Frontal and Executive Function. Psychology Press, London.

Rodgers, C. (1987) Maternal support for the Down's syndrome stereotype: The effect of direct experience of the condition. *Journal of Mental Deficiency Research* **31**, 217–78.

Rogers, S.J. (2009) What are infant siblings teaching us about autism in infancy? *Autism Research* **2**, 3, 125–37.

Rowe, J., Lavender, A. & Turk, V. (2006). Cognitive executive function in Down's syndrome. *British Journal of Clinical Psychology* **45**, 1, 5-17.

Sarimski, K. (1997) Communication, social-emotional development and parenting stress in Cornelia-de-Lange syndrome. *Journal of Intellectual Disability Research* **41**, 70–75.

Scheres, A**.**, Oosterlaan, J., Geurts, H. M., Morein-Zamir, S., Meiran, N., Schut, H., Vlasveld, L., & Sergeant, J. A.. (2004). Executive functioning in AD/HD: Primarily an inhibition deficit? Archives of Clinical Neuropsychology, 19, 569-594.

Selikowitz, M. (2008). Down Syndrome: The Facts. 3rd ed. Oxford: Oxford University Press.

Seltzer, M.M., Abbeduto, L., Krauss, M.W., Greenberg, J., Swe, A.(2004) Comparison groups in autism family research: Down Syndrome, Fragile X and Schizophrenia. *Journal of Autism and Developmental Disorders* **34**, 1, 41-48.

Sigman, M., & Ruskin, E. (1999) Continuity and change in the social competence of children with autism, Down syndrome, and developmental delays. *Monographs of the Society for Research in Child Development* **64**,114.

Sparrow, S.S., Balla, D.A., & Cicchetti, D.V., (1984) The Vineland Adaptive Behavior. Scales: Interview Edition, Survey Form. (Version II). Pearson Assessments.

Thomas, M. S.C. (2009) Worksheet on using SPSS to analyse and compare cross-sectional developmental trajectories. Developmental Neurocognition Lab. [Online] Available at www.psyc.bbk.ac.uk/research/DNL/stats/Thomas_trajectories.html#Section2 [accessed December 2009].

Thomas, M. S. C., Annaz, D., Ansari, D., Serif, G., Jarrold, C., & Karmiloff-Smith, A. (2009) Using developmental trajectories to understand developmental disorders. *Journal of Speech, Language, and Hearing Research* **52**, 336-58.

Tonkin, E., Wang, T-J., Lisgo, S., Bamshad, M. & Strachan, T. (2004) NIPBL, encoding a homologue of fungal Scc2-type sister chromatid cohesion proteins and Drosophila Nipped-B, is mutated in Cornelia de Lange syndrome. *Nature Genetics* **36**, 6, 636-41**.**

Turner, M. (1997) Toward an executive dysfunction account of repetitive behaviour. In: *Autism as an Executive Disorder* (ed J.Russell), pp. 57-100. Oxford University Press, Oxford.

Vuilleumier, N., Kövari, E., Michon, A., Hof, P.R., Mentenopoulos, G., Giannakopoulos, P. & Bouras, C. (2002) Neuropathological analysis of an adult case of the Cornelia de Lange syndrome. *Acta Neuropathologica* **104**, 3, 327-32.

Wilding, J., Cornish, K. & Munir, F. (2002) Further delineation of the executive deficit in males with fragile-X syndrome. *Neuropsychologia* **40**, 8, 1343-349.

Wilson, B.A., Alderman, N., Burgess, P.W., Emslie, H. & Evans, J.J. (1996) Behavioural Assessment of the Dysexecutive Syndrome. Pearson, Psycorp.

Wishart, J. G., & Johnston, F. H. (1990) The effects of experience on attribution of a stereotyped personality to children with Down's syndrome. *Journal of Mental Deficiency Research* **34**, 409-20.

Woodcock, K. A., Oliver, C., & Humphreys, G, W. (2009a) Hypothesis: A specific pathway can be identified between genetic characteristics and behaviour profiles in Prader-Willi syndrome via cognitive, environmental and physiological mechanisms. *Journal of Intellectual Disability Research* **53**, 493-500.

Zelazo, P.D. (2006) The Dimensional Change Card Sort (DCCS): a method of assessing executive function in children. *Nature Protocols* **1**, 297–301.

Zelazo, P. D., Carlson, S. M. & Kesek, A. (2008) Development of executive function in childhood. In: *Handbook of Developmental Cognitive Neuroscience*, 2nd ed, (eds C. A. Nelson and M. Luciana), pp553–574. MIT Press, Cambridge, MA.

APPENDIX A. SPSS output: Comparisons of background characteristics between participants who completed measures of executive functioning and those who did not.

1. **CdLS**

Group Statistics

	Completed EF tasks	N	Mean
age in years	EF tasks completed	17	22.71
	EF tasks not completed	12	24.42
Age in Months	EF tasks completed	17	277.882
	EF tasks not completed	12	296.667
BPVS: raw score	EF tasks completed	17	71.7647
	EF tasks not completed	8	57.2500
BPVS: vma in years (age equivalence)	EF tasks completed	17	6.5882
	EF tasks not completed	8	5.2500
BPVS: verbal mental age (months; age equivalence)	EF tasks completed	17	85.5294
	EF tasks not completed	8	67.7500
VABS- communication domain standard score	EF tasks completed	17	47.4706
	EF tasks not completed	11	52.1818
VABS- daily living skills domain standard score	EF tasks completed	17	58.8824
	EF tasks not completed	11	47.0909

VABS- socialization domain standard score	EF tasks completed	17	58.7059
	EF tasks not completed	11	51.6364
VABS-Adaptive Beavior Composite Standard Score	EF tasks completed	17	55.0588
	EF tasks not completed	11	49.1818

Group Statistics

	Completed EF tasks	Std. Deviation	Std. Error Mean
age in years	EF tasks completed	8.880	2.154
	EF tasks not completed	11.572	3.340
Age in Months	EF tasks completed	106.0141	25.7122
	EF tasks not completed	139.1613	40.1724
BPVS: raw score	EF tasks completed	18.81000	4.56210
	EF tasks not completed	19.83323	7.01211
BPVS: vma in years (age equivalence)	EF tasks completed	2.18114	.52900
	EF tasks not completed	1.75255	.61962
BPVS: verbal mental age (months; age equivalence)	EF tasks completed	24.60721	5.96812
	EF tasks not completed	22.42288	7.92769
VABS- communication domain standard score	EF tasks completed	17.34978	4.20794

	EF tasks not completed	21.91264	6.60691
VABS- daily living skills domain standard score	EF tasks completed	13.57333	3.29202
	EF tasks not completed	16.33680	4.92573
VABS- socialization domain standard score	EF tasks completed	19.10420	4.63345
	EF tasks not completed	17.90124	5.39743
VABS-Adaptive Beavior Composite Standard Score	EF tasks completed	17.70053	4.29301
	EF tasks not completed	17.97119	5.41852

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	T
age in years	Equal variances assumed	.282	.600	-.451
	Equal variances not assumed			-.430
Age in Months	Equal variances assumed	.334	.568	-.413
	Equal variances not assumed			-.394

BPVS: raw score	Equal variances assumed	.065	.802	1.770
	Equal variances not assumed			1.735
BPVS: vma in years (age equivalence)	Equal variances assumed	.065	.801	1.515
	Equal variances not assumed			1.643
BPVS: verbal mental age (months; age equivalence)	Equal variances assumed	.010	.920	1.730
	Equal variances not assumed			1.792
VABS- communication domain standard score	Equal variances assumed	.711	.407	-.633
	Equal variances not assumed			-.601
VABS- daily living skills domain standard score	Equal variances assumed	.256	.617	2.073
	Equal variances not assumed			1.990
VABS- socialization domain standard score	Equal variances assumed	.002	.967	.980
	Equal variances not assumed			.994
VABS-Adaptive Beavior Composite Standard Score	Equal variances assumed	.222	.642	.853
	Equal variances not assumed			.850

Independent Samples Test

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
age in years	Equal variances assumed	27	.656	-1.711
	Equal variances not assumed	19.704	.672	-1.711
Age in Months	Equal variances assumed	27	.683	-18.7843
	Equal variances not assumed	19.597	.698	-18.7843
BPVS: raw score	Equal variances assumed	23	.090	14.51471
	Equal variances not assumed	13.149	.106	14.51471
BPVS: vma in years (age equivalence)	Equal variances assumed	23	.143	1.33824
	Equal variances not assumed	16.977	.119	1.33824
BPVS: verbal mental age (months; age equivalence)	Equal variances assumed	23	.097	17.77941
	Equal variances not assumed	15.066	.093	17.77941
VABS- communication domain standard score	Equal variances assumed	26	.532	-4.71123
	Equal variances not assumed	17.916	.555	-4.71123

VABS- daily living skills domain standard score	Equal variances assumed	26	.058	11.79144
	Equal variances not assumed	18.608	.061	11.79144
VABS- socialization domain standard score	Equal variances assumed	26	.336	7.06952
	Equal variances not assumed	22.524	.331	7.06952
VABS-Adaptive Beavior Composite Standard Score	Equal variances assumed	26	.401	5.87701
	Equal variances not assumed	21.259	.405	5.87701

Independent Samples Test

		t-test for Equality of Means
		Std. Error Difference
age in years	Equal variances assumed	3.794
	Equal variances not assumed	3.974
Age in Months	Equal variances assumed	45.4794
	Equal variances not assumed	47.6963

BPVS: raw score	Equal variances assumed	8.20073
	Equal variances not assumed	8.36555
BPVS: vma in years (age equivalence)	Equal variances assumed	.88328
	Equal variances not assumed	.81472
BPVS: verbal mental age (months; age equivalence)	Equal variances assumed	10.27427
	Equal variances not assumed	9.92304
VABS- communication domain standard score	Equal variances assumed	7.44237
	Equal variances not assumed	7.83313
VABS- daily living skills domain standard score	Equal variances assumed	5.68737
	Equal variances not assumed	5.92454
VABS- socialization domain standard score	Equal variances assumed	7.21695
	Equal variances not assumed	7.11344
VABS-Adaptive Beavior Composite Standard Score	Equal variances assumed	6.88974
	Equal variances not assumed	6.91305

Independent Samples Test

		t-test for Equality of Means	
		95% Confidence Interval of the Difference	
		Lower	Upper
age in years	Equal variances assumed	-9.496	6.075
	Equal variances not assumed	-10.009	6.588
Age in Months	Equal variances assumed	-112.1003	74.5317
	Equal variances not assumed	-118.4083	80.8397
BPVS: raw score	Equal variances assumed	-2.44979	31.47920
	Equal variances not assumed	-3.53710	32.56652
BPVS: vma in years (age equivalence)	Equal variances assumed	-.48898	3.16545
	Equal variances not assumed	-.38085	3.05732
BPVS: verbal mental age (months; age equivalence)	Equal variances assumed	-3.47453	39.03335
	Equal variances not assumed	-3.36302	38.92185
VABS- communication domain standard score	Equal variances assumed	-20.00923	10.58677
	Equal variances not assumed	-21.17358	11.75112

VABS- daily living skills domain standard score	Equal variances assumed	.10090	23.48199
	Equal variances not assumed	-.62646	24.20935
VABS- socialization domain standard score	Equal variances assumed	-7.76513	21.90417
	Equal variances not assumed	-7.66298	21.80201
VABS-Adaptive Beavior Composite Standard Score	Equal variances assumed	-8.28507	20.03908
	Equal variances not assumed	-8.48881	20.24282

Crosstabs

Completed EF tasks * Gender Crosstabulation

Count

		Gender		
		Male	female	Total
Completed EF tasks	EF tasks not completed	6	6	12
	EF tasks completed	8	9	17
	Total	14	15	29

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.024[a]	1	.876		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.024	1	.876		
Fisher's Exact Test				1.000	.587
Linear-by-Linear Association	.024	1	.878		
N of Valid Cases	29				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.79.

b. Computed only for a 2x2 table

2. **DS group**

Group Statistics

	Completed EF tasks	N	Mean
age in years	EF tasks completed	19	23.58
	EF tasks not completed	2	32.00
Age in Months	EF tasks completed	19	287.842
	EF tasks not completed	2	393.000
BPVS: raw score	EF tasks completed	19	67.8421
	EF tasks not completed	2	61.0000
BPVS: vma in years (age equivalence)	EF tasks completed	19	6.3684
	EF tasks not completed	2	5.5000
BPVS: verbal mental age (months; age equivalence)	EF tasks completed	19	81.7895
	EF tasks not completed	2	68.5000
VABS- communication domain standard score	EF tasks completed	14	50.2143
	EF tasks not completed	2	40.0000
VABS- daily living skills domain standard score	EF tasks completed	14	56.6429
	EF tasks not completed	2	51.5000
VABS- socialization domain standard score	EF tasks completed	14	54.2143

	EF tasks not completed	2	41.0000
VABS-Adaptive Beavior Composite Standard Score	EF tasks completed	14	51.0000
	EF tasks not completed	2	43.0000

Group Statistics

	Completed EF tasks	Std. Deviation	Std. Error Mean
age in years	EF tasks completed	5.511	1.264
	EF tasks not completed	1.414	1.000
Age in Months	EF tasks completed	64.9010	14.8893
	EF tasks not completed	8.4853	6.0000
BPVS: raw score	EF tasks completed	24.84678	5.70024
	EF tasks not completed	5.65685	4.00000
BPVS: vma in years (age equivalence)	EF tasks completed	2.85210	.65432
	EF tasks not completed	.70711	.50000
BPVS: verbal mental age (months; age equivalence)	EF tasks completed	33.66762	7.72388
	EF tasks not completed	12.02082	8.50000
VABS- communication domain standard score	EF tasks completed	25.89974	6.92200
	EF tasks not completed	.00000	.00000

VABS- daily living skills domain standard score	EF tasks completed	11.73166	3.13542
	EF tasks not completed	3.53553	2.50000
VABS- socialization domain standard score	EF tasks completed	25.42010	6.79381
	EF tasks not completed	25.45584	18.00000
VABS-Adaptive Beavior Composite Standard Score	EF tasks completed	19.74842	5.27799
	EF tasks not completed	11.31371	8.00000

Crosstabs

Completed EF tasks * Gender Crosstabulation

Count

		Gender		
		Male	female	Total
Completed EF tasks	EF tasks not completed	0	2	2
	EF tasks completed	8	11	19
	Total	8	13	21

APPENDIX B. Background information questionnaire

BACKGROUND INFORMATION

Please tick or write your response to these questions concerning background details:

1. Today's date: _____

2. Your name: _____

3. Would you be happy to be contacted for future research? Yes ☐ No ☐

*The following questions regard information about the **person you care for**:*

1. Name of person: _____ Gender: Male ☐ Female ☐

2. Date of Birth: ___/___/____ **Age:_____**

3. Is the person verbal? (i.e. speaks / signs more than 30 words) Yes ☐ No ☐

4. Is the person able to walk unaided? Yes ☐ No ☐

5. Has the person been diagnosed with a syndrome? Yes ☐ No ☐

If yes, please answer the rest of this questionnaire. If no, please move on to question 9.

6. Which syndrome has the person been diagnosed with? _____

7. When was the person diagnosed? _____

8. Who diagnosed the person?

Paediatrician	☐	Clinical Geneticist	☐
GP	☐	Other _____	

9. Has the person experienced any of the following life events in the *past twelve months*:-

	Yes	No	N/A
9a. Significant change of staff or friends at residential unit? ……...	☐	☐	☐
9b. Significant change of staff or friends at day provision? …….….....	☐	☐	☐
9c. Significant change in day provision, e.g. school, college or job placement? ……	☐	☐	☐
9d. Significant change in place of residence? ……..	☐	☐	
9e. Serious illness and / or hospitalisation? ……..……	☐	☐	
9f. Serious illness of a close relative, close friend or close member of staff? …….	☐	☐	
9g. Death of a close relative, close friend or close member of staff? ……...	☐	☐	
9h. Parents divorced or separated? ……...	☐	☐	

Other (please give details) _____

_____

10. Is the person taking the medication Thyroxine? Yes ☐ No ☐

11. Has the person had their thyroid levels checked in the last 12 months?

Yes ☐ No ☐

APPENDIX C. RBQ

THE RBQ

INSTRUCTIONS:

1. The questionnaire asks about 19 different behaviours.

2. Each behaviour is accompanied by a brief definition and examples. The examples given for each behaviour are not necessarily a complete list but may help you to understand the definitions more fully.

3. Please read the definitions and examples carefully and circle the appropriate number on the scale to indicate how frequently the person you care for has engaged in each of the behaviours **within the last month**.

4. If a particular behaviour does not apply to the person you care for because they are not mobile or verbal please circle the number 0 on the scale

	Never	Once a month	Once a week	Once a day	More than once a day
1. Object stereotypy: repetitive, seemingly purposeless movement of objects in an unusual way *E.g. twirling or twiddling objects, twisting or shaking objects, banging or slapping objects.*	**0**	**1**	**2**	**3**	**4**
2. Body stereotypy: repetitive, seemingly purposeless movement of whole body or part of body (other than hands) in an unusual way. *E.g. body rocking, or swaying ,or spinning, bouncing, head shaking, body posturing.*. Does not include self-injurious behaviour.	**0**	**1**	**2**	**3**	**4**
3. Hand stereotypy: repetitive, seemingly purposeless movement of hands in an unusual way. *E.g. finger*	**0**	**1**	**2**	**3**	**4**

twiddling, hand flapping, wigging or flicking fingers, hand posturing. Does not include self-injurious behaviour.					
4. Cleaning: Excessive cleaning, washing or polishing of objects or parts of the body *E.g. polishes windows and surfaces excessively, washes hands and face excessively,*	**0**	**1**	**2**	**3**	**4**
5. Tidying up: Tidying away any objects that have been left out. This may occur in situations when it is inappropriate to put the objects away. Objects may be put away into inappropriate places. *E.g. putting cutlery left out for dinner in the bin, removes all objects from surfaces.*	**0**	**1**	**2**	**3**	**4**
6. Hoarding: Collecting, storing or hiding objects to excess, including rubbish, bits of paper, and pieces of string or any other unusual items.	**0**	**1**	**2**	**3**	**4**
7. Organising objects: Organising objects into categories according to various characteristics such as colour, size, or function. *E.g. ordering magazines according to size, ordering toy cars according to colour, ordering books according to topic.*	**0**	**1**	**2**	**3**	**4**
8. Attachment to particular people: Continually asking to see, speak or contact a particular 'favourite' person. *E.g. continually asks to see or speak to particular friend, carer, babysitter or schoolteacher.*	**0**	**1**	**2**	**3**	**4**
9. Repetitive questions: Asking specific questions over and over. *E.g. always asking people what their favourite colour is, asking who is taking them to school the next day over and over*	**0**	**1**	**2**	**3**	**4**
10. Attachment to objects: Strong preference for a particular object to be present at all times. *E.g. Carrying a particular piece of string everywhere, taking a particular red toy car everywhere, attachment to soft toy or particular blanket.*	**0**	**1**	**2**	**3**	**4**

11. Repetitive phrases/signing: Repeating particular sounds, phrases or signs that are unrelated to the situation over and over. *E.g. repeatedly signing the word 'telephone'.*	**0**	**1**	**2**	**3**	**4**
12. Rituals: carrying out a sequence of unusual or bizarre actions before, during or after a task. The sequence will always be carried out when performing this task and will always occur in the same way. *E.g. turning round three times before sitting down, turning lights on and off twice before leaving a room, tapping door frame twice when passing through it.*	**0**	**1**	**2**	**3**	**4**
13. Restricted conversation: Repeatedly talks about specific, unusual topics in great detail. *E.g. conversation restricted to: trains, buses, dinosaurs, particular film, country, or sport.*	**0**	**1**	**2**	**3**	**4**
14. Echolalia: Repetition of speech that has either just been heard or has been heard more than a minute earlier. *E.g.: Mum:' Jack don't do that' Jack: 'Jack don't do that'.*	**0**	**1**	**2**	**3**	**4**
15. Preference for routine: Insist on having the same household, school or work schedule everyday. *E.g. likes to have the same activities on the same day at the same time each week, prefers to eat lunch at exactly the same time every day, wearing the same jumper everyday.*	**0**	**1**	**2**	**3**	**4**
16. Lining up or arranging objects*: Arrangement of objects into lines or patterns E.g. placing toy cars in a symmetrical pattern, precisely lining up story books,*	**0**	**1**	**2**	**3**	**4**
17. Just right behaviour: Strong insistence that objects, furniture and toys always remain in the same place. *E.g. all chairs, pictures and toys have a very specific place that cannot be changed.*	**0**	**1**	**2**	**3**	**4**
18. Completing behaviour: Insists on having objects or activities 'complete' or 'whole' *E.g. Must have doors open or closed not in between, story must be read from*	**0**	**1**	**2**	**3**	**4**

beginning to end, not left halfway through.

