THE BEHAVIOURAL AND COGNITIVE PHENOTYPE OF RUBINSTEIN-TAYBI SYNDROME

by

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ABSTRACT

In a series of studies, repetitive behaviour, executive function development and the links between these constructs were explored in Rubinstein-Taybi syndrome (RTS). An overview of these constructs provided evidence that executive dysfunction might underpin repetitive behaviour and justified the use of a developmental trajectory approach. Repetitive behaviour was explored in RTS in relation to Autism Spectrum Disorder (ASD), Down and Fragile-X syndromes. Body stereotypy and repetitive questioning occurred at a similar frequency in RTS and ASD, but repetitive phrases occurred less frequently in RTS. A test battery was compiled and administered to profile the developmental trajectories of executive functions in RTS relative to typically developing children. Executive function development was delayed in RTS relative to mental age. Finally, the relationships between executive function development and repetitive behaviour were explored in RTS using correlational analyses. Repetitive questioning was related to poorer scores on verbal working memory and inhibition measures. Adherence to routines was related to poorer scores on a measure of shifting and emotional regulation, and completing behaviour was related to poorer scores on shifting measures. These findings highlight the merit of studying executive function development in disorder groups and that pathways can be mapped between cognition and behaviour. The implications of these findings for research and practice are discussed.

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DEDICATION

For my family

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Phenotypic Repetitive Behaviour and its Links to Executive Function Development

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1.1 Preface

This chapter provides an extended introduction to the core themes of this thesis and synthesises key research. The umbrella term 'repetitive behaviour' is introduced and it is argued that this term and the concept warrant clarification. Rubinstein-Taybi syndrome (RTS) is introduced as the syndrome of interest for this thesis and the repetitive behaviour profile of this syndrome is discussed. Repetitive behaviour is then linked to executive function (EF) to argue that impairment or a delay in the development of specific components of executive function may be associated with specific repetitive behaviours. The theme of *development* appears early on in the chapter in relation to executive function in typically developing (TD) children. It is argued that rare genetic syndromes such as RTS syndrome should be studied as developmental disorders and that adopting a developmental trajectory approach to explore the relationship between EF and repetitive behaviour can complement more traditional matching approaches that utilise control groups matched on chronological and/or mental age.

1.2 Introduction to Chapter 1

Genetic syndromes and neurodevelopmental disorders with associated intellectual disability can be described in terms of their behavioural phenotypes: a set of observable characteristics that are shown more frequently by people with a given syndrome than those without the syndrome (Dykens, Hodapp & Finucane, 2000). These observable characteristics can be either totally or partially specific to a syndrome or disorder. In genetic syndromes, total and partial specificity of phenotypic behaviours highlight the role of the genotype in determining these characteristics (Oliver, Woodcock & Adams, 2010).

Directly related to the behavioural phenotype is an endophenotype: the characteristics of a syndrome that are not directly observable but can be measured indirectly. This includes the cognitive, social and emotional characteristics of a syndrome group (Oliver et al., 2010). The endophenotype can be viewed as a component of the pathway between the genotype and certain types of phenotypic behaviour. In a given genetic syndrome, the genotype may underpin particular cognitive characteristics and these cognitive characteristics may underpin behavioural characteristics of the syndrome. Not everyone with a genetic syndrome will display every characteristic phenotypic behaviour so environmental factors, developmental processes and genetic variability are presumed to influence pathways (Oliver et al., 2010; Woodcock, Oliver & Humphreys, 2009a)

Repetitive behaviour is a phenotypic behaviour reported in a number of genetic syndromes and neurodevelopmental disorders (Moss, Oliver, Arron, Burbidge & Berg, 2009; Udwin & Dennis, 1995). According to Turner (1999), repetitive behaviour is in an umbrella term for behaviours associated by invariance, high frequency, rigidity and inappropriateness. A behaviour with these four characteristics will be classed as a repetitive behaviour irrespective of how qualitatively distinct it appears from other repetitive behaviours. Thus, a stereotyped motor movement (e.g. hand flapping) and adherence to strong routines can both be defined as repetitive behaviours.

The characteristics of repetitive behaviours are such that they may cause distress to an individual, interfere with other activities, and increase parent and care-giver stress (Lecavalier, Leone & Wiltz, 2006; Turner-Brown, Lam, Holtzclaw, Dichter & Bodfish, 2011; Woodcock Oliver & Humphreys, 2009b). There is merit in studying the causal mechanisms of these behaviours, so that effective interventions can be developed. One potential causal mechanism underpinning repetitive behaviour in syndrome groups is delay or deviant development of executive functions (EFs) (Turner, 1997). In this thesis the phenotypic repetitive behaviours and the development of EFs are described in an under studied syndrome group, Rubinstein-Taybi syndrome (RTS). The links between repetitive behaviours and EF constructs are then examined.

1.3 Repetitive Behaviour

1.3.1 Definition of repetitive behaviour

The term repetitive behaviour is an umbrella term that encompasses a diverse range of subclasses of behaviour including adherence to routines, insistence on sameness, compulsive behaviours, stereotyped behaviours and restricted interests (Turner, 1997). Each of these subclasses of repetitive behaviour can in turn be described as an umbrella term. For example, Moss et al. (2009) adopted a ‘fine grained’ approach to studying *stereotyped repetitive behaviour* by distinguishing body stereotypy, hand stereotypy and object stereotypy.

Historically, researchers dedicated very little attention to describing repetitive behaviour at a fine grained level (Turner, 1997). Research questions were often posed about the 'severity' of repetitive behaviour overall, and repetitive behaviours were grouped together using broad classification systems. Thus, repetitive behaviours were described using *composite* repetitive behaviour scores (e.g. Lopez, Lincoln, Ozonoff & Lai, 2005). However, Turner (1997) argued that any broad classification system is unsatisfactory because it fails to acknowledge the differences in presentation, and hence the potential difference in underlying causal mechanisms of 'fine grained' repetitive behaviours within and across clinical populations. This argument is appealing given the apparent qualitative differences between some types of repetitive behaviours and it is reasonable to think that behaviours that appear distinct might have different underlying mechanisms.