19. Spotless behaviour: Removing small, almost unnoticeable pieces of lint, fluff, crumbs or dirt from surfaces, clothes and objects. *E.g. Picking fluff off a jumper, removing crumbs from the kitchen table.*	**0**	**1**	**2**	**3**	**4**

APPENDIX D. Instructions and record form for executive functioning tasks

DIGIT SPAN

Digit Span Forward

Equipment needed:

Digit Span Forward Score sheet .

Administration:

"I am going to say some numbers. Listen carefully and when I have finished you say them after me".

Read the digits at the rate of one per second, dropping voice inflection slightly on the last digit in a series. After each sequence, pause to allow the participant to respond. Only fill in the columns labelled 'PARTICIPANT'S RESPONSE' and 'CORRECT/ INCORRECT'.

Digit Span Backward

Equipment needed:

Digit Span Backward Score sheet .

"Now I am going to say some more numbers but this time when I stop I want you to say them backwards. For example, if I say 8-2, what would you say? Pause for the participant to respond.

If the participant responds correctly say **"that's right".** Then proceed to item 1.

If the participant responds incorrectly say **"No, you would say 2-8. I said 8-2 so to say it backwards you would say 2-8. Now try these numbers. Remember, you are to say them backwards: 5-6"**

Whether the participant succeeds or fails with the second example, proceed to item 1. If the participant responds incorrectly to the 2nd example say, **"No, you would say 6-5. I said 5-6 so to say it backwards you would say 6-5. Let have a go at some more".**

Move on to the test items and give no help with these. Read the digits at the rate of one per second, dropping voice inflection slightly on the last digit in a series. After each sequence, pause to allow the participant to respond.

Discontinue after failure of all three trials on any item.

CORSI SPAN

Corsi Span Forward

Place the board on the table with the cube numbers facing the examiner and with the board centred at the examinee's midline so he / she can easily reach the cubes. All sequences should be tapped out at a rate of one cube per second.

"Now, I want you to do exactly what I do. Touch the blocks I touch, in the same order. Let's practice. If I touch this block (cube 1) **then this block** (cube 9)**, what would you do?"**

If the examinee gets it correct, administer trials on score sheet. If the examinee responds incorrectly say, **"No, I touched this one** (cube 1)**, then this one** (cube 9) **so you would do it in the same order** (examiner touches cube 1 then cube 9). **Let's have another go. So if I touch this block** (cube 3) **then this block** (cube 8)**, what would you do?"** Re-administer the same practice trial until the participant responds correctly.

When the examinee is ready for the test trials, say **"Great, let's try some more".**

Corsi Span Backward

"Now I am going to touch some more blocks. This time when I stop, I want you to touch the blocks backward, in the reverse order of mine. For example, if I touch this block (cube 3)**, then this one** (cube 5)**, you would touch them backwards,** (examiner touches

cube 5 then cube 3)**. In this example if I touch this block** (cube 9) **then this one** (cube 1)**, what would you do?**

If the examinee responds correctly say, **"That's right. Here's the next one. Remember to touch them in reverse order."**

If the examinee responds incorrectly, point appropriately and say **"No, I touched this one, then this one; so to do it in reverse, you would touch this one, then this one."**

VERBAL FLUENCY

Semantic Fluency

"See how many different animals you can name, like *cat* or *dog*. Say them as quickly as you can. Are you ready? Go.

Start timing. If the child does not produce any words within any 15-second period say **"Tell me some more animals".**

At 60 seconds say **"Stop".**

"Now see if you can name some more things you eat or drink. Say as many different ones as you can, like *pizza* or *milk*. Do it quickly. Ready? Go".

Start timing. If the child does not produce any words within any 15-second period say **"Tell me some more things you can eat or drink".**

At 60 seconds say **"Stop".**

Phonemic Fluency

"Now say all the different words you can think of that start with the letter *S* like sun or sand. Do not use any names of people or places, like *Susan* and *Spain*. Say the words as quickly as you can. Ready? Go".

Start timing. If the child does not produce any words within any 15-second period say **"Tell me some more words that start with the letter *S*".**

At 60 seconds say **"Stop".**

"The next letter is F. Tell me as many different words starting with *F* as you can think of, like fun and farm. Do not use any names of people or places, like *Frank* or *France*. Say the words as quickly as you can. Ready? Go".

Start timing. If the child does not produce any words within any 15-second period say **"Tell me some more words that start with the letter *F*".**

At 60 seconds say **"Stop".**

Time Interval	SEMANTIC		PHONEMIC	
	1. Animals	2. Food or Drink	3. S words	4. F words
1"-15"				

16”-30”				
31”-45”				
46”-60”				
Total words				

DESIGN FLUENCY

Structured Array

Present the Structured Array Teaching Example horizontally in front of the participant.

"Here are some boxes with dots. I want you to connect two or more dots using straight lines, to make a design in each box. Make sure that each design is different from he others. Let's practice".

Provide two examples: first a straight line connecting two dots and second, three lines connecting four dots.

"Now you do these".

Ask the participant to produce different designs on the two remaining boxes. Explain any errors.

Structured Array

Present the test page horizontally in front of the participant.

"In every box, coonect two or more dots with straight lines. Work as quickly as you can and make every design different. Start here (point to the upper left box) **and go this way** (left to right)**. When you finish this row, go to the next one** (point to the next line). **Ready? Begin".**

You may point to each box in turn, if it is helpful to guide participants acroos the page.

Start timing. Stop the participant after 60 seconds.

Random Array

Present the Random Array Teaching Example.

"Here are some more boxes with dots. Let's make as many different designs as we can by connecting two or more dots. Watch me"

Draw a line connecting two dots within the first box.

"Now you do these, making sure every design is different".

Ask the participant to produce different designs on the three remaining boxes. Explain any errors.

Present the test page horizontally (with arrows pointing away from the participant) in front of the participant.

"In every box, connect two or more dots with straight lines. Work as quickly as you can and make every design different. Start here. Ready? Begin".

Start timing. Stop the participant after 60 seconds.

DIMENSION CHANGE CARD SORTING TASK (DCCS)

Target cards**: Blue rabbit (on left tray) and red boat (one right tray)**

Pre-switch trials: colour game

Point at target cards. **"Here's a blue rabbit and a here's a red boat Now we're going to play a card game. This is the colour game. In the colour game, all the blue one's go here** (pointing to left tray) **and all the red ones go there** (pointing to right tray)".

The examiner sorts a 'blue boat' test card. **"See, here's a blue one. So it goes here".** Examiner places it face down in the left tray. **"If it's blue it goes here and if it's red it goes there".** The examiner then shows the participant a 'red rabbit' test card. **"Now here's a red one. Where does it go?"** Allow the participant to sort the card and whether correct or incorrect move on to the next card.

"Now it's your turn. So remember, if it's blue it goes here and if it's red it goes there". Here's a red one. Where does it go?"

For each trial say, **"Let's do another. If it's blue it goes here and if it's red it goes there** (select a test card). **Here's a red/blue one. Where does it go?"**

Order in which cards presented	Correct response	Tray selected by participant (Blue rabbit or Red boat)	Participant's response (correct / incorrect)
1. Red rabbit	Red boat		
2. Blue boat	Blue rabbit		
3. Blue boat	Blue rabbit		
4. Red rabbit	Red boat		
5. Blue boat	Blue rabbit		
6. Red rabbit	Red boat		

Post-switch trials: shape game

"Now we're going to play a new game. We're not going to play the colour game anymore. We're going to play the shape game. In the shape game, all the rabbits go here (pointing to left tray) **and all the boats go here** (pointing to right tray)**. Remember if it's a rabbit put it here but if it's a boat put it there. Okay?"**

For each trial say, **"Here's a boat/rabbit. Where does this one go?"**

Order in which cards presented	Correct response	Tray selected by participant (Blue rabbit or Red boat)	Participant's response (correct / incorrect)
1. Blue boat	Red boat		
2. Blue boat	Red boat		
3. Red rabbit	Blue rabbit		
4. Blue boat	Red boat		
5. Red rabbit	Blue rabbit		
6. Red rabbit	Blue rabbit		

Boarder version

Only do this game if participant gets at least 5/6 post-switch trials correct

Materials: 4 red rabbits, 3 blue boats, 4 red rabbits with border, 3 blue boats with border

"Okay, you did really well. Now I have a more difficult game for you to do. In this game, you sometimes get cards that have a black border around it, like this one (showing a red rabbit with a border)**. If you see cards with a black border you have to play the colour game. In the colour game, red ones go here and blue ones go there** (pointing to appropriate trays)**. This card's red so I'm going to put it there** (placing it face down in the appropriate tray). **But if the cards have no black border, like this one [showing a red rabbit without a border), you have to play the shape game. If it's a rabbit we put it here but if it's a boat we put it there** (pointing to appropriate trays). **This one's a rabbit so I'm going to put it here** (placing it face down in the appropriate tray).**Okay? Now it's your turn."**

One each trial say **"If there's a border, play the colour game. If there's no border, play the shape game."** Select a test card. **"This one has a border, where does it go? Let's do another"**

Order in which cards presented	**Correct response**	**Tray selected by participant (Blue rabbit or Red boat)**	**Participant's response (correct / incorrect)**
1. Red rabbit with border	Red boat		
2. Blue boat	Red boat		
3. Blue boat with border	Blue rabbit		
4. Red rabbit	Blue rabbit		
5. Blue boat	Red boat		
6. Blue boat with border	Blue rabbit		
7. Red rabbit	Blue rabbit		
8. Red rabbit with border	Red boat		
9. Blue boat with border	Blue rabbit		
10. Red rabbit	Blue rabbit		
11. Red rabbit with border	Red boat		
12. Blue boat	Red boat		

APPENDIX E. BRIEF-P

BRIEF-P

Below is a list of statements. We would like to know if the person has had *problems* with these behaviours *during the past 6 months*. Please answer *all the items* the best you can. Please do not skip any items. Think about the person as you read these statements and circle:

N if the behaviour is **Never** a problem

S if the behaviour is **Sometimes** a problem

O if the behaviour is **Often** a problem

	During the past 6 months, how often has each of the following behaviours been a *problem*?	**Never**	**Sometimes**	**Often**
1.	Over-reacts to small problems	**N**	**S**	**O**
2.	When given two things to do, remembers only the first or last	**N**	**S**	**O**
3.	Is unaware of how his/her behaviour affects or bothers others	**N**	**S**	**O**
4.	When instructed to clean up, puts things away in a disorganised, random way	**N**	**S**	**O**
5.	Becomes upset with new situations	**N**	**S**	**O**
6.	Has explosive, angry outbursts	**N**	**S**	**O**
7.	Has trouble carrying out the actions needed to complete tasks (such as, trying one puzzle piece at a time, cleaning up to earn a reward)	**N**	**S**	**O**
8.	Does not stop laughing at funny things or events when others stop	**N**	**S**	**O**
9.	Needs to be told to begin a task even when willing to do it	**N**	**S**	**O**
10.	Has trouble adjusting to new people (such as babysitter, teacher, friend or day care worker)	**N**	**S**	**O**

11.	Becomes upset too easily	**N**	**S**	**O**
12.	Has trouble concentrating on games, puzzles or activities	**N**	**S**	**O**
13.	Has to be more closely supervised than similar peers	**N**	**S**	**O**
14.	When sent to get something, forgets what he/she is supposed to get	**N**	**S**	**O**
15.	Is upset by a change in plans or routine (for example, order of daily activities, adding last minute errands to schedule, change in driving route to shop)	**N**	**S**	**O**
16.	Has outbursts for little reason	**N**	**S**	**O**
17.	Repeats the same mistakes over and over even after help is given	**N**	**S**	**O**
18.	Acts wilder or sillier than others in groups (such as, birthday parties, class at school/college, family gatherings)	**N**	**S**	**O**
19.	Cannot find clothes, shoes, toys or books even when he/she has been given specific instructions	**N**	**S**	**O**
20.	Takes a long time to feel comfortable in new places or situations (such as, visiting distant relatives or new friends)	**N**	**S**	**O**
21.	Mood changes frequently	**N**	**S**	**O**
22.	Makes silly mistakes on things he/she can do	**N**	**S**	**O**
23.	Is fidgety, restless or squirmy	**N**	**S**	**O**
24.	Has trouble following established routines for sleeping, eating or activities	**N**	**S**	**O**
25.	Is bothered by loud noises, bright lights or certain smells	**N**	**S**	**O**
26.	Small events trigger big reactions	**N**	**S**	**O**
27.	Has trouble with activities or tasks that have more than one step	**N**	**S**	**O**
28.	Is impulsive	**N**	**S**	**O**
During the past 6 months, how often has each of the following behaviours been a *problem*?		**Never**	**Sometimes**	**Often**
29.	Has trouble thinking of a different way to solve a problem or complete an activity when stuck	**N**	**S**	**O**
30.	Is disturbed by changes in the environment (such as, new furniture, things in room moved around or new clothes)	**N**	**S**	**O**

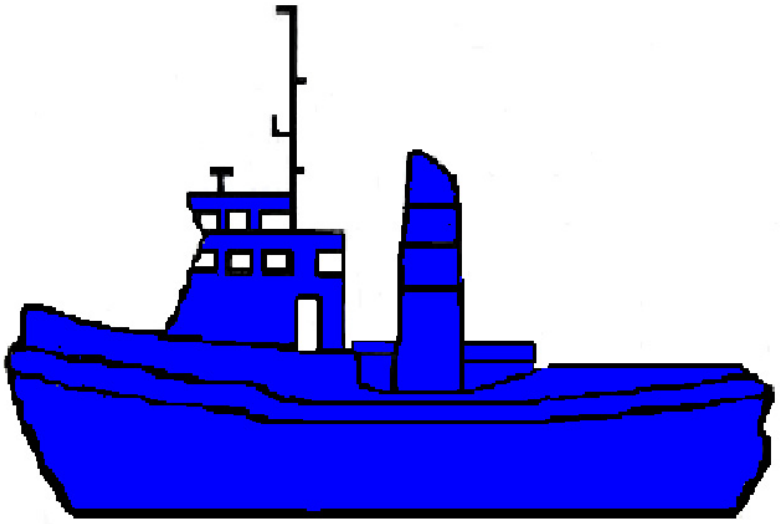
31	Angry or tearful outbursts are intensive but end suddenly	**N**	**S**	**O**
32.	Needs help from adult to stay on task	**N**	**S**	**O**
33.	Does not notice when his/her behaviour causes negative reactions	**N**	**S**	**O**
34.	Leaves messes that others have to clean up even after instruction	**N**	**S**	**O**
35.	Has trouble changing activities	**N**	**S**	**O**
36.	Reacts more strongly to situations than other peers	**N**	**S**	**O**
37.	Forgets what he/she is doing in the middle of an activity	**N**	**S**	**O**
38.	Does not realise that certain actions bother others	**N**	**S**	**O**
39.	Gets caught up in the small details of a task or situation and misses the main idea	**N**	**S**	**O**
40.	Has trouble "joining in" at unfamiliar social events (such as, birthday parties, picnics, holiday gatherings)	**N**	**S**	**O**
41.	Is easily overwhelmed or over stimulated by typical daily activities	**N**	**S**	**O**
42.	Has trouble finishing tasks (such as, games, puzzles or other activities)	**N**	**S**	**O**
43.	Gets out of control more than peers	**N**	**S**	**O**
44.	Cannot find things in room even when given specific instructions	**N**	**S**	**O**
45.	Resists change of routine, foods, places etc.	**N**	**S**	**O**
46.	After having a problem, will stay disappointed for a long time	**N**	**S**	**O**
47.	Cannot stay on the same topic when talking	**N**	**S**	**O**
48.	Talks or plays too loudly	**N**	**S**	**O**
49.	Does not complete tasks even after given directions	**N**	**S**	**O**
50.	Acts overwhelmed or over stimulated in crowded, busy situations (such as, lots of noise, activity or people)	**N**	**S**	**O**
51.	Has trouble getting started on activities or tasks even after instructed	**N**	**S**	**O**
52.	Acts too wild or out of control	**N**	**S**	**O**
53.	Does not try as hard as his/her ability on activities	**N**	**S**	**O**
54.	Has trouble putting the brakes on his/her actions even after being	**N**	**S**	**O**

	asked			
55.	Unable to finish describing an event, person or story	**N**	**S**	**O**
56.	Completes tasks or activities too quickly	**N**	**S**	**O**
57.	Is unaware when he/she does well and not well	**N**	**S**	**O**
58.	Gets easily sidetracked during activities	**N**	**S**	**O**
59.	Has trouble remembering something, even after a brief period of time	**N**	**S**	**O**
60.	Becomes too silly	**N**	**S**	**O**
61.	Has a short attention span	**N**	**S**	**O**
62.	Behaves carelessly or recklessly in situations where he/she could be hurt (such as, playground, swimming pool)	**N**	**S**	**O**
63.	In unaware when he/she performs a task right or wrong	**N**	**S**	**O**

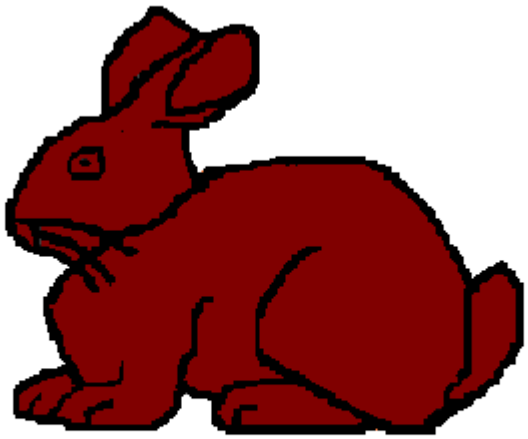
APPENDIX G. DCCS task pictures

There were two sorting trays- one with a picture of a blue rabbit, the other with a picture of a red boat. Participants had to sort a set of cards by colour (red/blue) in the first trial, and shape (boat/rabbit) in the second trial. In the third trial, if the shape was surrounded by a border, they were to sort by colour. If there were no border they were to sort by shape. (See Appendix * for full task instructions) The stimuli used are shown below.

i. Blue boat

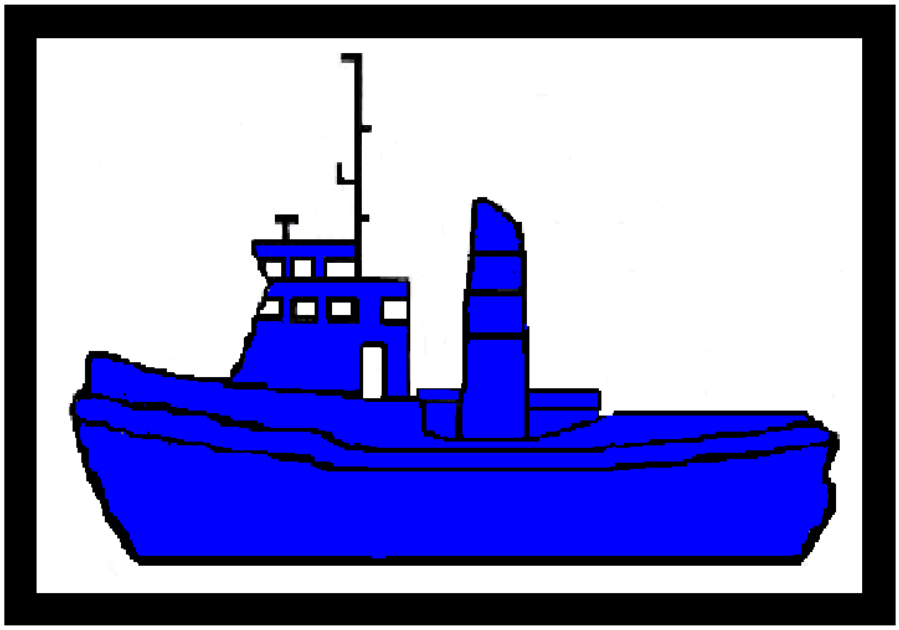


ii. Red Rabbit



iii

. Blue boat with border



APPENDIX H. Correlations BRIEF-P and performance on tasks.

Significant correlations BRIEF-P and EF measures

Inhibit Subscale

Digit span backwards r = -.43, p = .01, n = 35

Digit span backwards max r = -.47, p <.01, n = 35

Semantic animals r = -.46, p= .01, n =37

Semantic fluency total r = -.41, p=.01, n = 38

Phonemic 's' r = -.35, p = .03, n = 37

DCCS Border - r =.40, p = .01, n =39

Shift Subscale

Digit span forward max r = -.36, p = .04, n = 36

DCCS Shape r = -.38, p = .01, n = 40

DCCS Border r = -.40, p = .01, n = 39

Emotional control

Digit span forward max r = -.44, p <.01, n =.36

DCCS Border r = -.39, p <.02, n = 39

Working Memory subscale

Did not correlate with our measures of WM (Digit span, Corsi span)

Semantic fluency r = -.40, p = .01, n = 37

Phonemic fluency r = -.36, p = .03, n = 38

Design fluency r = -.34, p =.03, n = 39

Plan/organise

Digit span backward max r = -.40, p = .02, n =35

Corsi span backward max r = -.37, p = .02, n = 38

Semantic fluency r = -.42, p = .01, n= 38

Design fluency structured r = -.33, p = .03, n = 40

Design fluency unstructured r = -.34, p = .03, n = 40

Inhibitory self control index

Digit span forward max r = -.36, p = .03, n = 36

Digit span backward max r = -.40, p = .01, n = 35

Corsi span backward max r = -.33, p = .046, n = 38

Verbal fluency semantic r = -.39, p = .02, n = 38

DCCS border r = -.46, p = .003, n = 39

Design fluency structured r = -.38, p = .02, n = 40

Design fluency random r = - .36, p = ,02, n = 40

Flexibility Index

Digit span forward max r = -.46, p = ,01, n = 36

DCCS shape r = -.39, p = .01, n = 40

DCCS border r = -.34, p = .01, n = 39

Emergent meta cognition

Digit span backward max r = -.37, p = .03, n = 34

Semantic fluency r = -.44, p <.01, n = 37

Phonemic fluency r = -.33, p = .04, n = 38

Design fluency structured r = -.34, p = .03, n = 39

Global executive

Digit span backward max r = -40, p = .02, n = 34

Corsi span backwards max r = -.33, p= .048, n = 37

Semantic fluency r = -.49, p = .007, n = 32

Phonemic fluency r = -.34, p = .04, n = 38

Design fluency structured r = -.35, p = .03, n = 39

Design fluency unstructured r = -.33, p = .04, n = .39

Global executive and RBQ total: r = .60, p <.001, n = 42

RBQ total score

Digit span backward max -.48, p = .005, n = 33

Corsi span backward max -.45, p = .006, n = 37

Semantic fluency -.43, p = .01, n = 37

Phonemic fluency -.33, p = .046, n = 38

DCCS border -.38, p = .02, n = 38

Design fluency structured -.42, p = .01, n = 39

Design fluency random -.44, p <.01, n = 39

APPENDIX I. Results on the Digit Span tests

Digit Span Test			CdLS	DS	*t*	η^2	*p*
Forward	Number correct	*M*	5.56	6.67	-1.38	.05	n.s.
		SD	2.81	2.20			
	Maximum length	*M*	3.11	3.67	-1.91	.09	n.s.
		SD	1.02	.80			
Backward	Number correct	*M*	2.47	1.91	-.08	.00	n.s.
		SD	2.52	2.16			
	Maximum length	*M*	1.94	1.62	.75	.02	n.s.
		SD	1.25	1.35			

APPENDIX J. Correlations between chronological age and executive functioning measures.

Task		CdLS correlation with age	DS correlation with age
Digit Span Forward correct	*R*	-.21	.16
	p	.41	.48
	n	18	21
Digit Span Forward max	*r*	-.17	.11
	p	.51	.63
	n	18	21
Digit Span Backward Correct	*R*	-.46	.08
	P	.06	.74
	N	17	21
Digit Span Backward max	*R*	-.49*	.21
	P	.04	.37
	n	17	21
Corsi Span Forward Correct	*r*	-.27	.03

	p	.24	.90
	n	21	21
Corsi Span Forward	*r*	-.23	-.12
max	*p*	.31	.62
	n	21	21
Corsi Span Backward	*R*	-.30	.16
Correct	*p*	.19	.50
	n	21	21
Corsi Span Backward	*R*	-.26	-.01
max	*p*	.26	.96
	n	21	21
Verbal fluency semantic	*R*	.33	.05
animals	*p*	.16	.82
	n	20	21
Verbal fluency animal	*R*	.28	-.14
repeats	*p*	.23	.54
	n	20	21

Verbal fluency semantic food	*r*	.15	.20
	p	.52	.40
	n	20	21
Verbal fluency food repeats	*r*	.39	.37
	p	.09	.09
	n	20	21
Semantic total score	*r*	.29	.14
	p	.20	.55
	n	22	21
Verbal fluency phonemic S	*r*	.25	.26
	p	.29	.25
	n	20	21
Verbal fluency S repeats	*r*	.65**	-.32
	p	.002	.16
	n	20	21
Verbal fluencyphonemic F	*R*	.25	-.001
	p	.29	.99

	n	20	21
Verbal fluency f repeats	*r*	.47*	-.24
	p	.04	.30
	n	20	21
Phonemic total score	*r*	.14	.15
	p	.52	.52
	n	23	21
DCCS colour (5 to pass)	*r*	-.13	.
	p	.56	.
	n	23	21
DCCS shape (5 to pass)	*r*	-.11	.19
	p	.63	.40
	n	23	21
DCCS border (9-pass)	*r*	-.14	.51*
	p	.53	.02
	n	22	21
DCCSB colour as shape error	*r*	.50	-.59**

	p	.08	.01
	n	13	19
DCCSB shape as colour error	*r*	-.19	-.36
	p	.528	.13
	n	13	19
Design Fluency Structured Array Correct	*r*	-.107	-.01
	p	.627	.96
	n	23	21
Design Fluency Structured Array Incorrect	*r*	.271	-.12
	p	.210	.61
	n	23	21
Design Fluency Random Array Correct	*r*	.022	-.01
	p	.922	.98
	n	23	21
Design Fluency Random Array Incorrect	*r*	.230	-.05
	p	.290	.83
	n	23	21

APPENDIX K. Mental age and Performance Correlations

BPVS calculation of mental age

As young people with developmental disorders may develop slower in respect to their cognitive capabilities, chronological age may not be that insightful or useful as a measure of development. As is typical with research in this area, mental age (MA) was used to examine correlations with measures of executive functioning.

Table 1 shows the significant correlations of both the DS and CdLS groups combined. As can be seen there are significant positive correlations of MA with Digit Span Forward and Backward, Corsi Span Forward and Backward, Verbal fluency, DCCS border version and Design fluency. These correlations are as you would expect from a typically developing population. As people get older from childhood through to mid twenties their brains continue to develop and executive functioning capabilities mature.

Table 1. *Verbal Mental age and Executive function measures correlations*.

		BPVS: verbal mental age (months; age equivalence)
Digit Span Forward correct	Pearson Correlation	.466**
	Sig. (2-tailed)	.003

	N	39
Digit Span Forward max	Pearson Correlation	.411**
	Sig. (2-tailed)	.009
	N	39
Digit Span Backward Correct	Pearson Correlation	.567**
	Sig. (2-tailed)	.000
	N	38
Digit Span Backward max	Pearson Correlation	.627**
	Sig. (2-tailed)	.000
	N	38
Corsi Span Forward Correct	Pearson Correlation	.446**
	Sig. (2-tailed)	.003
	N	42
Corsi Span Forward max	Pearson Correlation	.473**
	Sig. (2-tailed)	.002
	N	42

Corsi Span Backward Correct	Pearson Correlation	.537**
	Sig. (2-tailed)	.000
	N	42
Corsi Span Backward max	Pearson Correlation	.486**
	Sig. (2-tailed)	.001
	N	42
Verbal fluency semantic animals	Pearson Correlation	.596**
	Sig. (2-tailed)	.000
	N	41
Verbal fluency semantic food	Pearson Correlation	.510**
	Sig. (2-tailed)	.001
	N	41
Semantic total score	Pearson Correlation	.603**
	Sig. (2-tailed)	.000
	N	42
Verbal fluency phonemic S	Pearson Correlation	.587**

	Sig. (2-tailed)	.000
	N	41
Verbal fluency phonemic F	Pearson Correlation	.627**
	Sig. (2-tailed)	.000
	N	41
Phonemic total score	Pearson Correlation	.647**
	Sig. (2-tailed)	.000
	N	42
DCCS border (9-pass)	Pearson Correlation	.407**
	Sig. (2-tailed)	.007
	N	43
Design Fluency Structured Array Correct	Pearson Correlation	.638**
	Sig. (2-tailed)	.000
	N	44
Design Fluency Random Array Correct	Pearson Correlation	.630**
	Sig. (2-tailed)	.000

	N	44

Table 2 shows the significant correlations between MA and executive functioning with the two groups separated for analysis. As can be seen from the table, the Down Syndrome group show positive correlations between MA and all the executive functioning tasks. The CdLS group also showed positive correlations with the exception of Digit Span where there were found to be no evidence of significant correlations.

Table 2. *Verbal Mental age and Executive function measures correlations for CdLS and DS individually*.

Group			BPVS: verbal mental age (months; age equivalence)
CdLS			
	Digit Span Forward correct	Pearson Correlation	.413
		Sig. (2-tailed)	.089
		N	18

Digit Span Forward max	Pearson Correlation	.405
	Sig. (2-tailed)	.095
	N	18
Digit Span Backward Correct	Pearson Correlation	.457
	Sig. (2-tailed)	.065
	N	17
Digit Span Backward max	Pearson Correlation	.451
	Sig. (2-tailed)	.069
	N	17
Corsi Span Forward Correct	Pearson Correlation	.527*
	Sig. (2-tailed)	.014
	N	21
Corsi Span Forward max	Pearson Correlation	.591**
	Sig. (2-tailed)	.005
	N	21
Corsi Span Backward Correct	Pearson Correlation	.470*

	Sig. (2-tailed)	.032
	N	21
Corsi Span Backward max	Pearson Correlation	.433*
	Sig. (2-tailed)	.050
	N	21
Verbal fluency semantic animals	Pearson Correlation	.735**
	Sig. (2-tailed)	.000
	N	20
Verbal fluency semantic food	Pearson Correlation	.502*
	Sig. (2-tailed)	.024
	N	20
Semantic total score	Pearson Correlation	.674**
	Sig. (2-tailed)	.001
	N	21
Verbal fluency phonemic S	Pearson Correlation	.615**
	Sig. (2-tailed)	.004

	N	20
	N	20
Verbal fluencyphonemic F	Pearson Correlation	.671**
	Sig. (2-tailed)	.001
	N	20
Phonemic total score	Pearson Correlation	.681**
	Sig. (2-tailed)	.001
	N	21
DCCS shape (5 to pass)	Pearson Correlation	.393
	Sig. (2-tailed)	.064
	N	23
DCCS border (9-pass)	Pearson Correlation	.540**
	Sig. (2-tailed)	.009
	N	22
Design Fluency Structured Array Correct	Pearson Correlation	.660**
	Sig. (2-tailed)	.001

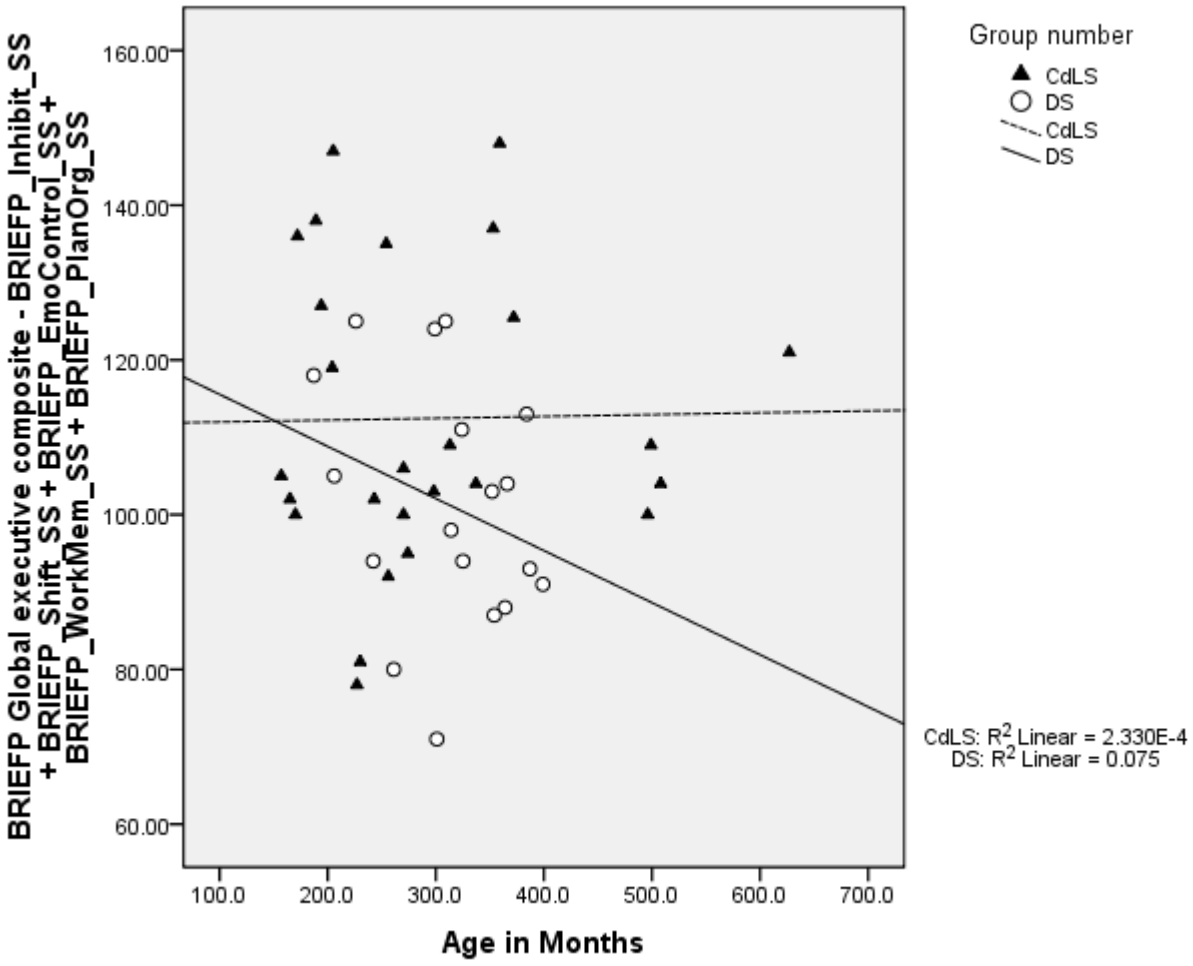
		N	23
	Design Fluency Random Array Correct	Pearson Correlation	.569**
		Sig. (2-tailed)	.005
		N	23
DS			
	Digit Span Forward correct	Pearson Correlation	.599**
		Sig. (2-tailed)	.004
		N	21
	Digit Span Forward max	Pearson Correlation	.528*
		Sig. (2-tailed)	.014
		N	21
	Digit Span Backward Correct	Pearson Correlation	.633**
		Sig. (2-tailed)	.002
		N	21

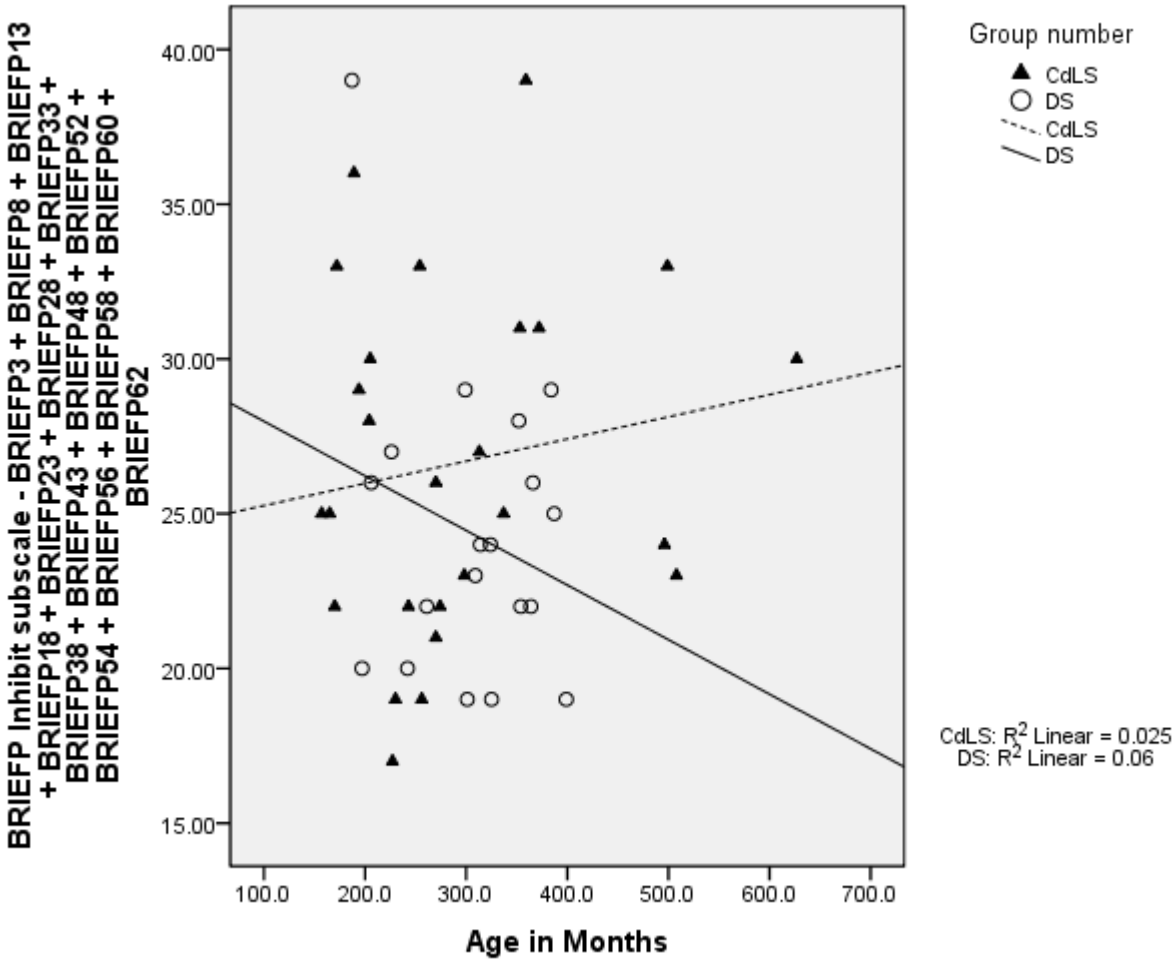
Digit Span Backward max	Pearson Correlation	.723**
	Sig. (2-tailed)	.000
	N	21
Corsi Span Forward Correct	Pearson Correlation	.509*
	Sig. (2-tailed)	.019
	N	21
Corsi Span Forward max	Pearson Correlation	.534*
	Sig. (2-tailed)	.013
	N	21
Corsi Span Backward Correct	Pearson Correlation	.693**
	Sig. (2-tailed)	.000
	N	21
Corsi Span Backward max	Pearson Correlation	.593**
	Sig. (2-tailed)	.005
	N	21
Verbal fluency semantic animals	Pearson Correlation	.538*