A number of 'fine grained' classification systems have been proposed that split repetitive behaviour into more specific categories. Turner (1997) proposed eleven narrow categories of repetitive behaviour grouping behaviours similar in content, form and presentation. For example, the class 'stereotyped manipulation of objects' was operationalised to include spinning objects, repetitively examining a toy, and lining up objects; however, this category was distinct from the class 'abnormal object attachment' that was operationalised to include the behaviour: preoccupation with carrying a stick, rubber glove, etc. A similar approach was taken by Moss et al. (2009) who developed the Repetitive Behaviour Questionnaire (RBQ) for parents of children with intellectual disabilities. Moss et al. (2009) selected items for the RBQ based on five established repetitive behaviour measures. The items formed five broad classes of repetitive behaviour consisting of nineteen specific behaviours (see Table 1.1; Appendix A). The RBQ has both subscale and item level reliability, allowing it to be used to study repetitive behaviours at a fine-grained level.

Table 1.1
The subscales, items and item descriptions from the Repetitive Behaviour Questionnaire (RBQ; Moss et al., 2009).

Subscale	Item	Item Description (taken directly from Moss et al. 2009)
Stereotyped behaviour	Q1 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.
	Q2 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.
	Q3 Hand stereotypy	Repetitive, seemingly purposeless movement of hands in an unusual way. E.g. finger twiddling, hand Flapping, wigging or flicking fingers, hand posturing. Does not include self-injurious behaviour.
Compulsive behaviour	Q4 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.
	Q5 Tidying	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.
	Q6 Hoarding	Collecting, storing or hiding objects to excess, including rubbish, bits of paper, and pieces of string or any other unusual items.
	Q12 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.
	Q16 Lining up objects	Arrangement of objects into lines or patterns E.g. placing toy cars in a symmetrical pattern, precisely lining up story books.

Table 1.1 continued.

The subscales, items and item descriptions from the RBQ (Moss et al., 2009)

Subscale	Item	Item Description (taken directly from Moss et al. 2009)
	Q18 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 beginning to end, not left halfway through.
	Q19 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.
Restricted preferences	8 Attachment to 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 school teacher.
	Q10 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.
	Q13 Restricted conversation	Repeatedly talks about specific, unusual topics in great detail. E.g. conversation restricted to: trains, buses, dinosaurs, particular film, country, or sport.
Insistence of sameness	Q15 Preference for routine	Insist on having the same household, school or work schedule every day. 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 every day.
	Q17 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.
Repetitive speech	Q9 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
	Q11 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'.
	Q14 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.'

At a theoretical level a 'fine grained' approach to studying repetitive behaviour appears warranted given the breadth of behaviours that fall under the repetitive behaviour umbrella. The diversity of repetitive behaviours suggests that these behaviours are likely to impact on an individual's environment in different ways leading to different outcomes for that individual. Furthermore, there is emerging evidence that when a fine grained approach is adopted rich profiles of repetitive behaviour emerge that vary across syndrome groups.

1.3.2 Variation in repetitive behaviour profiles across genetic syndromes and neurodevelopmental disorders

Moss et al. (2009) demonstrated the marked differences between repetitive behaviour profiles in individuals with genetic syndromes. The Repetitive Behaviour Questionnaire was administered to 797 people across seven syndromes (Cri du Chat, Angelman, Fragile-X, Prader-Willi, Cornelia de Lange, Smith-Magenis & Lowe syndromes). Individuals with Fragile-X syndrome engaged in significantly more types of repetitive behaviour overall (generalised heightened specificity). They also engaged in the majority of these behaviours more frequently than at least two other syndrome groups. In contrast, individuals with Angelman syndrome engaged in fewer types of repetitive behaviour, and these were largely limited to stereotyped behaviours. Individuals with Prader-Willi syndrome had the most mixed profiles of repetitive behaviour and engaged in hoarding and adherence for routine more frequently than at least two other groups. This finding fits with previous reports of behaviour in Prader-Willi syndrome (Dykens, Leckman & Cassidy, 1996; Woodcock et al., 2009b).

Moss et al. (2009) also found evidence for syndrome *specific* repetitive behaviours in people with Cri du Chat and Smith-Magenis syndromes. These were attachment to objects and attachment to people respectively. These findings concur with previous reports of behaviour in these syndromes. For example, Cornish and Pigram (1996) collected questionnaire data on the behavioural phenotype of children with Cri du Chat syndrome from 26 families of children living in the community. A control group was not included so syndrome specific claims could not be made; however, they did find that a large proportion of the children (51.8%) had a specific object that they were attached to. Given the agreement across these studies, attachment to objects may be a syndrome specific repetitive behaviour in Cri du Chat syndrome. This behaviour is of particular interest in Cri du Chat because it does not appear to be associated with ASD phenomenology (Moss et al., 2009). In individuals with Smith-Magenis syndrome attachment to particular people is also reflected in anecdotal accounts of social behaviour. Haas-Givler (1994) noted that one of the key features of individuals with Smith-Magenis syndrome is a desire for an 'inordinate' and 'sometimes-insatiable' amount of attention from a particular adult.

1.3.3 Rubinstein-Taybi Syndrome (RTS)

Although research has started to emerge that profiles repetitive behaviour in a range of genetic syndromes there is still a dearth of research on repetitive behaviour relative to other syndrome characteristics, and for some populations no detailed research studies have been conducted that focus specifically on repetitive behaviour. Rubinstein-Taybi syndrome (RTS) is an example of a population where little is known about repetitive behaviour or its underlying mechanisms.

RTS is a rare genetic syndrome that occurs in approximately 110,000 - 125,000 live births. The syndrome is caused by microdeletions on chromosome 16p13.3 or by a mutation in the E1A-binding protein (p300) or CREB-binding protein (CBP). Individuals with RTS have intellectual disability that can range from mild to profound; however, the majority of individuals have a moderate intellectual disability (Hennekam, 2006). This associated intellectual disability may be underpinned by long-term memory deficits associated with mutations in the CREB binding protein (Alarcon et al., 2004; Bartsch et al., 1995; Josselyn, 2005; Korzus, Rosenfeld & Mayford, 2004; Oike et al., 1999; Petrij et al., 1995; Tanaka et al., 1997; Wood et al., 2005; Weeber & Sweatt, 2002). Despite these genetic markers, individuals are usually diagnosed by clinical features such as the characteristic facial phenotype that includes a broad nasal bridge, beaked nose, high arched eyebrows and downwards slanting palpebral fissues. Other characteristics include growth deficiency, microcephaly, broad thumbs and big toes (Hennekam, 2006; Udwin & Dennis, 1995).

RTS has a number of phenotypic behavioural characteristics, of which one is repetitive behaviour. Stevens, Carey and Blackburn (1990) conducted a study of 50 children with RTS to identify problems associated with the syndrome. Using parental report they found that over 50% of individuals engaged in stereotyped motor movements including hand stereotypy, spinning and rocking. Over 75% of individuals were reported to insist on sameness. Recently, Galéra et al. (2009) found that parents of individuals with RTS reported higher rates of repetitive motor movements than parents of individuals from a matched heterogeneous intellectual disability group. However, because this study did not contain syndrome specific comparison groups, conclusions cannot be drawn about how these repetitive behaviours compare to the repetitive behaviours observed in other syndromes.

The social behaviour of children with RTS is also worth noting, particularly when considered in conjunction with repetitive behaviour. Parents of individuals with RTS describe their children as friendly, particularly around adults (Goots & Liemohn, 1977; Baxter & Beer, 1992; Stevens et al., 1990) and reports suggest individuals with RTS have more interest in social interaction when compared to matched controls (Galéra et al., 1990). High levels of repetitive behaviour have been associated with Autism Spectrum Disorder (ASD) and this forms part of the diagnostic criteria for this disorder (World Health Organisation, 1993; American Psychiatric Association, 1994). However, ASD is also associated with social deficits such as eye gaze aversion, a small number of facial expressions, reduced motivation to pursue common interest in activities with others, and reduced social and emotional reciprocation (Hollander & Nowinski, 2003). Hence, reports of behaviour suggest that individuals with RTS may present with a dissociation of key ASD characteristics. This profile of behavioural characteristics will be explored in detail in the introduction to chapter 2; however, it serves here to introduce RTS as a syndrome whose repetitive behaviour profile warrants further investigation.

1.3.4 Repetitive behaviours in typical development – a comparison with developmental disorders

Apart from being classified as a rare genetic syndrome, RTS can also be described as a developmental disorder. According to Pillitteri (2009), "Developmental disorders, although not related by etiology, typically share a common feature in that there is a delay in one or more areas of development" (p.1618). Delays in development can occur across a breadth of domains including attention, cognition, language, emotional regulation and social communication. A delay to the development of one domain can impact on the development of other domains because these domains are connected (Pillitteri, 2009).

Individuals with developmental disorders may be described as having atypical repetitive behaviour if they engage in behaviour that does not occur in the typical population. However, behaviour may also be labelled as atypical if it is similar in form to behaviour in the typically developing population but persists for a longer time, is out of sequence with typical developmental progression, or occurs at a higher frequency than would be expected in typical development. The occurrence of repetitive behaviours in typically developing (TD) children should be considered in relation to individuals with developmental disorders because similarities in presentation may suggest similar underlying etiology.

TD infants engage in a wealth of stereotyped behaviours during the first year of development, including body rocking, kicking and swaying (Thelen, 1979, 1996). These behaviours are very similar to the behaviours engaged in by individuals with developmental disorders (Symons, Sperry, Dropik & Bodfish, 2005; Thelen, 1980). Thelen (1979) argued that in TD children these behaviours are tied to motor development and are generated by the central nervous system. The behaviours fade when developmental milestones, such as crawling, are reached (Thelan, 1979; Sprague & Newall, 1996); however, this is not to say that they do not persist beyond this age in some form. For example, Soussignan and Koch (1985) noted stereotyped leg-swinging behaviours in school aged children. Apart from a few exceptions there is limited literature on stereotyped behaviours in older TD children, which suggests that if stereotyped behaviours occur in older children they do not persist for a lengthy duration, or to a degree that they have elicited interest from researchers.

Other types of repetitive/ritualistic behaviour have been described in TD children aged between two and five years (Leekam et al. 2007; Evans & Gray, 2000; Evans et al., 1997; Pietrefesa & Evans, 2007; Tregay, Gilmour & Charman, 2009). Evans et al. (1997) developed a parental report questionnaire, the Childhood Routines Inventory (CRI), to measure these ritualistic/repetitive behaviours in early childhood. Items on the CRI reflect many of the repetitive behaviours displayed in individuals with developmental disorders such as RTS. For example, CRI items focus on preference for routine and sameness, attachment to objects, hoarding, ordering and lining up.

Evans et al. (1997) asked 1,492 parents of children aged 8-72 months to complete the Childhood Routines Inventory. Behaviours clustered around two factors: just right and repetitive behaviours. Just right behaviours were captured by items describing ordering and arranging objects or events, and striving for an action to meet a 'subjective standard,' whereas repetitive behaviours referred to repeating the same thing. TD children aged between 2-4 years engaged in more repetitive behaviour than younger and older children (Evans et al., 1997).

Although the repetitive behaviour engaged in by preschool children may be similar in form to that displayed by individuals with developmental disorders, the frequency and persistence of repetitive behaviours in TD children has rarely been directly compared to people with developmental disorders. There are a few exceptions: Turner-Brown et al. (2011) used parental report measures to compare the circumscribed interests of 50 children and adolescents with high functioning ASD to 50 TD controls. Individuals with ASD did not engage in more topographies of circumscribed interests than the TD children, however, the groups differed in respect to the content and intensity of the interests. The individuals with

ASD had a heightened interest in 'folk physics' relative to TD children and pursued their interests more intensely.

Evans and Gray (2000) used a developmental approach to compare repetitive behaviours in TD children and individuals with Down syndrome (DS). This involved measuring changes in compulsive behaviour relative to mental age in the two groups. Individuals with DS exhibited the same number of topographies of compulsive behaviour as the TD children; however, the DS group engaged in compulsive behaviour more frequently and intensely. In both groups younger children engaged in more compulsive behaviour than older children, and Evans and Gray argued that this provided evidence that individuals with DS follow a similar sequence of development as TD children.

In summary, there is evidence to suggest that repetitive behaviour in TD children is similar in form to those behaviours observed in individuals with developmental disorders. However, it has been found that in some disorder groups repetitive behaviours (circumscribed interests and compulsive behaviour) occur at a greater intensity than in TD children.

Evans and Gray (2000) highlight the importance of considering developmental progression when studying repetitive behaviours. The observation of similar developmental changes in TD children and individuals with DS suggests that the same underlying processes may be leading to a decrease in repetitive behaviour in DS and TD. These developmental changes would have been missed if behaviour in DS had only been considered at group level.