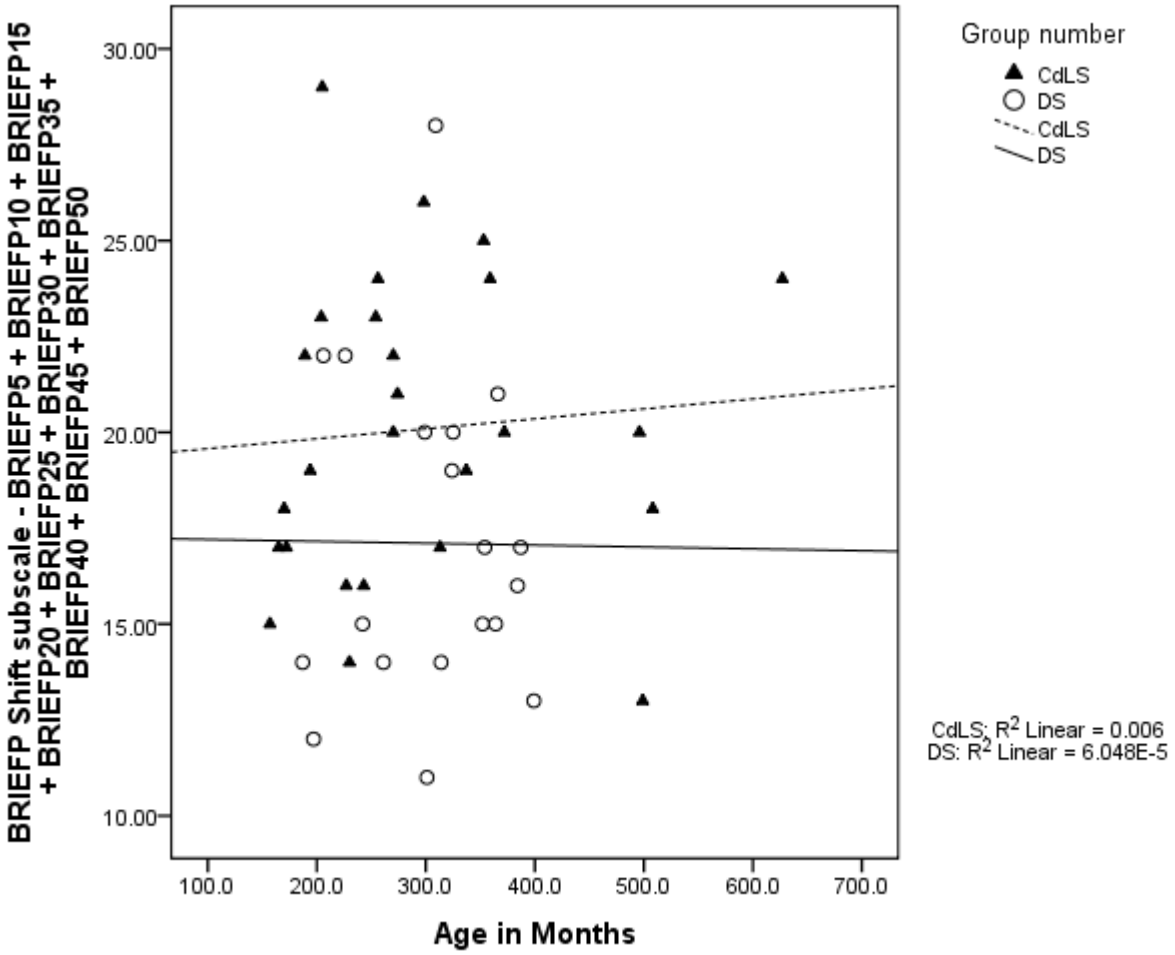
	Sig. (2-tailed)	.012
	N	21
Verbal fluency semantic food	Pearson Correlation	.658**
	Sig. (2-tailed)	.001
	N	21
Verbal fluency food repeats	Pearson Correlation	.480*
	Sig. (2-tailed)	.028
	N	21
Semantic total score	Pearson Correlation	.655**
	Sig. (2-tailed)	.001
	N	21
Verbal fluency phonemic S	Pearson Correlation	.671**
	Sig. (2-tailed)	.001
	N	21
Verbal fluencyphonemic F	Pearson Correlation	.690**
	Sig. (2-tailed)	.001

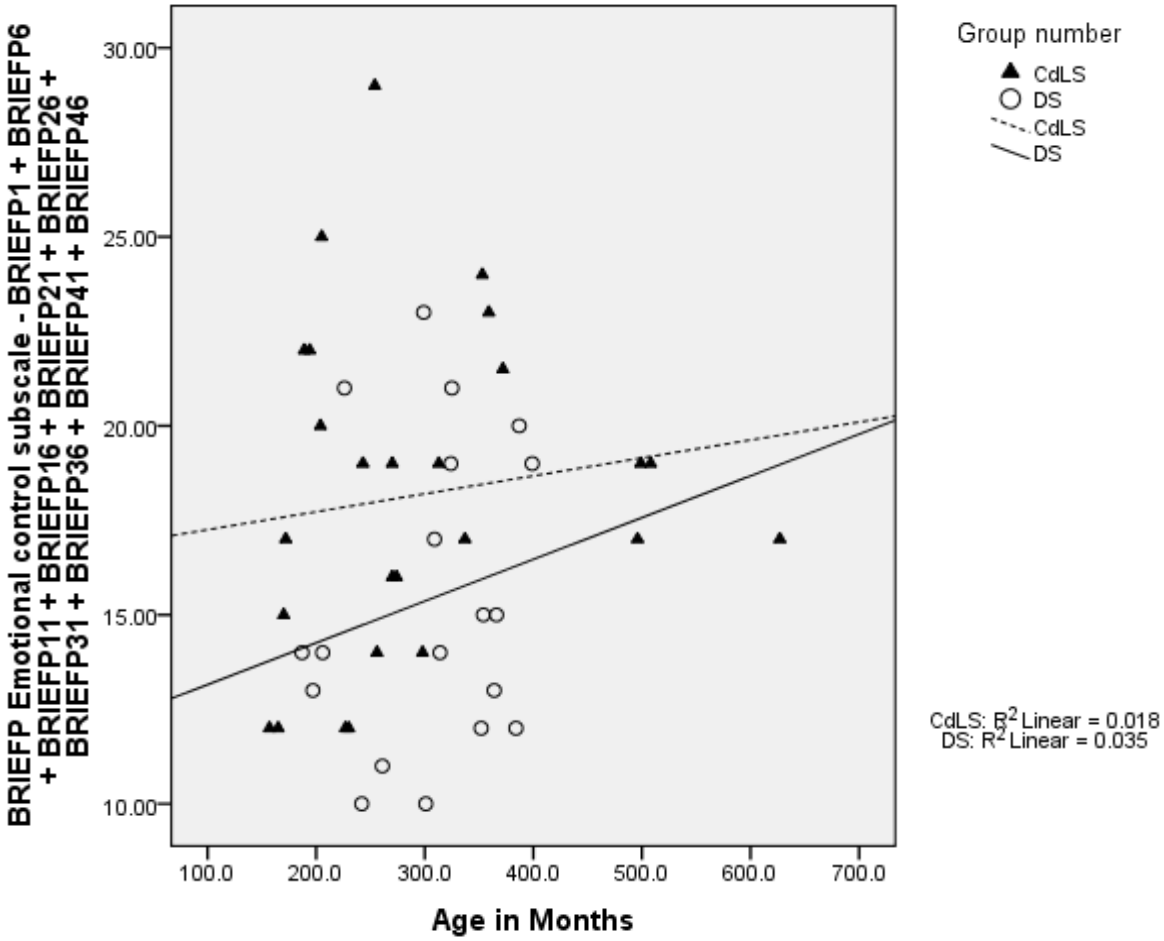
	N	21
Phonemic total score	Pearson Correlation	.734**
	Sig. (2-tailed)	.000
	N	21
DCCS shape (5 to pass)	Pearson Correlation	.263
	Sig. (2-tailed)	.250
	N	21
DCCS border (9-pass)	Pearson Correlation	.446*
	Sig. (2-tailed)	.043
	N	21
Design Fluency Structured Array Correct	Pearson Correlation	.672**
	Sig. (2-tailed)	.001
	N	21
Design Fluency Random Array Correct	Pearson Correlation	.711**
	Sig. (2-tailed)	.000
	N	21

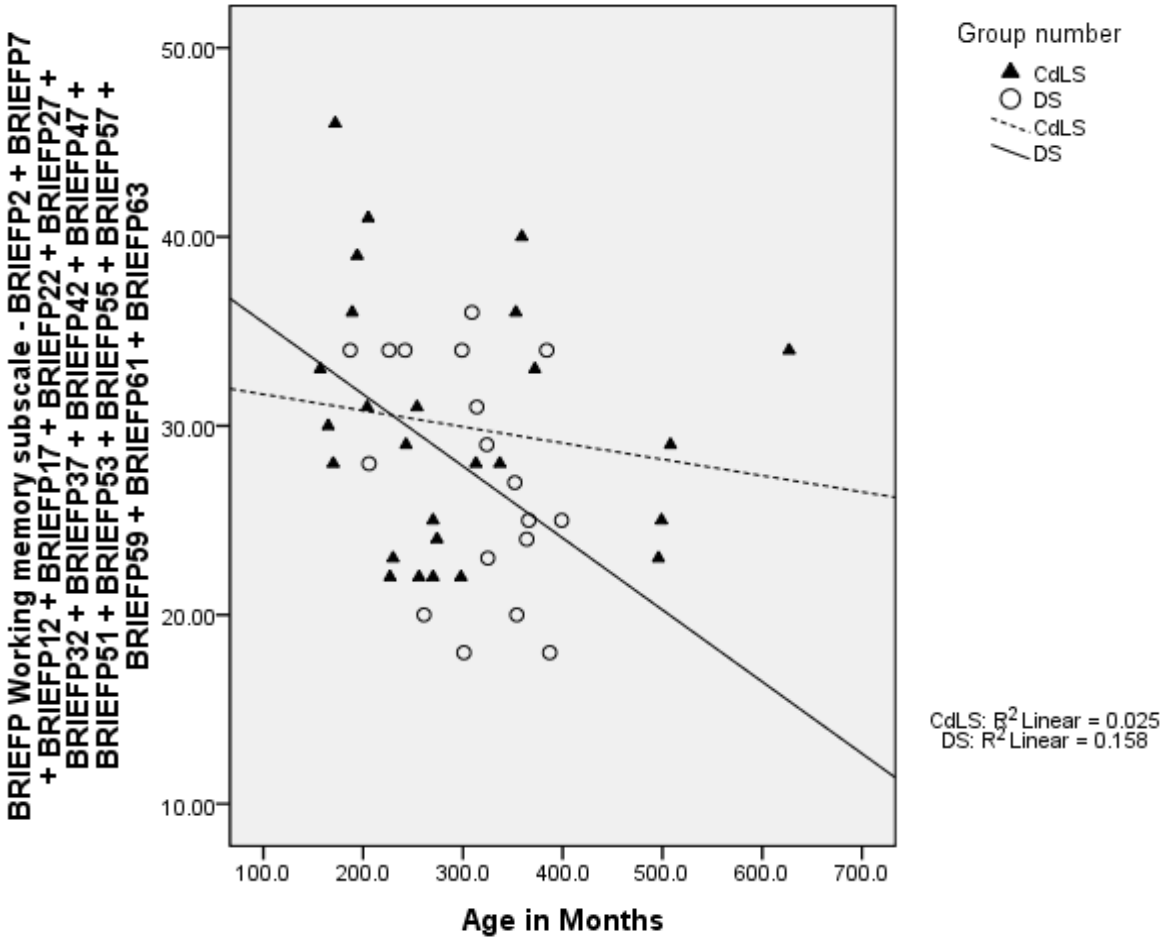
APPENDIX L. Developmental trajectories

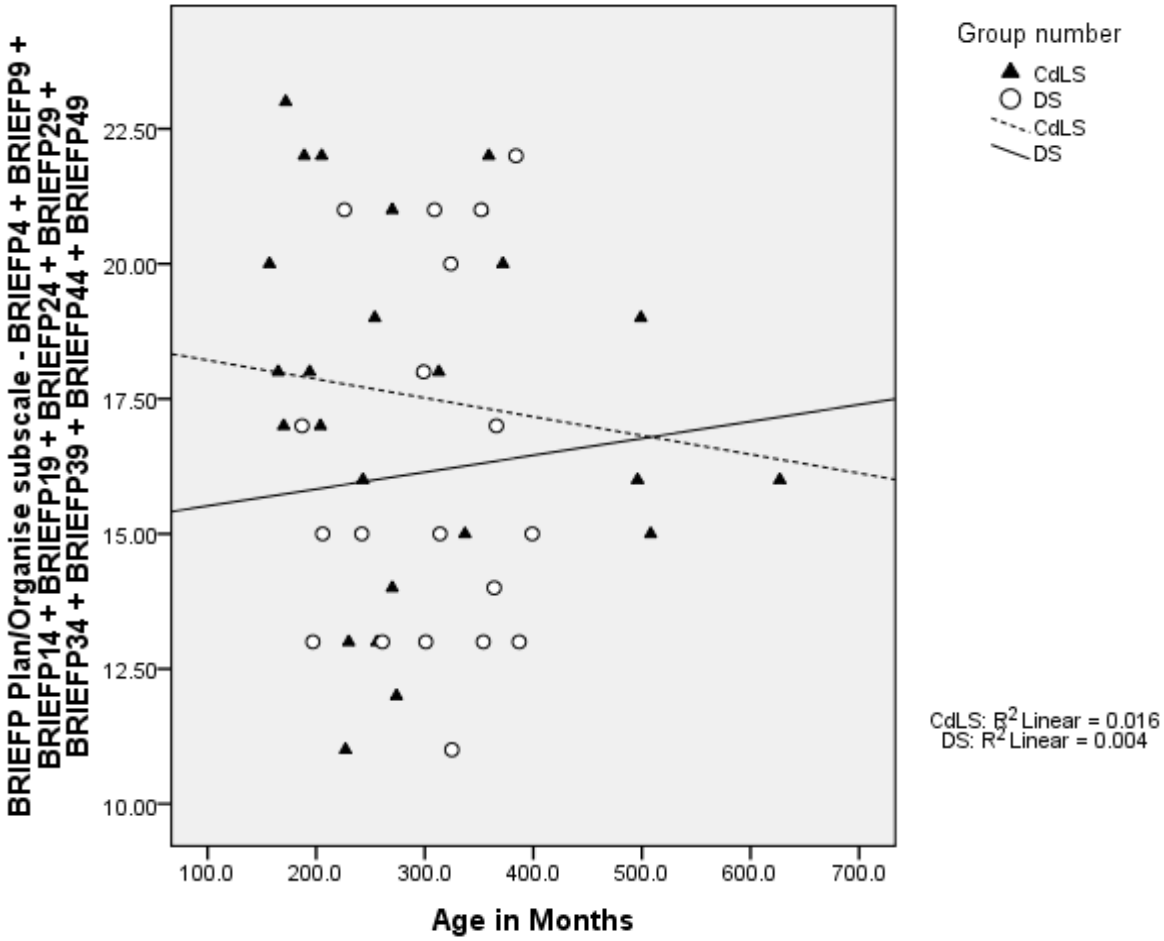


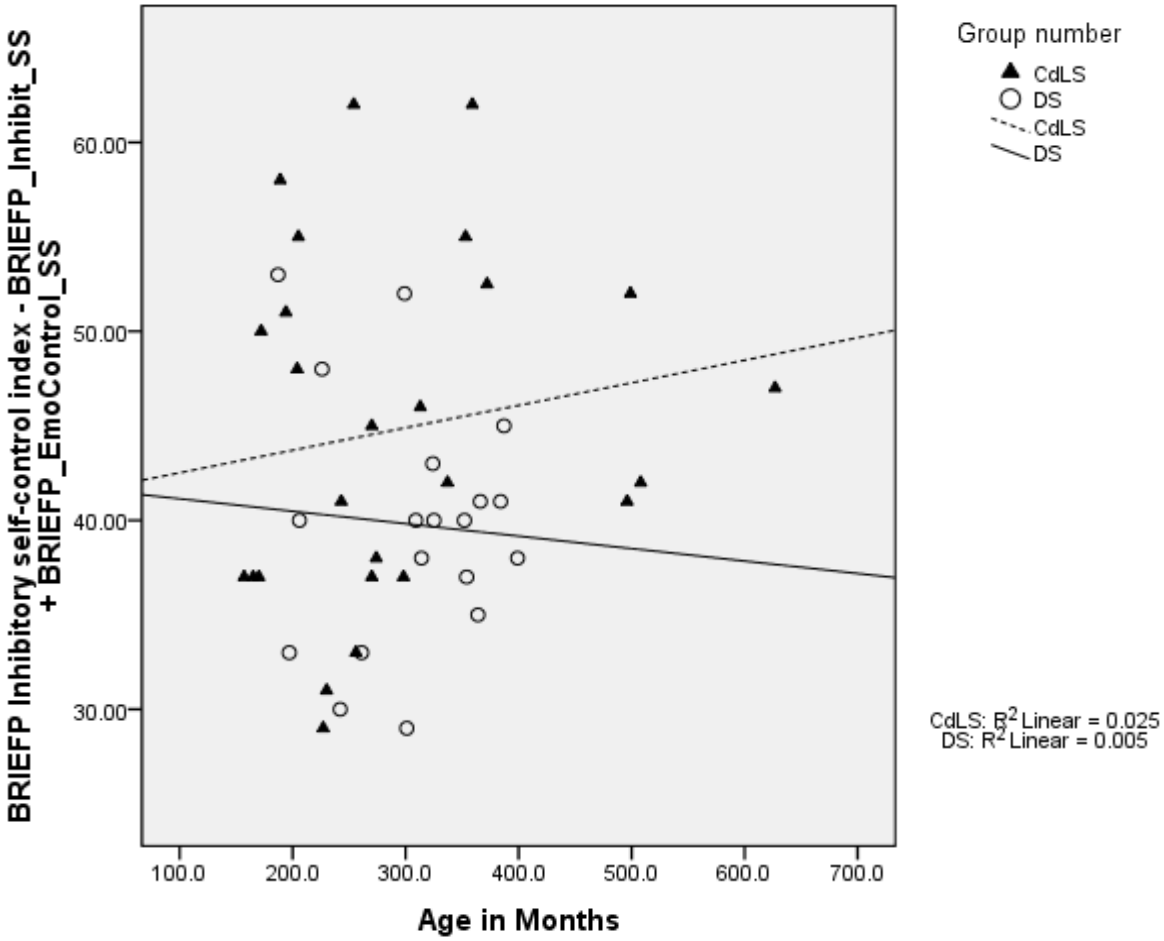

BRIEFP Inhibit subscale - BRIEFP3 + BRIEFP8 + BRIEFP13 + BRIEFP18 + BRIEFP23 + BRIEFP28 + BRIEFP33 + BRIEFP38 + BRIEFP43 + BRIEFP48 + BRIEFP52 + BRIEFP54 + BRIEFP56 + BRIEFP58 + BRIEFP60 + BRIEFP62
40.00
35.00
30.00
25.00
20.00
15.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.025
DS: R2 Linear = 0.06