1.3.5 Interim Summary

In the previous four sections the term repetitive behaviour has been presented and operational definitions of its component parts have been discussed. The importance of focusing on specific classes of repetitive behaviours has been highlighted and attention has been drawn to the variation in repetitive behaviour profiles across syndromes**.** RTS has been introduced as the syndrome of interest and repetitive behaviour was noted as a key component of this syndrome. Finally, an overview of repetitive behaviour in TD children was presented emphasising that genetic syndromes and neurodevelopmental disorders are 'developmental disorders'. Indeed, repetitive behaviours may not be limited to clinical populations and it is important to think about repetitive behaviour relative to developmental processes. The following section of this thesis is concerned with the mechanisms underpinning repetitive behaviour. While this thesis is concerned primarily with the relationship between EF and repetitive behaviour, there are a number of alternative theories of repetitive behaviour in genetic syndromes and neurodevelopmental disorders.

1.3.6 Alternative theories of repetitive behaviour

Alterative theories of repetitive behaviour include those that conceptualise repetitive behaviour as a homeostatic mechanism and as behaviour maintained by socially mediating variables. It has also has been suggested that repetitive behaviour may occur in ASD because of poor mentalizing ability, or weak central coherence (Rapp & Vollmer, 2005; Lovaas, Newson & Hickman, 1987; Turner, 1997). Finally, changes to the cortical-basal ganglia circuitry have been linked to repetitive behaviour (Lewis, Tanimura, Lee & Bodfish, 2007).

There are two competing arguments surrounding repetitive behaviour as a homeostatic mechanism. The first is that stereotyped behaviour functions to increase arousal. This theory was developed after captive animals in deprived environments were observed engaging in stereotypic movements (Dantzer, 1986), and it was strengthened further by evidence that enriching the environments of people with intellectual disabilities reduced stereotypy in some instances (see Rapp & Vollmer (2005) for a review). The second argument is that repetitive behaviour serves as a homeostatic mechanism that helps counteract over arousal by blocking sensory activity (Hutt & Hutt, 1965). This theory was based largely on observations of repetitive behaviour in individuals with ASD (Turner, 1997).

The argument that repetitive behaviour is a homeostatic mechanism cannot account for why repetitive behaviour often persists across contexts in individuals with developmental disorders (see Rapp & Vollmer, 2005; Turner, 1997). Furthermore, Turner argued that the over arousal hypothesis is circular because high levels of repetitive behaviour are thought to indicate high levels of arousal, but repetitive behaviour is also explained as a mechanism to reduce this arousal.

A further limitation of the homeostatic mechanism argument is that neither version of this argument can explain the heterogeneous profiles of repetitive behaviours across syndrome groups. For example, there is no evidence to suggest that individuals Prader-Willi syndrome need more stimulation than individuals with Angelman Syndrome, as would be predicted by based on their repetitive behaviour profiles if the low arousal hypothesis was adopted (profiles described in section 1.3.2). Furthermore, the homeostatic argument cannot explain why specific repetitive behaviours appear to be heightened in some syndrome groups (e.g. attachment to objects in Cri du Chat syndrome) and it does not provide an adequate explanation for more complex high level repetitive behaviours such as adherence to routines.

An alternative theory was proposed by Lovaas et al. (1987) who employed the term perceptual reinforcement, arguing that the perceptual consequences of repetitive behaviour are automatically reinforcing (e.g. tapping and echolalia provide auditory feedback). In support of this hypothesis, giving an individual access to alternative object that has similar properties to that generated by the stereotyped behaviour has been found to compete with, or replace, the original behaviour for some individuals (see Rapp & Vollmer (2005 for a review). However, it is difficult to use this theory to account for higher level repetitive behaviours. Leekam, Prior & Uljarevic (2011) agree, stating that some repetitive behaviours do not seem directly sensory in nature e.g. stacking chairs.

It is possible that repetitive behaviours are reinforced by social contact in some individuals. It is well established that social reinforcement, as well as escape from social stimuli can serve to increase the likelihood of a behaviour occurring again (Iwata, 1987). Despite the wealth of evidence for the role of operant conditioning in maintaining behaviours outside of the context of repetitive behaviour, there is little robust evidence that repetitive behaviour is socially reinforced (Rapp & Vollmer, 2005). In a review of the literature, Rapp and Vollmer (2005) argue that the few studies that link social reinforcement to repetitive behaviour have methodological flaws that make it impossible to separate the effects of social reinforcement from automatic reinforcement.

A theory that was developed to explain repetitive behaviour specifically in ASD was that poor metalizing ability, in the form of deficits to theory of mind, made it difficult for individuals with ASD to judge other people's thoughts and intentions. Baron-Cohen (1989) argued that these deficits in social comprehension make the world unpredictable and anxiety provoking, and that repetitive behaviour such as insistence on sameness and just right behaviour exercise control over this potentially threatening environment. At face value this theory seems adequate to explain complex repetitive behaviours such as adherence to routine; however, it does not adequately account for lower level stereotyped behaviours (Turner, 1997), nor does the theory seem an appropriate explanation for high level repetitive behaviours that are observed in syndromes described as sociable and 'friendly', such as RTS. Finally, Turner (1995) (as cited in Turner, 1997) did not find evidence for a relationship between the performance on a battery of four traditional theory of mind tasks and a Repetitive Behaviour Interview in ASD.

In ASD it has also been proposed that repetitive behaviour occurs due to weak central coherence. Frith (1989) proposed that individuals with ASD experience the world in a 'fragmented' manner. According to Frith (1989) this drives attention towards minor details in the environment rather than global elements. It is argued that a focus on minor details in the environment may increase resistance to minor changes to these details. Turner (1995) (as cited in Turner, 1997) tested this hypothesis but found no links between scores on the Repetitive Behaviour Interview and scores on the Children's Embedded Figures Test in individuals with ASD.

Finally, there has been a number of studies that have explored the role of the cortical-basal ganglia circuitry in repetitive behaviour. Evidence comes mainly from: observations of repetitive behaviour in genetically altered knockout mice, pharmacologically induced repetitive behaviour, and alterations in cortical-basal ganglia circuitry and the links to repetitive behaviour (see Lewis, et al. (2007) for a review). Problems with the cortical-basal ganglia circuitry have traditionally been associated with increased motor inhibition, such as bradykinesia and akinesia in Parkinson's Disease; however, the basal ganglia circuitry is also related to cognition because it projects to the frontal lobes (Mink, 1996; Cameron, Watanabe, Pari & Munoz, 2010). EF deficits and repetitive behaviour observed in some clinical groups have been attributed to this region i.e. task switching deficits and compulsive-like hoarding, cleaning and ordering engaged in individuals with Parkinson's disease (Cools, Barker, Sahakian & Robbins, 2003; Kurlan, 2004). The relationships between, the frontal lobes, the basal ganglia, EF and repetitive behaviour indicate that current biological theories of repetitive behaviour may be compatible with an EF hypothesis of repetitive behaviour.