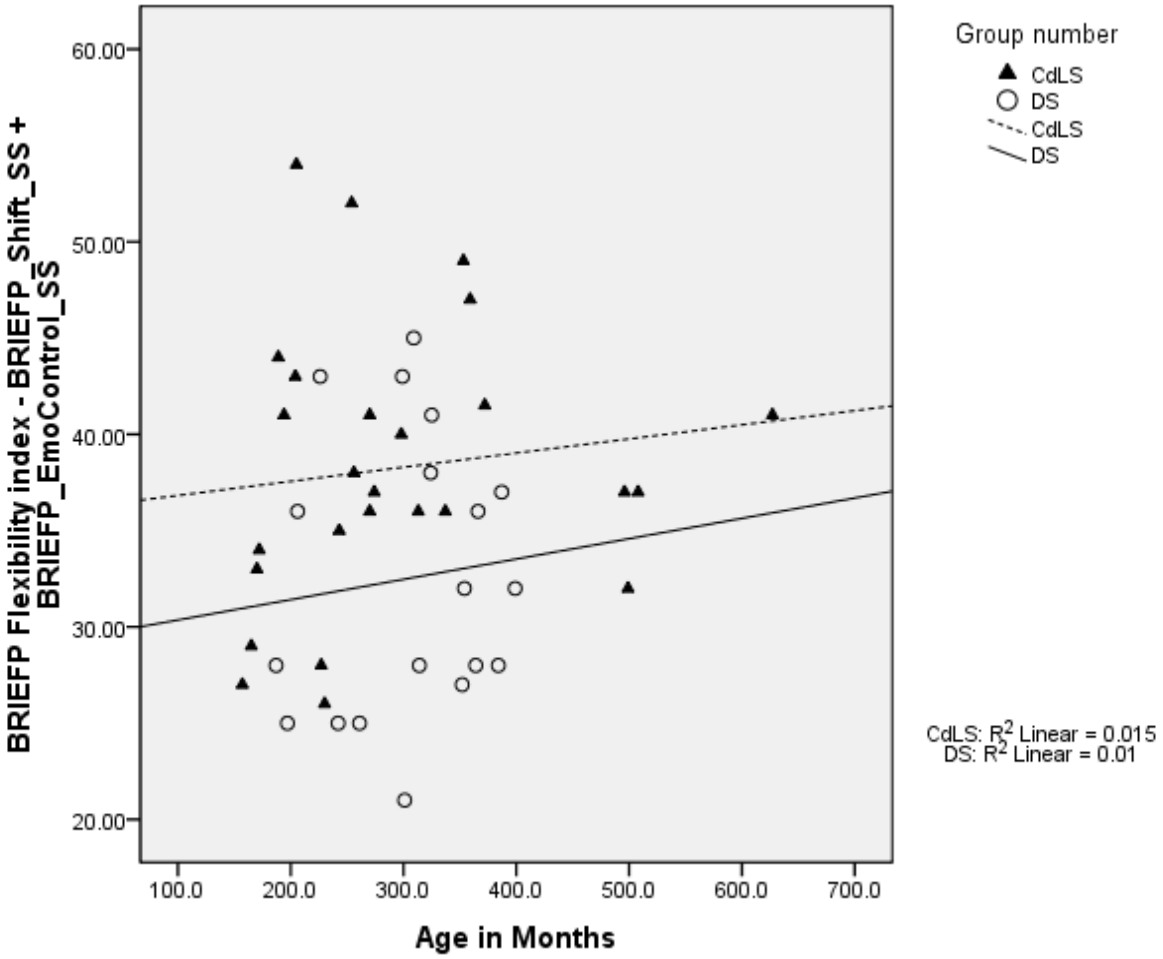

BRIEFP Shift subscale - BRIEFP5 + BRIEFP10 + BRIEFP15 + BRIEFP20 + BRIEFP25 + BRIEFP30 + BRIEFP35 + BRIEFP40 + BRIEFP45 + BRIEFP50
30.00
25.00
20.00
15.00
10.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS; R2 Linear = 0.006
DS: R2 Linear = 6.048E-5

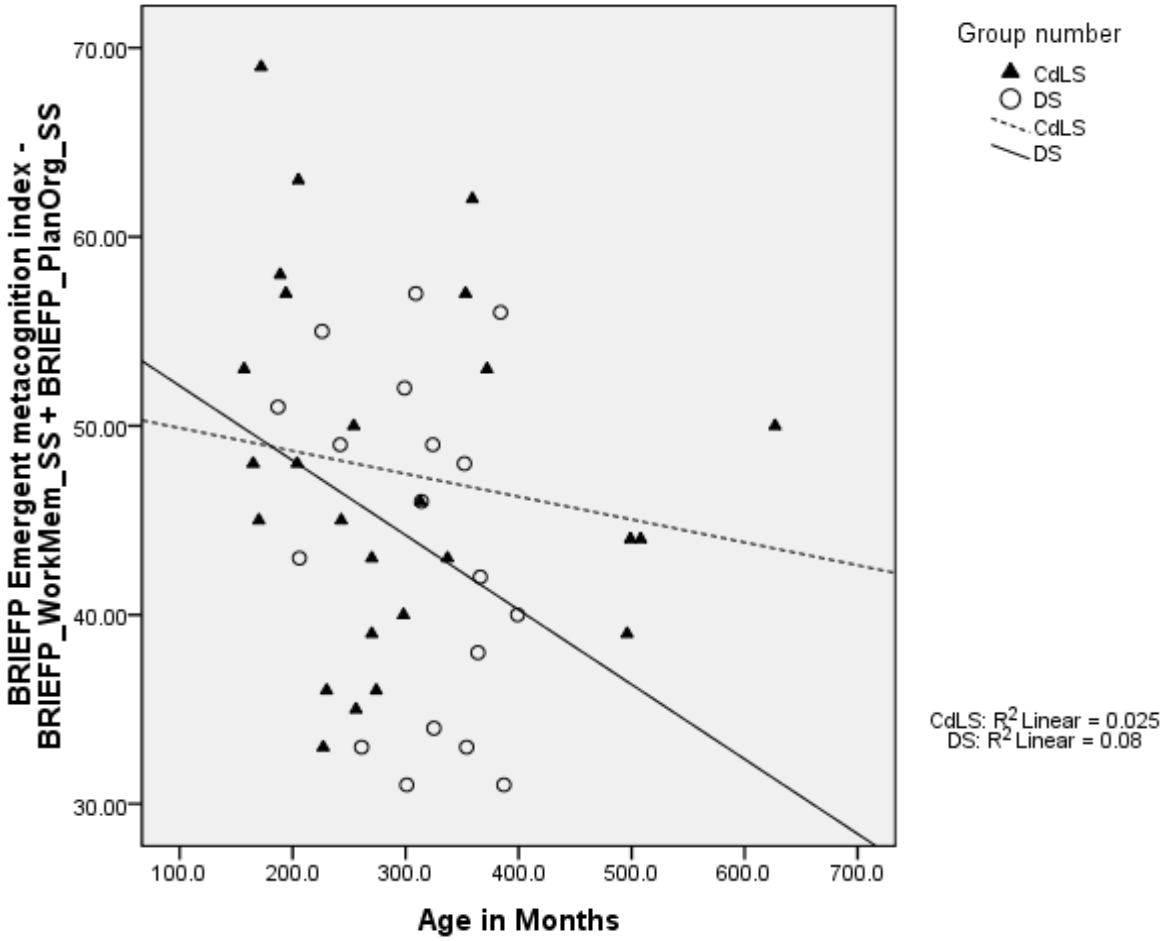

BRIEFP Emotional control subscale - BRIEFP1 + BRIEFP6 + BRIEFP11 + BRIEFP16 + BRIEFP21 + BRIEFP26 + BRIEFP31 + BRIEFP36 + BRIEFP41 + BRIEFP46
30.00
25.00
20.00
15.00
10.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.018
DS: R2 Linear = 0.035

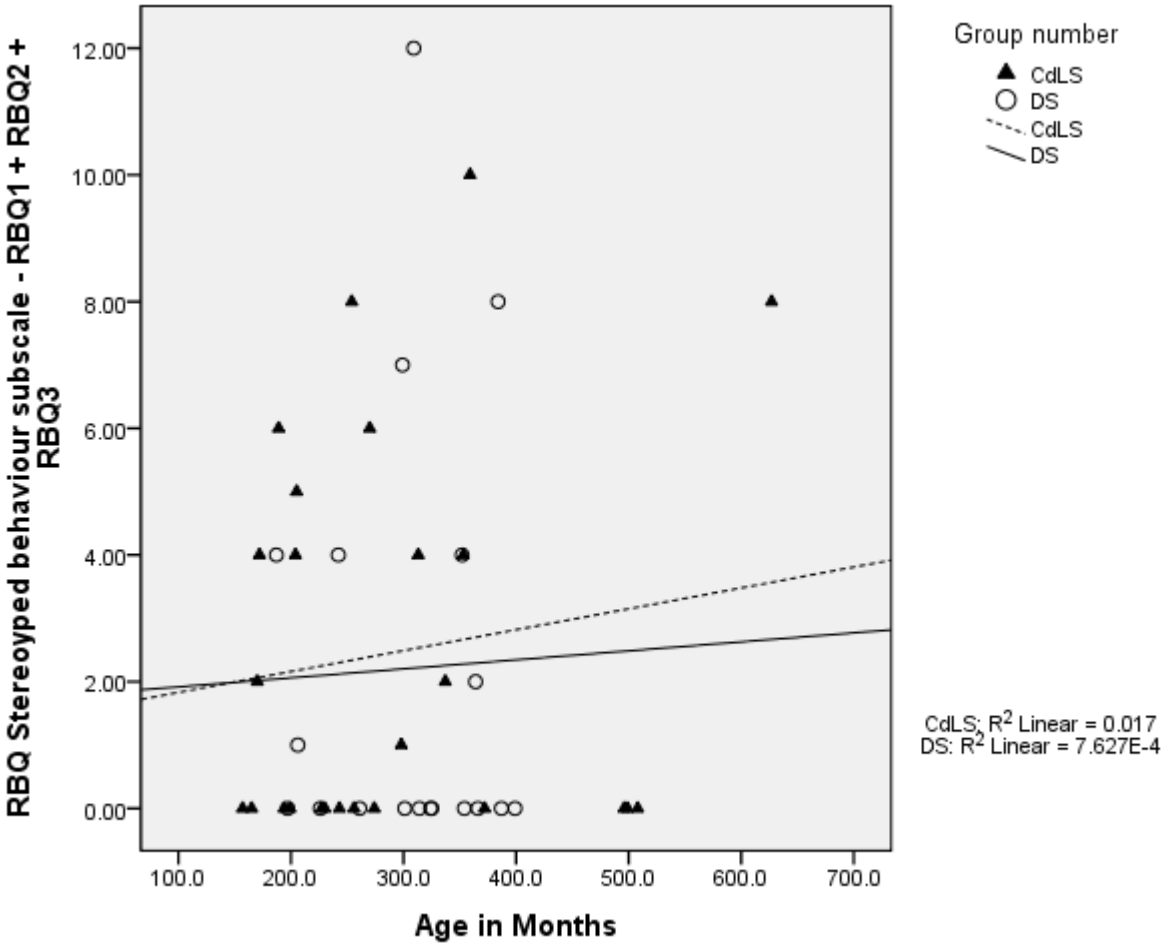

BRIEFP Working memory subscale - BRIEFP2 + BRIEFP7 + BRIEFP12 + BRIEFP17 + BRIEFP22 + BRIEFP27 + BRIEFP32 + BRIEFP37 + BRIEFP42 + BRIEFP47 + BRIEFP51 + BRIEFP53 + BRIEFP55 + BRIEFP57 + BRIEFP59 + BRIEFP61 + BRIEFP63
50.00
40.00
30.00
20.00
10.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.025
DS: R2 Linear = 0.158

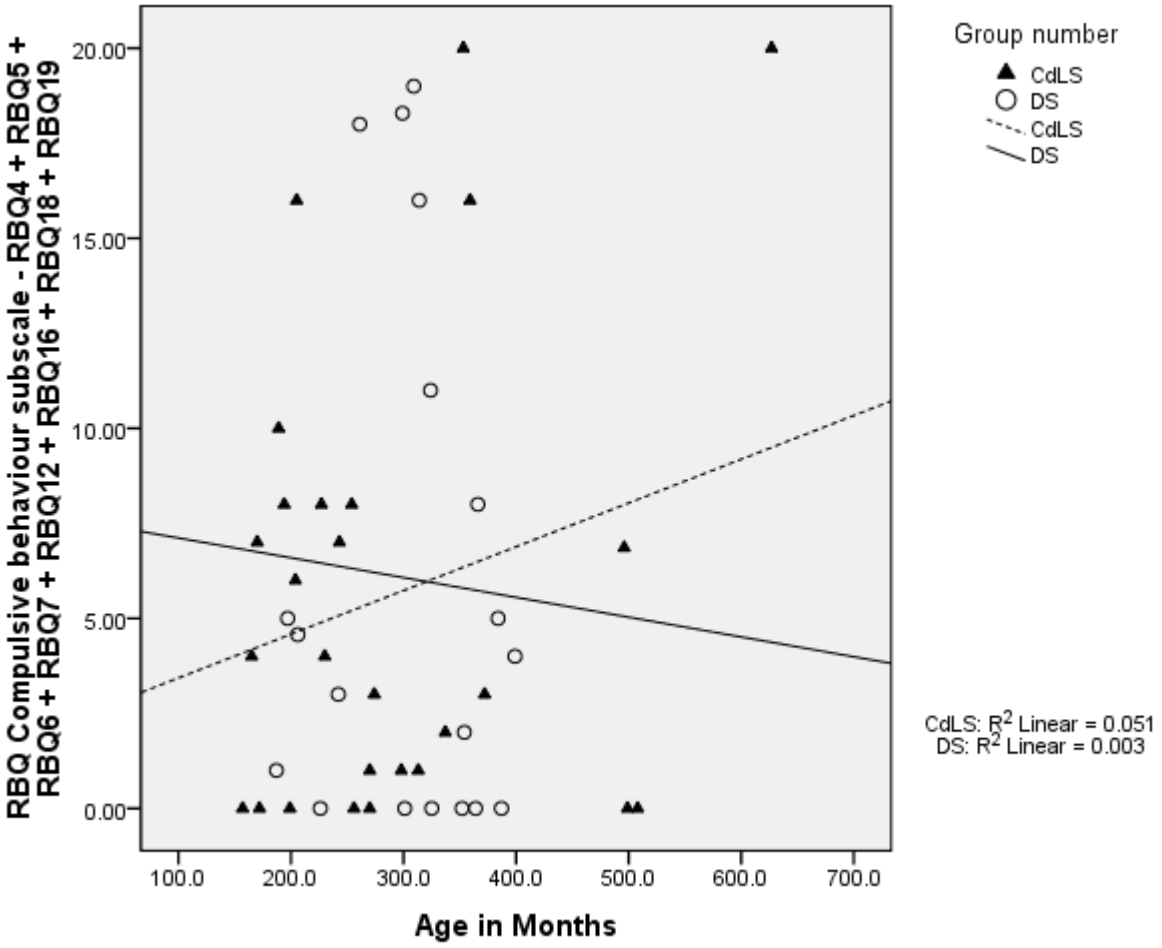

BRIEFP Plan/Organise subscale - BRIEFP4 + BRIEFP9 + BRIEFP14 + BRIEFP19 + BRIEFP24 + BRIEFP29 + BRIEFP34 + BRIEFP39 + BRIEFP44 + BRIEFP49
22.50
20.00
17.50
15.00
12.50
10.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.016
DS: R2 Linear = 0.004

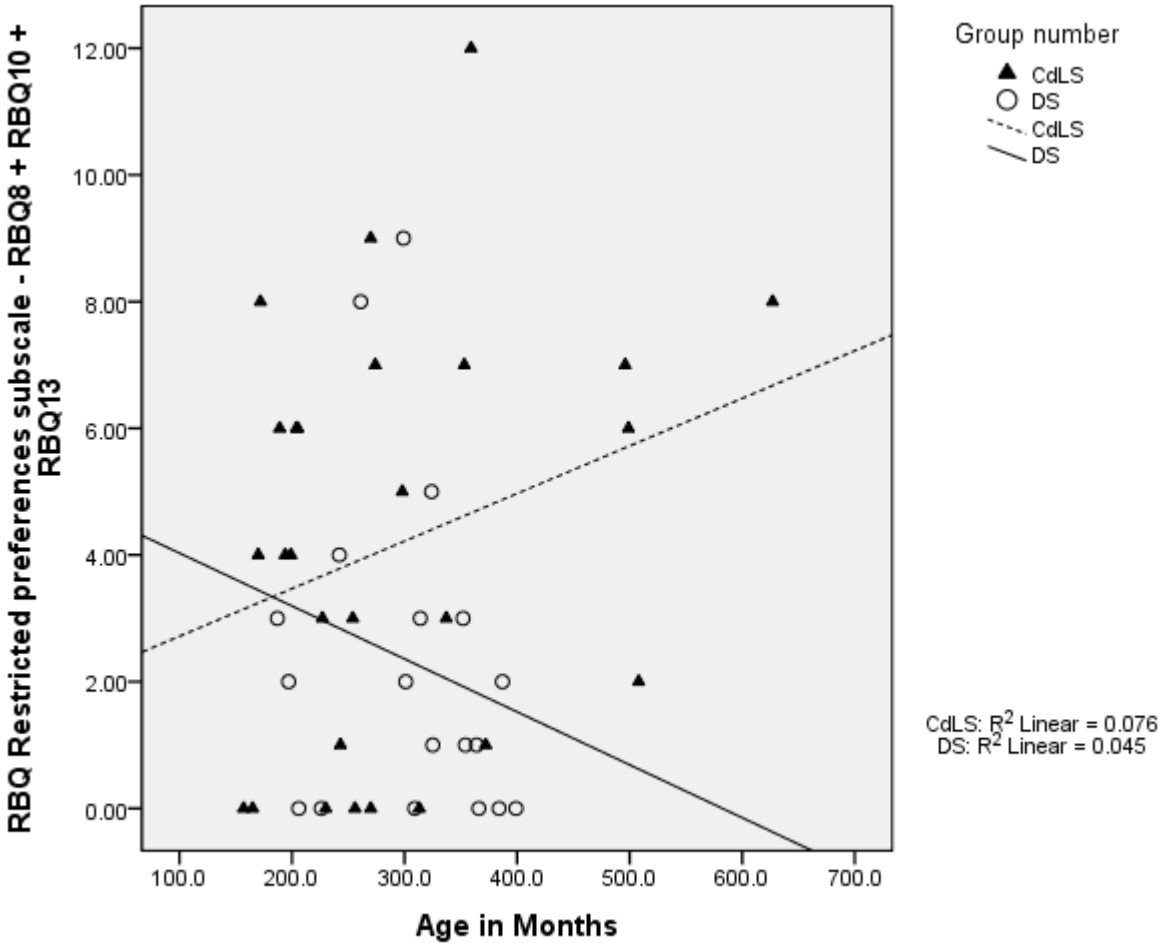

BRIEFP Inhibitory self-control index - BRIEFP_Inhibit_SS + BRIEFP_EmoControl_SS
60.00
50.00
40.00
30.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.025
DS: R2 Linear = 0.005