In conclusion, there are a number of theories that attempt to explain repetitive behaviour; however, the majority of these theories do not adequately explain the variation and range of repetitive behaviours within and across syndrome groups, nor do they explain the pervasiveness of repetitive behaviours across contexts. While there is evidence for the role of the cortical basal-ganglia circuitry in repetitive behaviour, alternations to the cortical basal-ganglia may be linked to EF. Thus, an alternative explanation is warranted to account for heterogeneous profiles of repetitive behaviour which incorporates EF.

1.4 Executive Function (EF)

1.4.1 Introduction to Executive Function (EF)

Over the last sixteen years the executive dysfunction hypothesis of repetitive behaviour has gained momentum as an explanation of repetitive behaviour in a number of clinical populations and TD children (Pietrefesa & Evans, 2007; Lysaker, Whitney & Davis, 2009; Woodcock, Oliver & Humphreys, 2009c). Turner (1997) was a proponent of this hypothesis in ASD arguing that specific classes of repetitive behaviour could be explained by deficits to specific components of EF. This hypothesis grew in popularity because of its potential to explain the varied profiles of repetitive behaviour within a syndrome group, as well as across groups. Before exploring the mechanics of this hypothesis and the evidence that supports it, it is first necessary to define EF and describe its component parts. The theoretical argument that encapsulates the executive dysfunction hypothesis, and the evidence in support of it, will then be presented.

EF has been defined in a number of different ways by a variety of authors and Elliott (2003) notes that "most attempts to define EF resorts to a list of examples" (p. 49). These lists often encompass processes such as inhibition, organising, working memory, shifting, planning, emotional regulation and generativity (Suchy, 2009; Garon, Bryson & Smith, 2008). The general consensus is that EF is an umbrella term that incorporates higher-level cognitive processes used in the conscious control and regulation of lower-level thought and action (Zelazo & Müller, 2002; Alvarez & Emory, 2006). It is now widely accepted that these cognitive processes are associated with the dorsal frontal, lateral frontal and orbital frontal anatomical regions (see Suchy, 2009 for a review).

These higher order cognitive processes can be divided into microlevel and macrolevel constructs depending on their level of complexity (Senn, Espy & Kaufmann, 2004; Miyake et al., 2000). For example, planning and organising are considered complex macrolevel EFs because they contain other micro level EFs (e.g. inhibition). For example, the Tower of London task is a well established measure of planning ability. In this task individuals are presented with a wooden board with three sticks on it. Discs are placed onto the sticks and the individual is required to plan how to move these discs to match them to a set of discs presented by the experimenter (Phillips, Wynn, McPherson & Gilhooly, 2001). Welsh, Satterlee-Cartmell and Stine (1999) found that to be successful on this task an individual needs to remember the rules while planning, initiating, monitoring and updating actions in *working memory*. Furthermore, successful completion of the task requires counter-intuitive moves – thus the *inhibition* of obvious but incorrect moves. Micro level constructs such as inhibition and working memory were found to account for over half of the variance in performance of typical adults on this task.

When an individual performs a complex EF task such as the Tower of London Task it becomes difficult to draw conclusions about which components of EF are contributing to their performance. Miyake et al. (2000) described this as the 'task impurity' problem, and advocated a more reductionist approach to studying EF that focuses on the microlevel constructs of *inhibition, working memory* and *set-switching*. Indeed, within the developmental literature this is often the approach adopted (Garon et al., 2008).

1.4.2 An overview of inhibition, working memory and shifting

This section expands on each of these micro constructs in turn. Garon et al. (2008) noted that response inhibition "involves withholding or restraint of a motor response" (p. 40). Simpson and Riggs (2006) use a broader definition noting that inhibitory control is not only the ability to "stop an inappropriate response" but also the ability to "ignore irrelevant information" (p.19). Often this may involve overriding or withholding well rehearsed or strong habitual behaviour in response to salient stimuli. Thus, inhibition allows an individual to respond in a flexible and novel way to the environment rather than in an automatic way that may be irrelevant or inappropriate to the task at hand (Garon et al., 2008).

Inhibition is conceptualised in Norman and Shallice's model of the executive system as a higher level supervisory attentional system that regulates and controls the processes of lower level subsystems (Norman & Shallice, 1986). The lower level subsystems consist of schemas (organised plans) that can be executed automatically to cues in the external environment unless supervisory attentional system exercises deliberate control over them. Execution of automatic organised plans is quick and requires less processing speed than higher level controlled actions; however, the supervisory system can choose to override these plans if they are deemed inappropriate for the task at hand. Hence, a deficit in inhibitory control can be conceptualised as the inability of the supervisory system to exercise control over the subsystems, leading to the inappropriate selection of fast, automatic organised plans in response to external cues in the environment.

Working memory is essential for integrating incoming information and holding information in mind for a task at hand (Baddeley & Hitch, 1974). Richardson et al. (1996) concluded that,

> "Insofar as there is a core to the general concept of working memory, it is the assumption that there is mechanism responsible for the temporary storage and processing of information and that the resources available to this mechanism are limited (p.23)."

Baddeley's model of working memory has, arguably, been the most dominant (Garon et al., 2008). The model consists of a central executive (defined as attention) and two slave systems: a visuo-spatial sketchpad that stores visual information and a phonological loop that stores verbal information (Baddeley & Hitch, 1974; Baddeley, 1986).

Finally, shifting refers to the ability to shift to a different pattern of responding (response shifting) or shift focus from one dimension of an object to another dimension of the same object in order to respond to it in a different way (attention shifting) (see Garon et al., 2008 for review). Shifting may appear somewhat similar to inhibition; however, in order for a shift to be necessary an individual must first establish set, a way of responding or focusing attention, to *actively shift* away from. Conversely, inhibition is concerned with *suppressing* habitual automatic responses to stimuli (Simpson & Riggs, 2009).