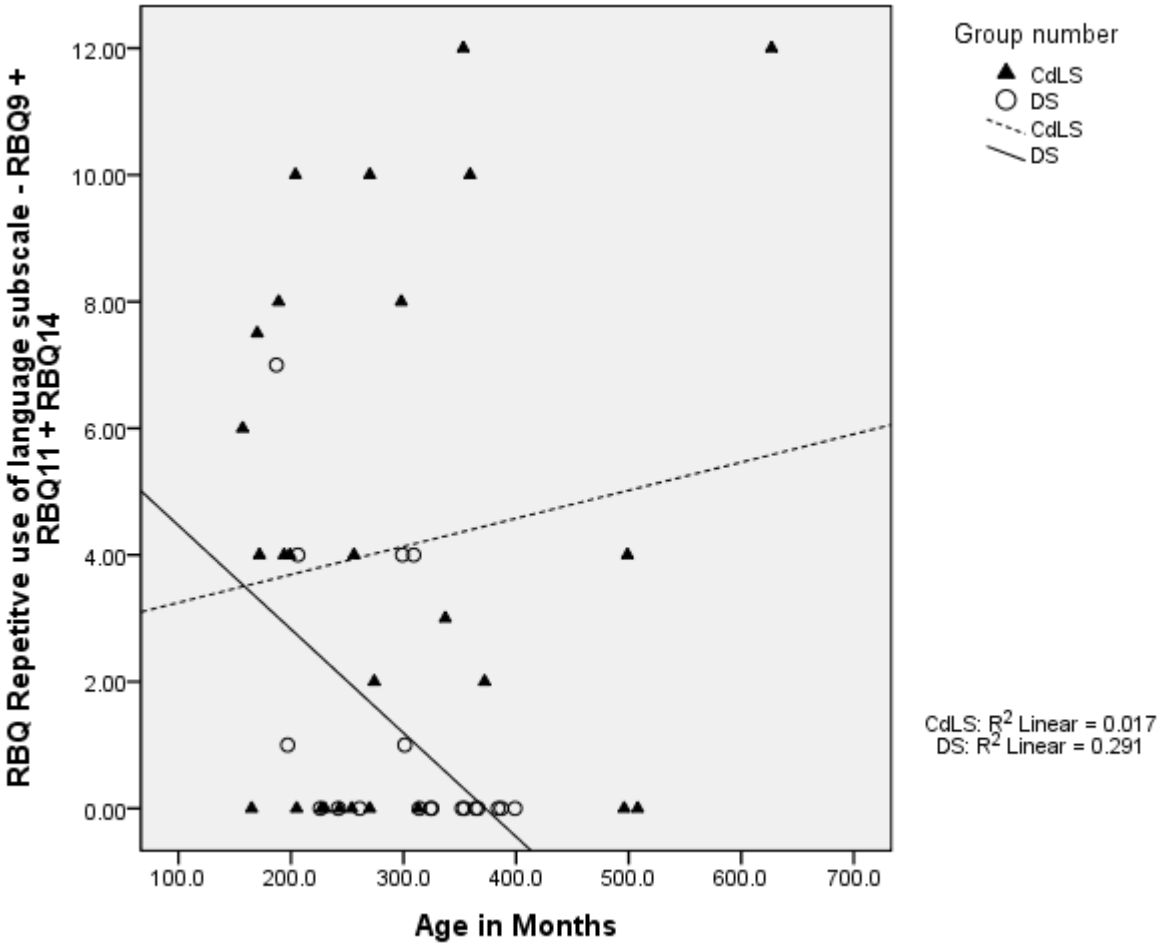

BRIEFP Flexibility index - BRIEFP_Shift_SS + BRIEFP_EmoControl_SS
60.00
50.00
40.00
30.00
20.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.015
DS: R2 Linear = 0.01

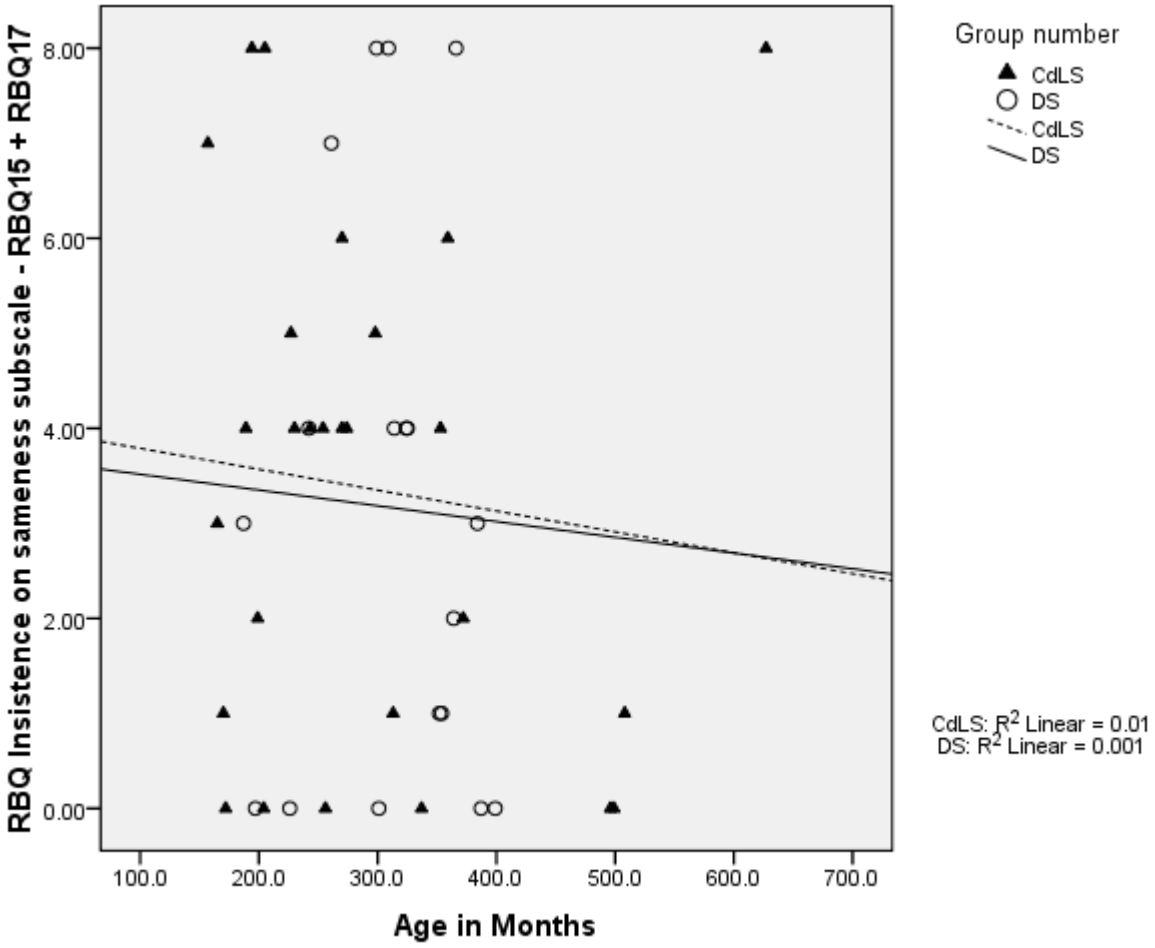

BRIEFP Emergent metacognition index - BRIEFP_WorkMem_SS + BRIEFP_PlanOrg_SS
70.00
60.00
50.00
40.00
30.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R² Linear = 0.025
DS: R² Linear = 0.08

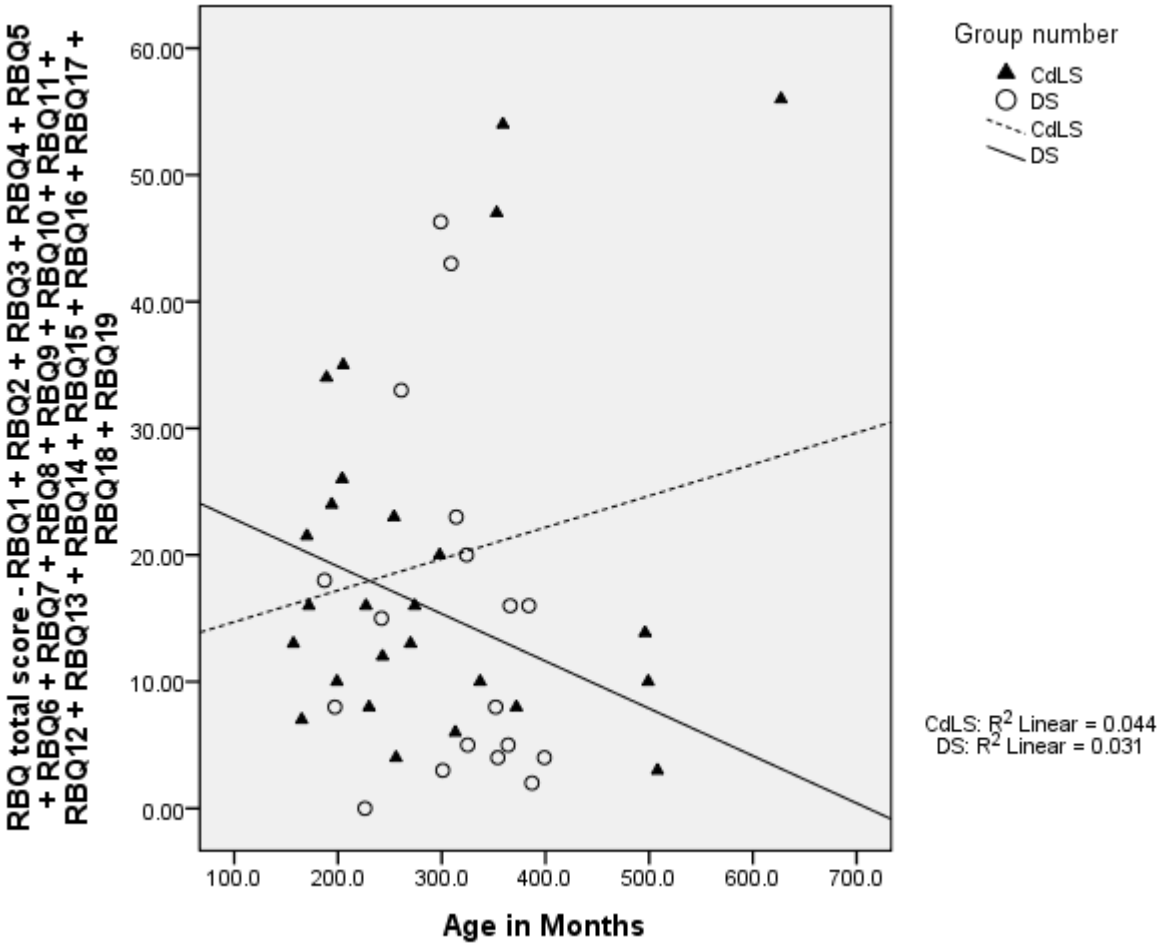

RBQ Stereoyped behaviour subscale - RBQ1 + RBQ2 + RBQ3
12.00
10.00
8.00
6.00
4.00
2.00
0.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS; R2 Linear = 0.017
DS: R2 Linear = 7.627E-4

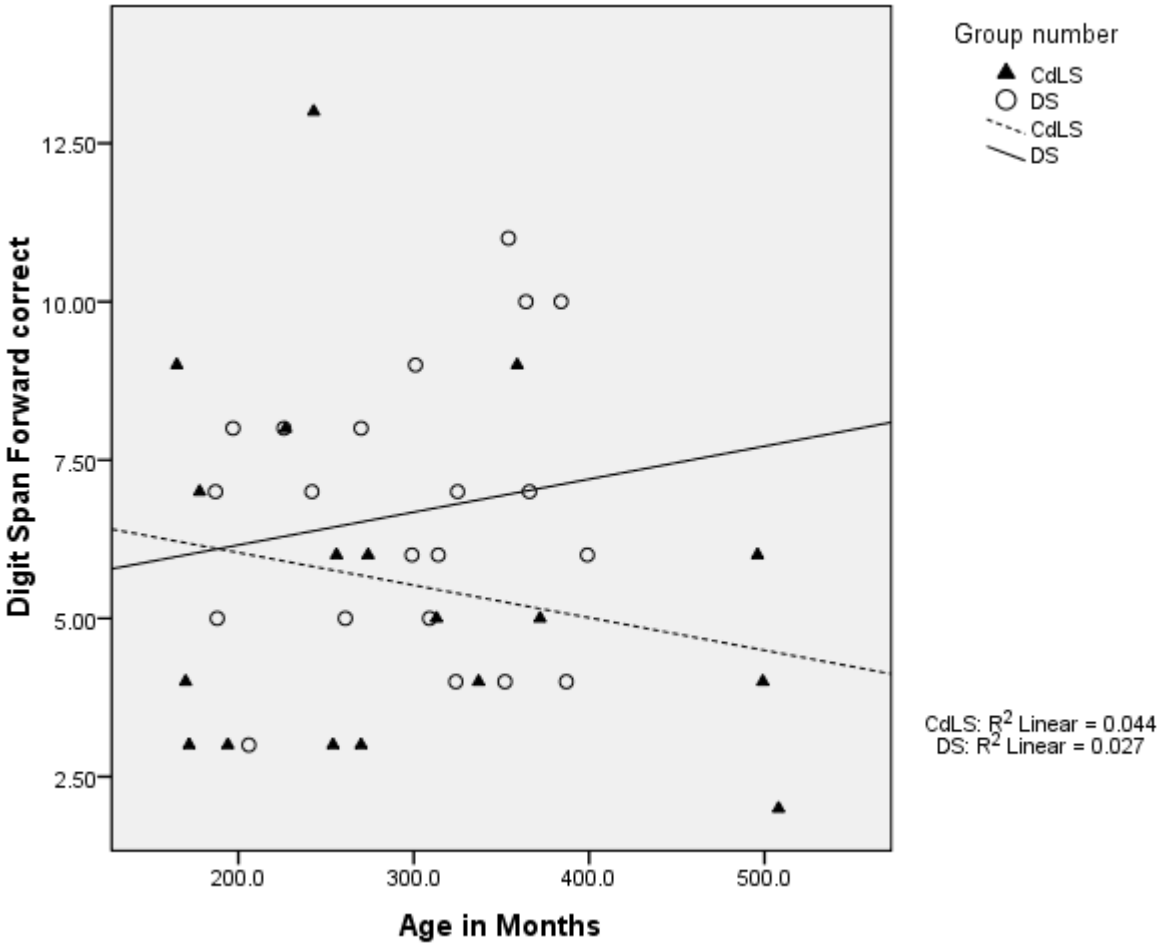

RBQ Compulsive behaviour subscale - RBQ4 + RBQ5 + RBQ6 + RBQ7 + RBQ12 + RBQ16 + RBQ18 + RBQ19
20.00
15.00
10.00
5.00
0.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.051
DS: R2 Linear = 0.003

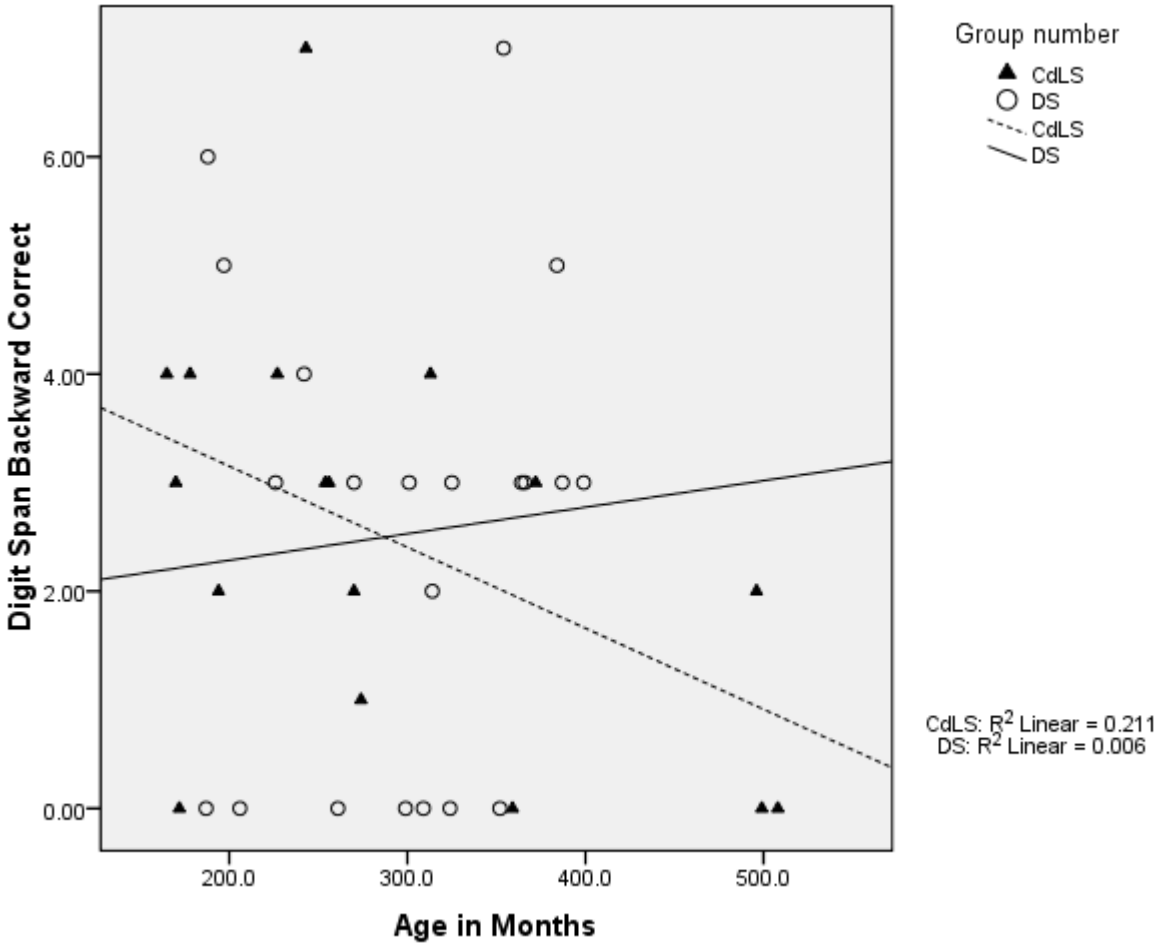

RBQ Restricted preferences subscale - RBQ8 + RBQ10 + RBQ13
12.00
10.00
8.00
6.00
4.00
2.00
0.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.076
DS: R2 Linear = 0.045