1.4.3 Are inhibition, working memory and shifting dissociable?

As previously described, Moss et al. (2009) has demonstrated that repetitive behaviour is not a unitary construct and that repetitive behaviour profiles vary across syndrome groups (see section 1.3.2). A robust EF hypothesis of repetitive behaviour would, ideally, explain this variability and define clear pathways between cognitive processes and specific types of behaviour. If EF is truly fractionated into the micro level components proposed in the literature (i.e. inhibition, working memory and shifting) it is possible that impairments to one component of EF may underpin specific types of repetitive behaviour. Hence, a fractionated EF system is equipped to explain the variability in repetitive behaviour because it is possible that one domain of EF may be compromised relative to another. However, if there are substantial overlaps between the micro level EFs it would suggest EF might be best conceptualised as a unitary function. Hence, the constructs 'inhibition' and 'working memory' and 'shifting' would be merely descriptive labels of the behavioural manifestations of one underlying 'executive' process. It is less likely that a unified EF system could explain the variability in repetitive behaviour profiles.

To date, there have been a number of studies that have explored the dissociable nature of the executive system in clinical populations and typical adults. Welsh, Pennington and Groisser (1991) administered a number of EF measures to children aged 3-12 years and to adults. These were mainly 'complex' EF tasks such as the Tower of Hanoi task, which is a more difficult version of the Tower of London task. Based on low correlations between measures, the authors concluded that EF was fractionated into three distinct areas: speeded responding, set maintenance, and planning.

Lehto (1996) conducted a large scale study comparing performance on a battery of working memory tasks, the Tower of London Task (TOL), the Wisconsin Card Sorting Task (WSCT), and the Goal Search Task (GST). The WCST is a measure of attentional shifting whereby individuals are required to sort cards according to one dimension of a stimulus displayed on the cards, and then switch to sort them by another dimension of this stimulus. The GST is a planning task whereby an individual observes a sequence of box tapping demonstrated by the experimenter and must copy this sequence. The sequence is very long and difficult to retain in memory so the individual can choose to tap a shorter version of this sequence. If they execute a shorter sequence correctly they are awarded points according to the length of the sequence, however, if they make an error they are not awarded any points. Therefore, to be successful an individual needs to hold the sequence in mind, plan a strategy for obtaining the maximum number of points relative to their abilities, and then initiate this strategy. Scores on the TOL, WSCT, and GST did not correlate, and none of the working memory measures correlated with the TOL or GST. Lehto (1996) concluded that these results supported the conclusions of Welsh et al. (1991) that EF was fractionated.

While studies support the existence of a fractionated EF system there are a number of methodological issues that limit the findings. Weak correlations between EF tasks do not necessarily indicate a fractionated EF system. Correlations may be weakened by other demands across tasks (e.g. language) that obscure the relationships between the executive components (Miyake et al., 2000). Aside from this, to accept that EF is fractionated on the basis of these studies may be to accept that speeded responding, set-maintenance, planning, shifting and working memory are dissociable. However, because a number of these constructs are global macrolevel EFs it is difficult to conclude which factors are driving this dissociation. Miyake et al. (2000) noted that the interpretation of performance on these macrolevel tasks is often arbitrary and post hoc, and is further complicated because individuals often adopt different strategies when asked to repeat a macrolevel task; hence, it becomes unclear what the task is measuring (see Denckla, 1996; Rabbitt, 1997).

To overcome these weaknesses Miyake et al. (2000) conducted a study of the dissociable nature of EFs by asking 137 undergraduate students to complete tasks measuring inhibition, updating and monitoring, and shifting. In this study the updating and monitoring construct can be argued to be an alternative name for working memory. Commonly used complex EF tasks were also included such as the WCST, and TOH. The methodological weaknesses of previous studies were overcome using confirmatory factor analysis that employed latent variables as opposed to manifest variables. Latent variables are variables that are not directly observed but are inferred from other manifest variables (observable variables) that are considered to measure the construct of interest. Miyake et al. (2000) created latent variables by essentially extracting shared variance across several measures of a particular EF. This provided purer measures of each EF that were compared to see how they related to each other. By employing this method the researchers demonstrated that while inhibition, working memory and shifting are moderately correlated they are also clearly dissociable (Miyake et al., 2000).

A study by Lehto, Juujärvi, Kooistra and Pulkkinen (2003) supported the findings of Miyake et al (2000). The researchers investigated EF in 108 TD 8-13 year olds. The children completed a battery of EF tasks and data were analysed using both exploratory factor analysis and confirmatory factor analysis. In line with Miyake et al. (2000) the results indicated a three factor solution of working memory, inhibition and shifting. This study strengthens the results of Miyake et al. (2000) because the researchers were able to generate a similar factor structure in children to that found in adults using a different battery of EF tests.

1.5 Linking executive function to repetitive behaviour

The theoretical argument for linking specific repetitive behaviours to specific types of executive dysfunction is plausible given evidence of a fractionated EF system. A number of authors have postulated how executive dysfunction might lead to particular classes of repetitive behaviour and there is an emerging body of evidence that links repetitive behaviour to poorer inhibitory control, working memory and shifting. However, this research has often been limited because repetitive behaviours were not measured at the 'fine grained' level of description. This body of evidence comes from a range of clinical populations including rare genetic syndromes and neurodevelopmental disorders. A selection of evidence linking each component of EF to repetitive behaviour is summarised below alongside an appraisal of the methods used in these studies.

1.5.1 Inhibition

It is possible that an inhibitory control deficit could underpin repetitive behaviour if an environmental cue triggered a prepotent response and this response was not inhibited to allow for more flexible behaviour. It may be, particularly in the case of motor movements, that once the response had been triggered then an individual with an inhibitory control deficit might continue to respond in this way until the behaviour is interrupted by an external stimulus (Turner, 1997).

Lopez et al. (2005) measured EF using the Delis-Kaplin Executive Function Scales and compared scores on this measure with several measures of repetitive behaviour (The Autism Diagnostic Observation Schedule, Autism Interview-Revised, Gilliam Autism Rating Scale, and the Aberrant Behavor Checklist). Inhibition was related to restricted repetitive behaviour and not intellectual ability in adults with high functioning ASD. However, Lopez et al. used a repetitive behaviour composite score and so it is not possible to comment on whether specific types of repetitive behaviour may be driving the association with inhibition in this study.

Turner (1995) (cited in Turner, 1997) has also provided evidence for a possible link between inhibition and stereotyped behaviour in a study of individuals with high functioning ASD. These individuals engaged in more 'recurrent perseveration' than a heterogeneous intellectual disability control group when asked to guess where a computerised target would appear from two possible locations. Participants were instructed to find as many targets as they could, and were not told that the locations of the target were chosen at random by the computer. Turner interpreted returning repetitively to the same response choice as a failure to inhibit the previous location. Returning repetitively to the same location positively correlated with parental report of stereotyped repetitive behaviours in ASD but not with other repetitive behaviours. These results were robust when degree of intellectual disability was controlled. A measure of shifting was not related to recurrent perseveration in this study.

Evidence of a link between inhibition and EF has also been found outside genetic syndromes and neurodevelopmental disorders. Executive dysfunction is associated with Schizophrenia and Alzheimer's disease and individuals with these disorders also engage in a range of repetitive behaviours. Lysaker, Whitney and Davis (2009) used the Maudsley Obsessive-Compulsive Inventory to measure checking, cleaning behaviour, slowness and doubting (compulsive like repetitive behaviours) in individuals with Schizophrenia. A lesser ability to inhibit thoughts and behaviour on tests from the Delis Kaplan Executive Function System was positively related to self report of a larger range of topographies of compulsive behaviours. In Alzheimer's patients, Cullen et al. (2005) found that poorer inhibitory control on a trail-making task was linked to repetitive actions, which is in agreement Turner (1997) whose research suggests a link between inhibition and repetitive motor movements in ASD.

In summary, there are several studies that suggest a link between inhibition and repetitive behaviour. There is some evidence to suggest that poor inhibition may be linked to low-level stereotypic behaviours and repetitive motor movements in individuals with ASD and individuals with Alzheimer's disease (Turner, 1997; Lysaker et al., 2009), and evidence of a link between compulsive behaviour and poorer EF in Schizophrenia (Lysaker, et al., 2009). These studies also illustrate the methodological variation that is common in the literature. Often a fine-grained approach will be taken when measuring one construct such as repetitive behaviour, while the other construct (e.g. EF) will be measured globally.

1.5.2 Shifting

It has been argued that shifting deficits may lead to repetitive behaviour in that an individual may have difficulty shifting away from their previous way of responding so that they become "stuck-on-set," repeating strategies that may no longer be useful. Turner (1997) argues that being unable to set-shift may explain why some individuals with Autism have 'high level' repetitive behaviours such as insistence on sameness and restricted interests. High level repetitive behaviour is in contrast to 'low level' repetitive behaviours like stereotyped movements. Turner (1997) argues that because individuals with Autism have difficulty performing the necessary cognitive action they may find change distressing.

In support of this, Turner (1995) (cited in Turner, 1997) found that individuals with high functioning ASD who performed poorly on a card sorting task that measures 'stuck-in-set perseveration,' were more likely to insist on sameness than participants who had mastered the task. It is important to note that Turner defined stuck-in-set perseveration as a failure of behavioural inhibition rather than shifting and grouped stuck-in-set perseveration together with recurrent perseveration to argue that an inhibition deficit might underpin repetitive behaviour in ASD. However, stuck-in-set perseveration as measured by Turner is comparable to 'shifting' that has been described as an independent component of EF by Miyake et al. (2000).

Several recently published studies lend further support for a link between shifting and restricted/repetitive behaviour in Autism Spectrum Disorder. However, in a similar manner to the studies conducted by Lopez et al. (2005) and Lysaker et al. (2009), the construct of repetitive behaviour was not split into its component parts to allow for the exploration of links between specific classes of behaviour and shifting (Yerys et al., 2009; South, Ozonoff, McMahon, 2007). For example, Yerys et al. (2009) studied shifting in children with high-functioning Autism. Shifting was measured using the Intra-dimensional Extra-dimensional Card Sorting Test while the 'total amount' of repetitive behaviour was calculated from the Autism Diagnostic Interview– Revised (ADI-R). A positive correlation was found between extra-dimensional reversal shifts and repetitive behaviours in the ASD group.

An exception to this general methodological approach is a series of studies conducted by Woodcock, Oliver, Humphreys & Hansen (2010) and Woodcock, Oliver and Humphreys (2009a, 2009b, 2009c) with individuals with Prader-Willi syndrome. Woodcock et al. utilised neuropsychological testing, naturalistic observation and brain imaging to demonstrate that adherence to strong routines and repetitive questions in people with Prader-Willi syndrome were linked to a shifting deficit irrespective of mental age. The work by Woodcock et al. (2010, 2009a, 2009b, 2009c) demonstrates the utility of studying discrete classes of EF rather than EF as a global construct, and linking these discrete classes of EF to highly specific repetitive behaviours in rare genetic syndromes and developmental disorders.

Links between shifting and repetitive behaviour have also been found in people with schizophrenia and obsessive-compulsive disorder using fine-grained methodology, although arguably not as sophisticated as the highly specific methods used by Woodcock et al. (2010, 2009a, 2009b & 2009c). For example, Lawrence at al. (2006) measured shifting in people with obsessive compulsive disorder (OCD) using the Wisconsin Card Sorting Test (a test of shifting). An association was found between a set shifting deficit in people with OCD and specific repetitive behaviours: ordering/symmetry. Morrens, Hulstijin, Lewi, de Hert and Sabbe (2006) developed the Stereotypy Test Apparatus (STA), on which participants were required to generate random sequences of motor responses. The apparatus is thought to capture stereotyped behaviour in the form of stereotyped response patterns. The participants also completed the Wisconsin Card Sorting Test. It was found that participants with schizophrenia engaged in more stereotyped response patterns on the Stereotypy Test Apparatus than a normative control group. The differences between groups on the WCST were only marginally significant; however, there was a weak but significant negative relationship between participants' performance on the STA and the WCST in the absence of correlation with measures of short term memory and working memory. This lends some support to the hypothesis that a shifting deficit may underpin stereotyped repetitive behaviour.

In summary, it is clear from these studies that the link made by Turner (1997) between set-shifting deficits in ASD and complex (higher order) repetitive behaviours such insistence to sameness may generalise to other clinical populations such as Prader-Willi syndrome. However, studies of people with OCD and schizophrenia suggest shifting, like inhibition, may also be related to low-level stereotyped motor movements, ordering and symmetry. It is difficult to be certain of the domain of EF that underpins the relationship between performance on the designated shifting task (Wisconsin Card Sort Task) and low-level repetitive behaviour in these studies. It may be that shifting and inhibition both contribute to low-level repetitive behaviours, or alternatively, the WCST may also have an inhibitory component. Indeed, the WCST was described as an inhibition task by Morrens et al. (2006) despite usually being classified as a task of shifting.