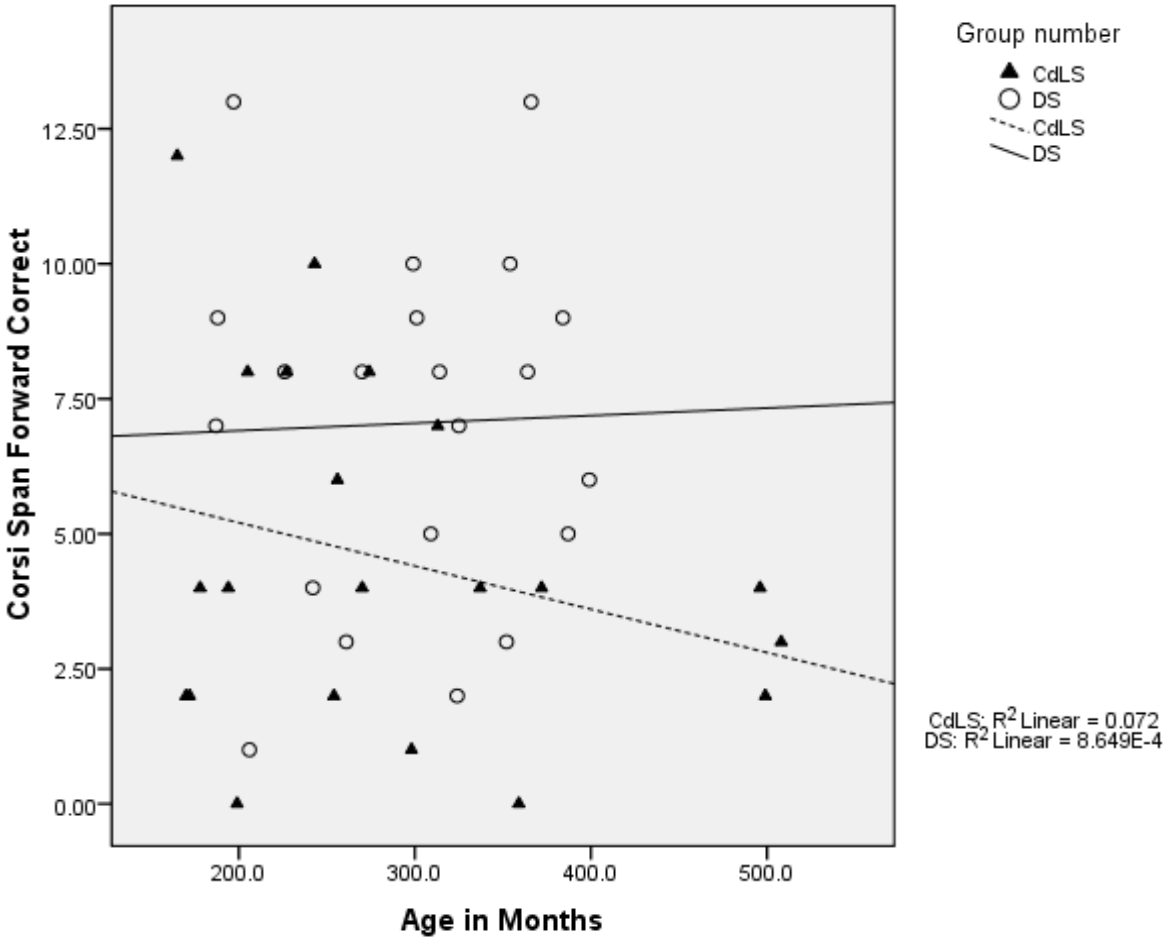

RBQ Repetitve use of language subscale - RBQ9 + RBQ11 + RBQ14
12.00
10.00
8.00
6.00
4.00
2.00
0.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.017
DS: R2 Linear = 0.291

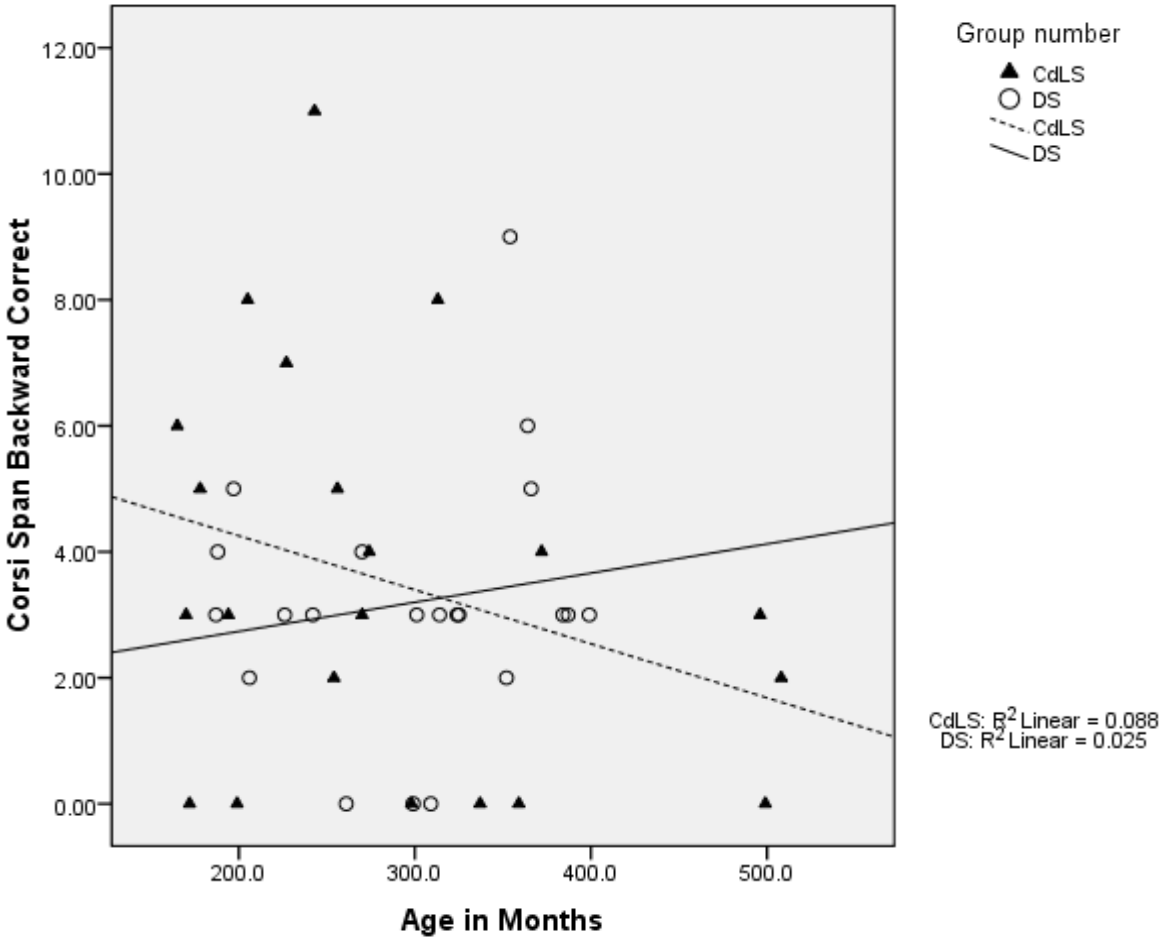

RBQ Insistence on sameness subscale - RBQ15 + RBQ17
8.00
6.00
4.00
2.00
0.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.01
DS: R2 Linear = 0.001

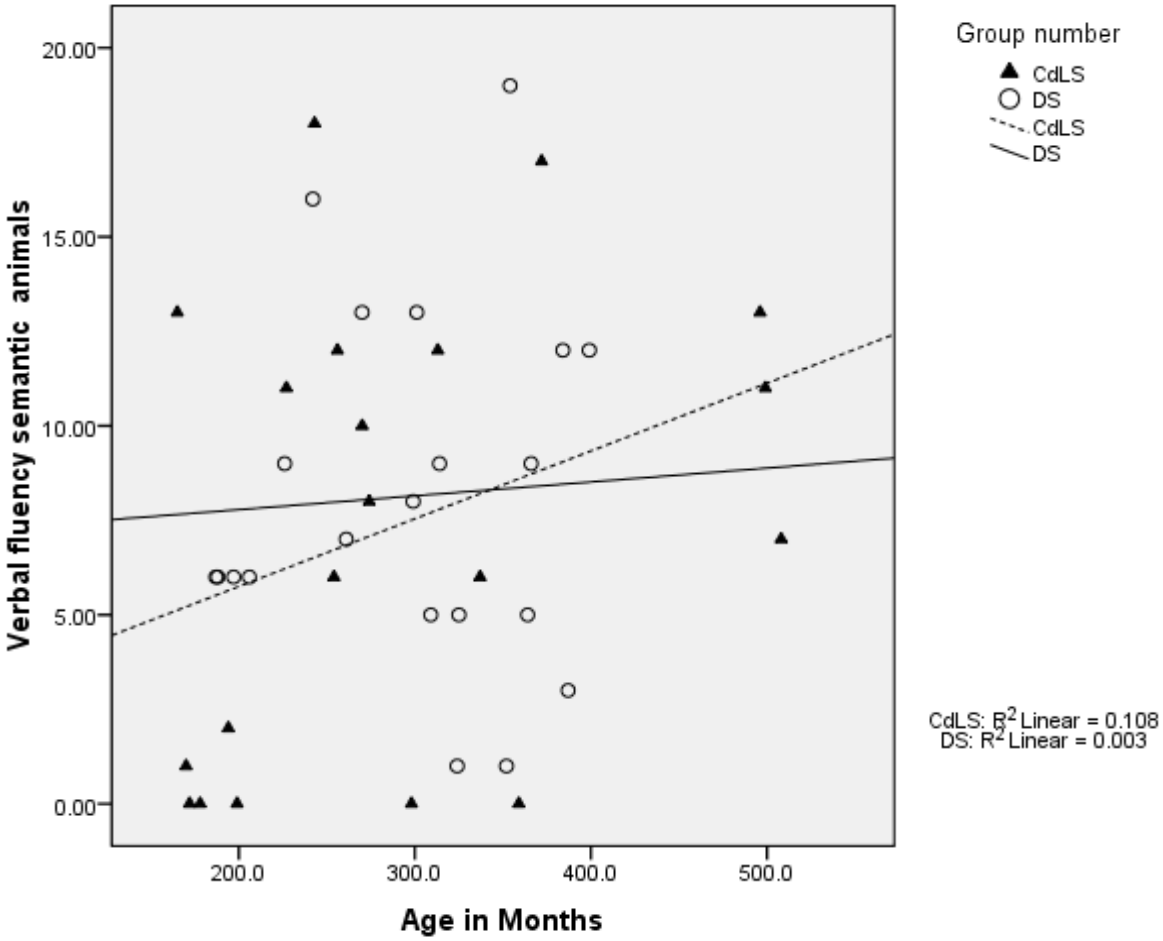

RBQ total score - RBQ1 + RBQ2 + RBQ3 + RBQ4 + RBQ5 + RBQ6 + RBQ7 + RBQ8 + RBQ9 + RBQ10 + RBQ11 + RBQ12 + RBQ13 + RBQ14 + RBQ15 + RBQ16 + RBQ17 + RBQ18 + RBQ19
60.00
50.00
40.00
30.00
20.00
10.00
0.00
100.0
200.0
300.0
400.0
500.0
600.0
700.0
Age in Months
Group number
CdLS
DS
CdLS
DS
CdLS: R2 Linear = 0.044
DS: R2 Linear = 0.031

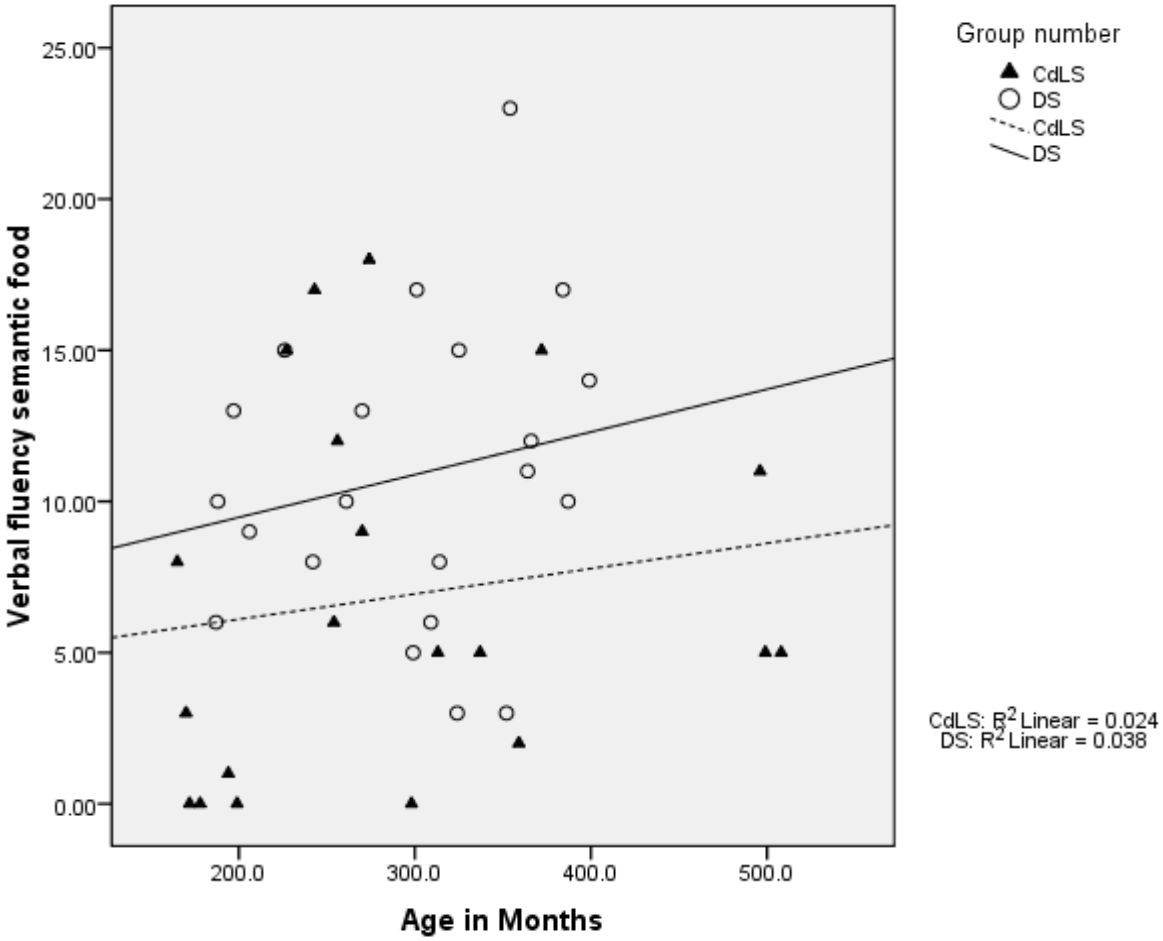

Group number
CdLS
DS
CdLS
DS
Digit Span Forward correct
12.50
10.00
7.50
5.00
2.50
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.044
DS: R2 Linear = 0.027

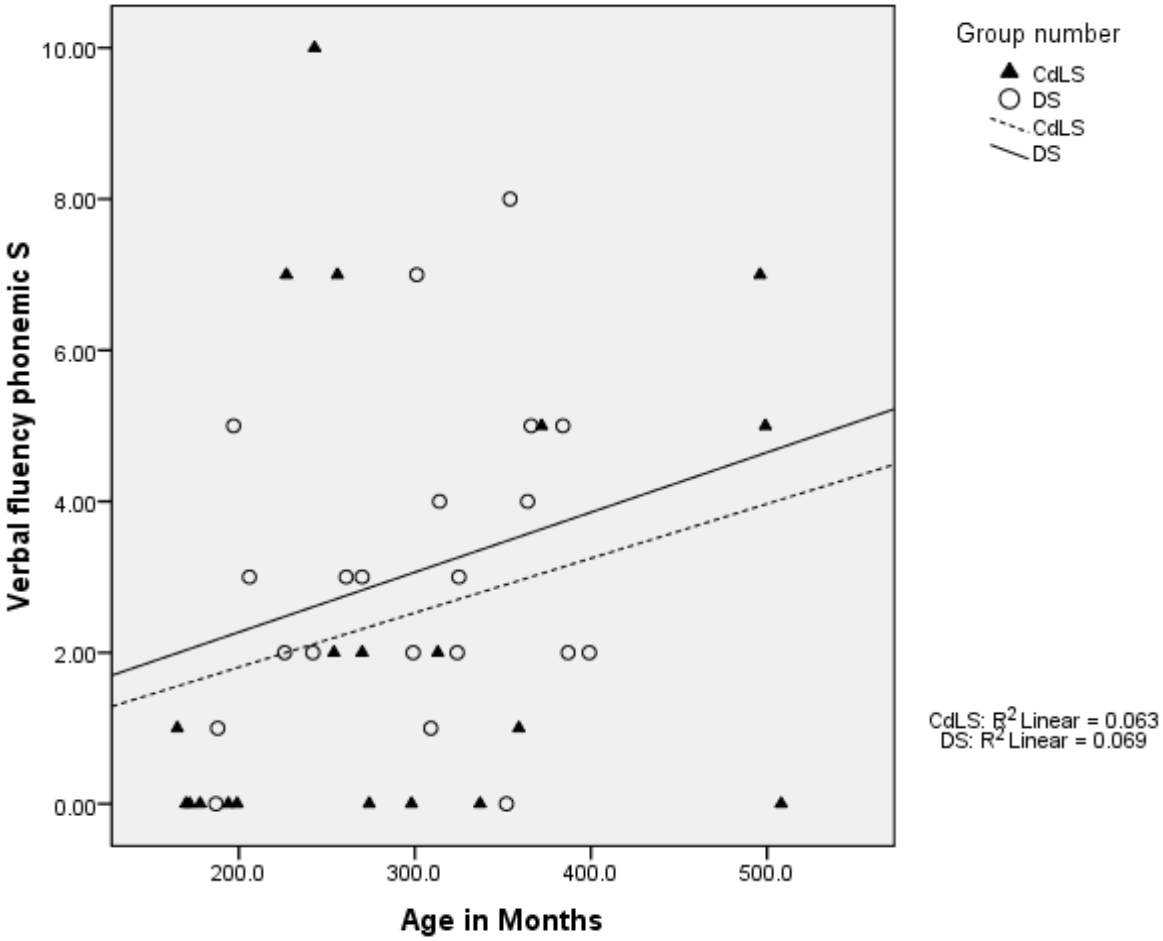

Group number
CdLS
DS
CdLS
DS
Digit Span Backward Correct
6.00
4.00
2.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.211
DS: R2 Linear = 0.006

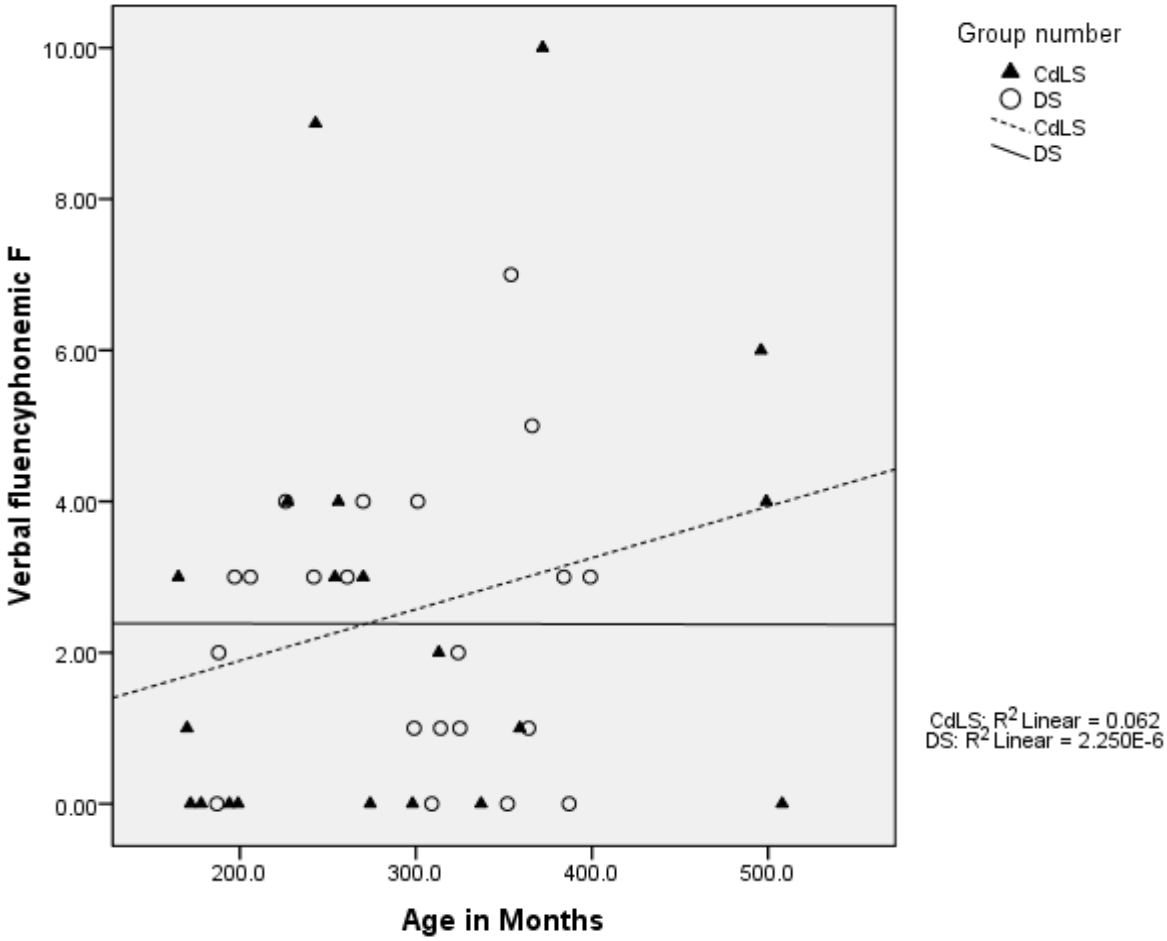

Group number
CdLS
DS
CdLS
DS
Corsi Span Forward Correct
12.50
10.00
7.50
5.00
2.50
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.072
DS: R2 Linear = 8.649E-4

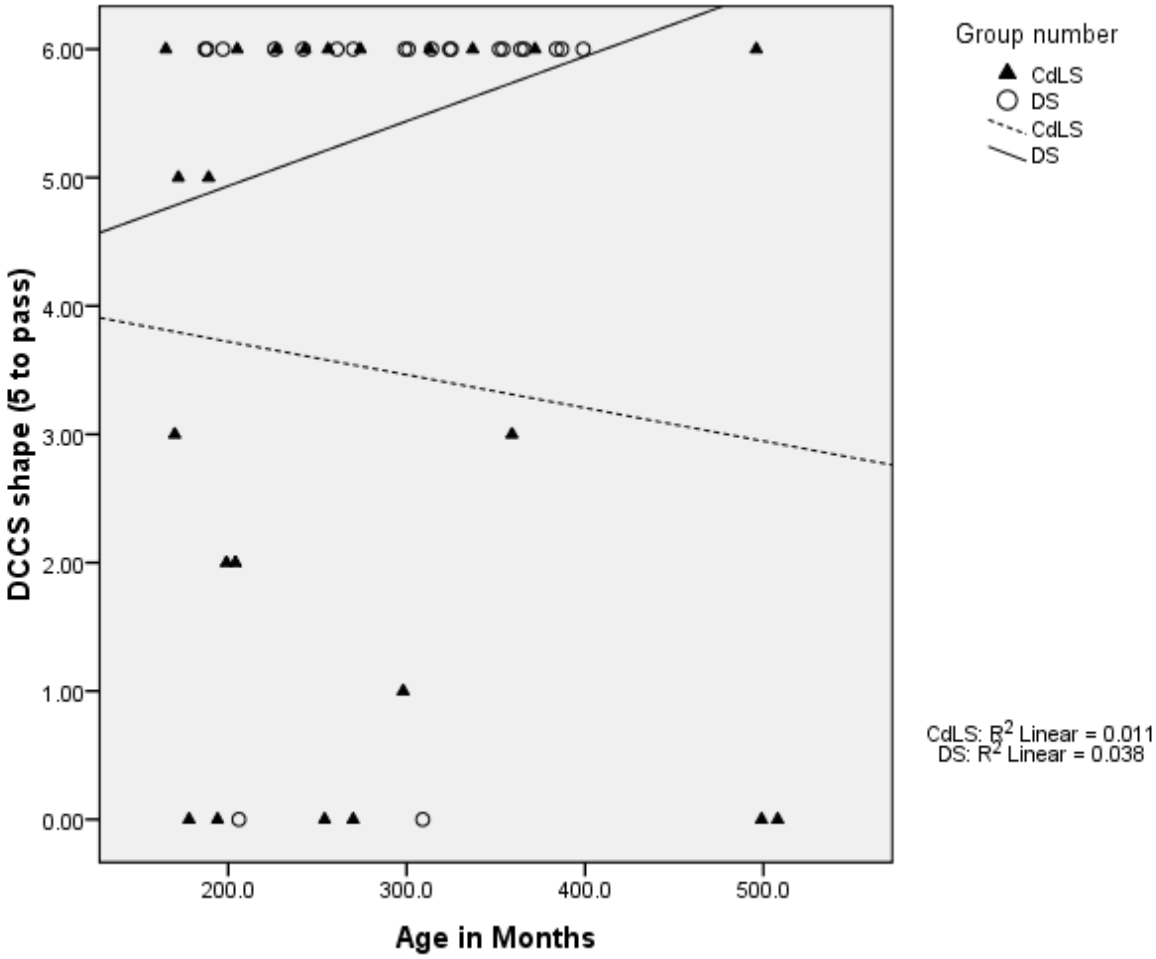

Group number
CdLS
DS
CdLS
DS
Corsi Span Backward Correct
12.00
10.00
8.00
6.00
4.00
2.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.088
DS: R2 Linear = 0.025

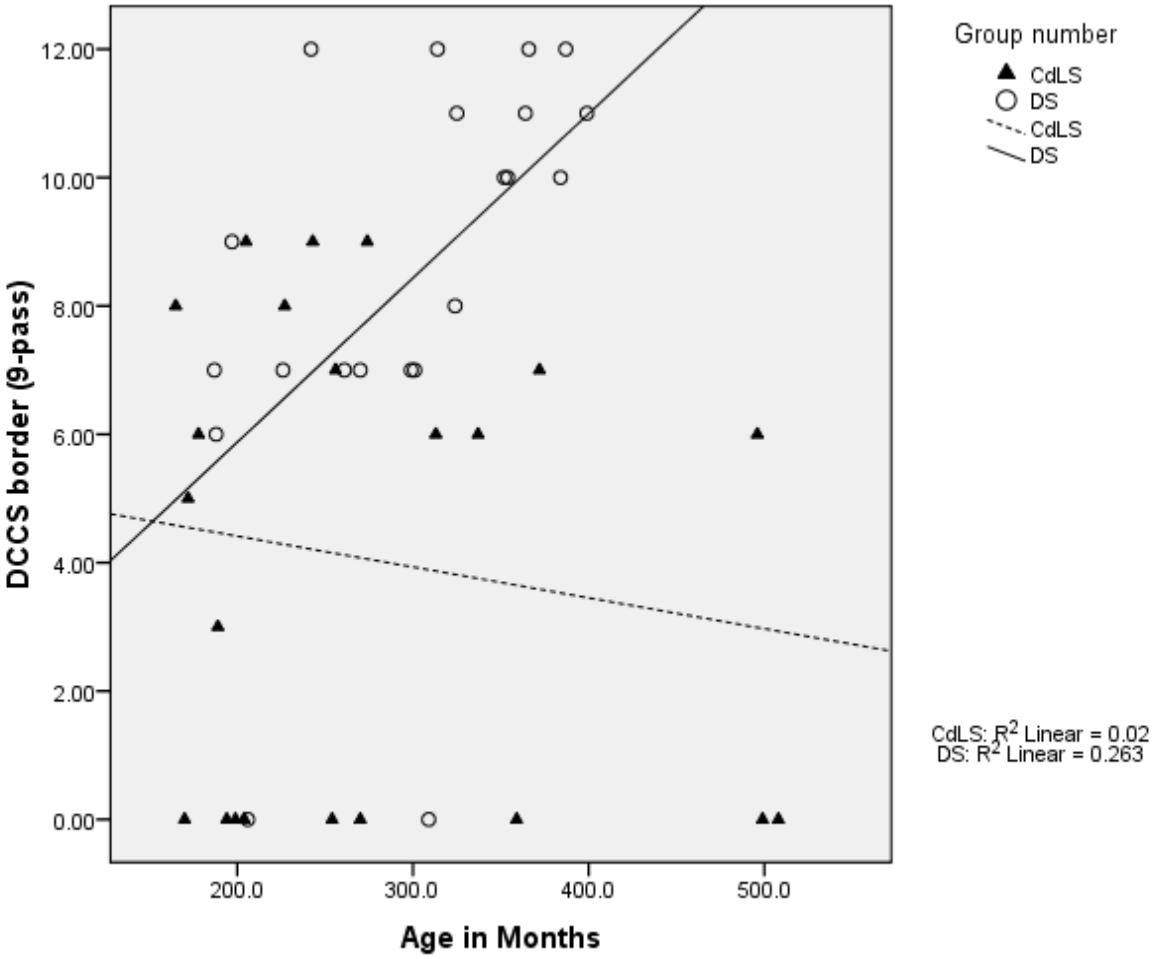

Group number
CdLS
DS
CdLS
DS
Verbal fluency semantic animals
20.00
15.00
10.00
5.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.108
DS: R2 Linear = 0.003


Group number
CdLS
DS
CdLS
DS
Verbal fluency semantic food
25.00
20.00
15.00
10.00
5.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.024
DS: R2 Linear = 0.038


Group number
CdLS
DS
CdLS
DS
Verbal fluency phonemic S
10.00
8.00
6.00
4.00
2.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.063
DS: R2 Linear = 0.069


Group number
CdLS
DS
CdLS
DS
Verbal fluencyphonemic F
10.00
8.00
6.00
4.00
2.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.062
DS: R2 Linear = 2.250E-6


Group number
CdLS
DS
CdLS
DS
DCCS shape (5 to pass)
6.00
5.00
4.00
3.00
2.00
1.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.011
DS: R2 Linear = 0.038


Group number
CdLS
DS
CdLS
DS
DCCS border (9-pass)
12.00
10.00
8.00
6.00
4.00
2.00
0.00
200.0
300.0
400.0
500.0
Age in Months
CdLS: R2 Linear = 0.02
DS: R2 Linear = 0.263

APPENDIX M. Correlations between RBQ subscales and tests of executive functioning.

		Stereotyped behaviour	Compulsive behaviour	Insistence on sameness subscale
Digit Span Forward max	Correlation	-.148	.006	-.006
	Significance (2-tailed)	.426	.974	.973
	Df	29	29	29
Digit Span Backward max	Correlation	-.454	-.315	-.271
	Significance (2-tailed)	.010	.084	.140
	Df	29	29	29
Corsi Span Forward max	Correlation	-.402	-.362	.142
	Significance (2-tailed)	.025	.046	.446
	Df	29	29	29
Corsi Span Backward max	Correlation	-.508	-.300	-.326
	Significance (2-tailed)	.004	.101	.073
	Df	29	29	29
Semantic total score	Correlation	-.327	-.309	-.130
	Significance (2-tailed)	.072	.091	.487
	Df	29	29	29
Phonemic total score	Correlation	-.072	-.076	-.076
	Significance (2-tailed)	.701	.683	.686

	Df	29	29	29
DCCS shape (5 to pass)	Correlation	.003	-.305	-.217
	Significance (2-tailed)	.989	.096	.242
	df	29	29	29
DCCS border (9-pass)	Correlation	-.228	-.536	-.079
	Significance (2-tailed)	.217	.002	.671
	df	29	29	29
Design Fluency Structured Array Correct	Correlation	-.304	-.286	-.168
	Significance (2-tailed)	.096	.119	.366
	df	29	29	29
Design Fluency Random Array Correct	Correlation	-.344	-.130	-.170
	Significance (2-tailed)	.058	.486	.362
	df	29	29	29

Control Variables			Restricted preferences subscale	Repetitive use of language subscale
	Digit Span Forward max	Correlation	-.148	.006
		Significance (2-tailed)	.426	.974
		df	29	29
	Digit Span Backward max	Correlation	-.454	-.315
		Significance (2-tailed)	.010	.084
		df	29	29

	Corsi Span Forward max	Correlation	-.402	-.362
		Significance (2-tailed)	.025	.046
		df	29	29
	Corsi Span Backward max	Correlation	-.508	-.300
		Significance (2-tailed)	.004	.101
		df	29	29
	Semantic total score	Correlation	-.327	-.309
		Significance (2-tailed)	.072	.091
		df	29	29
	Phonemic total score	Correlation	-.072	-.076
		Significance (2-tailed)	.701	.683
		df	29	29
	DCCS shape (5 to pass)	Correlation	.003	-.305
		Significance (2-tailed)	.989	.096
		df	29	29
	DCCS border (9-pass)	Correlation	-.228	-.536
		Significance (2-tailed)	.217	.002
		df	29	29
	Design Fluency Structured Array Correct	Correlation	-.304	-.286
		Significance (2-tailed)	.096	.119
		df	29	29
	Design Fluency Random Array Correct	Correlation	-.344	-.130

	Significance (2-tailed)	.058	.486

3. Public Domain Briefing Paper

Executive Functioning in Neurodevelopmental Disorders

Dr. Donna Jane Reid, University of Birmingham, UK.

Summary

This research was conducted by Donna Reid from the Department of Clinical Psychology at the University of Birmingham, UK, as partial fulfilment of the Doctor of Clinical Psychology training programme. The research was supervised by Professor Chris Oliver, head of the Cerebra Centre of Neurodevelopmental Disorders at the University of Birmingham. Ethical approval was obtained from the University of Birmingham Ethics Committee.

The research consists of a literature review and an empirical paper. The literature review examines research that has been conducted into executive functioning in neurodevelopmental disorders. It focuses on the genetic disorders of Fragile X, Prader Willi and Williams syndrome, concluding with a summary of the research carried out, and directions for future work. The empirical paper focuses on the exploration of executive functioning in Cornelia de Lange syndrome. An overview of the empirical paper is presented below.

Background

Cornelia de Lange Syndrome (CdLS) is a genetic disorder caused by mutations to Chromosomes 5, 10 or X. In addition to mild to profound intellectual disability and the distinctive physical phenotype, emerging evidence has suggested that there are a number of age-related changes in behaviour occurring during adolescence and early adulthood (Collis, Oliver & Moss, 2006), including an increase in preference for routine, difficulty coping with

change, obsessive-compulsive behaviours, and selective mutism. Research into executive functioning and behaviour in other neurodevelopmental disorders (e.g. Woodcock, Oliver & Humphreys, 2009), suggests that behaviours that are phenotypic of a syndrome are underpinned by specific executive functioning impairments. Given this evidence, it seems likely that the emotional and behavioural difficulties reported in adolescents and adults with CdLS are underpinned by specific executive functioning impairments.

Aims

This study aims to examine the main areas of executive functioning in adolescents and adults with CdLS and identify whether there is a profile of executive functioning specific to these individuals.

Participants

Twenty-four participants with Cornelia de Lange Syndrome (14 females and 10 males) aged 13-42 years (M = 22), and a comparable contrast group of 21 individuals with Down syndrome (13 females and eight males) aged 15-33 years (M = 24), participated in the study.

Method

Each participant was visited at their home and asked to complete a number of executive functioning tasks in order to assess their executive functioning abilities. Two parent/carer rated questionnaire measures and seven participant completed tasks were used. Tests of executive functioning included the Digit Span and Corsi Span tasks (for verbal and

visuospatial working memory), Verbal and Design Fluency tests and a measure of flexibility and inhibition (the dimensional card change sorting task, DCCS; Frye *et al.*, 1995). To get a general overview, a well used parent/carer rated questionnaires of executive functioning was used- the BRIEF-P (Gioia, Isquith, Guy & Kenworthy, 2000).

Summary of Findings

The group of participants with CdLS showed significantly more impairment on tasks requiring generativity (verbal fluency), flexibility and inhibition (DCCS) compared to the group with DS, despite there being no significant differences in working memory. These impairments were also reported in the parent/carer-rated questionnaire measures. There was also anecdotal evidence suggesting that there may be difficulties with initiation in the CdLS group, explaining their difficulties starting and or/completing some of the tasks. The relative deficits in executive functioning task performance may be important in understanding the behavioural phenotype of CdLS.

Limitations

As there are many elements to executive functioning, there are some that have not been addressed, for example planning, and as such will need to be looked at in future research to complete the picture of executive functioning in these groups.

A general limitation of all the tests used to assess executive functioning is that they have all been designed for use on a typically developing population- as such the terms used can be too advanced for some populations. This was one of the reasons another syndrome group was

used as a comparison group to demonstrate any differences were not just due to the tests not being appropriately normed on the syndrome group.

The use of a group of participants with Down Syndrome also needs mentioning. One difficulty with using this group is related to their increased risk of dementia as they age. The DS sample in the current study were all under 40, however it may be possible some of these may have early stages of dementia that may impact on their results. The use of a longitudinal study would help rule out this alternative explanation.

The battery of tests presented to the participants was quite long, requiring a day to administer with the inclusion of several breaks. Ideally the tests would have been conducted over several sessions however due to the logistics and time restraints this was not possible.

Recommendations for Further Research

Future research should involve examining executive functioning across both children and adults with CdLS in order to understand whether there is a change in the trajectory of executive functioning with age. A longitudinal follow-up of executive functioning will help to determine whether there are any change in executive functioning with age without the possibility of cohort effects. Also, it is important to conduct research examining the links between cognition and behaviour in adolescents and adults with CdLS so that we can identify whether there is a common causal pathway underpinning the number of behavioural changes reported with age in CdLS or whether there are specific pathways underpinning the different behavioural changes with age. A fMRI scanning study in children and adults with CdLS will also be important in order to understand, at a biological level, the changes that may be occurring with age. A subsequent examination of the relationship between the results of the

scanning study, with cognition, behaviour and age will go some way to aid understanding of the pathways from genes to behaviour via cognition, and how these pathways may change with age.

Implications

From a pedagogical perspective, this research can begin to give ideas to inform the design of more effective education and rehabilitation strategies that are tailored to the syndrome to help develop executive functioning in different areas or to help compensate for deficits, so optimising a person's potential.

Ultimately, research looking at cognitive and behavioural phenotypes will help forge a greater understanding of neurodevelopmental disorders, and help parents, teachers and society understand the disorders much better, helping optimise the quality of life that the individuals with the disorders may have.

Further Details

The literature review and empirical paper are reported in more detail in the following:

Literature Review

D.Clin.Psy. Volume I

University of Birmingham, Department of Clinical Psychology

To be submitted to the Journal of Intellectual Disability Research (JIDR).

Empirical Paper

D.Clin.Psy. Volume I

University of Birmingham, Department of Clinical Psychology

To be submitted to the Journal of Intellectual Disability Research (JIDR).

5. Instructions to Authors for the Journal of Intellectual Disability Research (JIDR)

Journal of Intellectual Disability Research

Published on behalf of MENCAP and in association with IASSID

Edited by:
A.J. Holland Mental Health Special Issue Editor: Sally-Ann Cooper

Print ISSN: 0964-2633 0964-2633
Online ISSN: 1365-2788
Frequency: Monthly
Current Volume: 54 / 2010
ISI Journal Citation Reports® Ranking: 2008: 3/29 Education, Special; 5/51 Rehabilitation (Social Science)
Impact Factor: 1.853

Author Guidelines

Content of Author Guidelines: 1. General, 2. Ethical Guidelines, 3. Submission of Manuscripts, 4. Manuscript Types Accepted, 5. Manuscript Format and Structure, 6. After Acceptance.