1.5.3 Working Memory

Deficits in working memory might lead to specific repetitive behaviours. For example, it is possible that an individual who is unable to hold information in their mind for a task at hand may attempt to elicit unknown information from others by asking repetitive questions, or use repetitive questions as a means to reduce anxiety associated with uncertainty that arises from poor integration of information in working memory (Cullen et al., 2005). Alternatively, repetitive questioning could be argued to serve as a rehearsal strategy to compensate for limited working memory.

Hwang, Tsai, Yang, Liu & Lirng (2000) found that repetitive behaviour is common in Alzheimer's disease including repetitive questioning. Out of 141 individuals sampled it was found that 74.7% exhibited repetitive questioning, and 35.5% had repetitive actions. It has been reported that executive dysfunction is characteristic of Alzheimer's disease (Chen, Sultzer, Hinkin, Mahler & Cummings, 1998).

Cullen et al. (2005) examined the links between repetitive behaviour and executive dysfunction in people with Alzheimer's disease. The authors found that repetitive questioning was associated with poorer recall on word list learning. Although a word list learning task primarily measures short term memory, it may also make higher demands on working memory in a similar manner to simple verbal span tasks. Cullen et al. (2005) also found that repetitive phrase/stories were associated with more severe generalised executive dysfunction in this study.

Other evidence that links poorer working memory to repetitive behaviour comes from the study by Lopez et al. (2005), who as well as finding a negative correlation between inhibitory control and restricted repetitive behaviours, and between task switching and restricted/repetitive behaviours, found a negative correlation between the repetitive behaviours and working memory in people with ASD. Furthermore, Lopez et al. (2005) did not find links between repetitive behaviour and more complex macrolevel EFs such as planning and fluency despite measuring them. Therefore, this study also lends support to focusing on microlevel EFs when investigating the underpinnings of repetitive behaviour in syndrome groups.

In summary, there is limited evidence for a relationship between working memory and repetitive behaviour; however, the evidence does highlight the necessity of including this construct in any study that is concerned with exploring associations between repetitive behaviour and EF. Furthermore, because working memory is often involved to some degree in most EF tasks (i.e. to hold in mind the rules of the task) it may have an important influence on performance on tasks measuring shifting and inhibition.

1.5.4 Links between executive function and repetitive behaviour in typical development

Early in this thesis it was acknowledged that ritualistic behaviour commonly occurs in young children, particularly between the ages of 2-5 years (Evans et al., 1997; Leekam et al., 2007; Evans & Gray, 2000). It was also acknowledged that rare genetic syndromes are developmental disorders and that atypical behaviours in these syndromes might be similar to behaviours engaged in by TD children in certain stages of development. Thus, it is important to consider this when hypothesising about the underpinnings of repetitive behaviour in syndrome groups because there may be similarities between the underlying mechanisms of these behaviours and repetitive behaviours engaged in by young children.

A number of studies have demonstrated that EF develops rapidly during the developmental window of 2-5 years in TD children (Carlson, 2005; Diamond & Taylor, 1996; Frye, Zelazo & Palfal, 1995; Simpson & Riggs, 2005). This is not to say that inhibition, working memory and shifting develop at the same rate. Davidson, Amso, Anderson and Diamond (2006) examined the development of EF in children aged 4 to 12 years. Participants completed a computerised battery of tests that measured inhibition, working memory and shifting. One of the key findings was that shifting had a longer developmental progression than inhibition even when working memory demands were decreased. Huizinga, Dolan & van der Molen (2006) found shifting continued to develop into adolescence and that working memory developed into adulthood.

There is emerging evidence that ritualistic/repetitive behaviours are associated with poorer inhibitory control and shifting in young children. For example, Pietrefesa and Evans (2007) administered tests of inhibitory control and shifting to 44 children aged between 48 and 96 months. Parents completed the Childhood Routine Inventory (CRI: Evans et al, 1997). In younger children a combination of inhibitory control and set shifting explained a significant proportion of variance in repetitive/ritualistic type behaviours. In older children a combination of response inhibition and non executive factors (i.e. affective factors) predicted compulsive like behaviours. Tregay et al. (2009) used a similar method to Pietrefesa and Evans (2007). They studied children aged 37-107 months and compared their scores on three EF tests (inhibitory control, shifting and generativity) to their scores on the Childhood Routines Inventory. They found that shifting was significantly associated with repetitive/ritualistic behaviours in both the younger and older children. No associations were found between generativity or inhibition and repetitive/ritualistic behaviours.

In conclusion, while there is only partial agreement about the components of EF that may underpin specific repetitive behaviours in TD children, there does appear to be a clear link between these constructs generally. The merit of employing a developmental perspective to studying the link between EF and repetitive behaviour is clearly demonstrated because when executive performance was studied across development subtle relationships between constructs emerged. Davidson et al. (2006) also highlight potentially differing rates of developmental progression across EFs. Therefore, in rare genetic syndromes it is possible that EFs may develop at differing rates, and that development of specific EFs may correspond to increases and decreases in specific repetitive behaviours.

1.5.5 Interim Summary

This section has reviewed EF, explored the dissociable nature of its component parts, presented evidence that links poorer EF to increased rates of repetitive behaviour, and considered the relationship between EF and repetitive behaviour from a developmental perspective. Although links between specific types of repetitive behaviour and specific components of EF have been noted these links are not always consistent across studies. For example, low-level repetitive behaviours were linked to shifting and inhibition. This inconsistency may be due to methodological problems such as poorly defined constructs and inadequate measures of repetitive behaviour and EF. Inconsistency may also arise due to overlapping task demands.

This section has also reviewed evidence that the EFs develop rapidly in TD children between the ages of 2-5 years. It has been acknowledged that TD children engage in less repetitive behaviour after this period of development, and studies that have linked poor EF to repetitive behaviour in TD children have been presented.

1.6 Rationale for matching and developmental approaches

Developmental processes may be related to EF and repetitive behaviour in TD children, so one aim of this thesis was to maintain a developmental perspective whenever possible. This aim was further strengthened by a commitment to RTS as a developmental disorder. For this reason a developmental trajectory approach to studying the development of EF in RTS has been adopted within chapters 3 and 4. The developmental trajectory approach has a number of advantages over the traditional matching approach, but the nature of this method makes it difficult to apply in all instances. Therefore, this thesis serves to demonstrate proof of principle with regard to the developmental trajectory approach, but remains flexible in that it adopts the matching approach where necessary. The following section provides a theoretical overview of these two approaches, discusses the strengths and weakness of each approach, and summarises evidence to support the use of developmental a trajectory approach.

1.6.1 Adopting matching and developmental trajectory approaches when studying cognition and behaviour in disorder groups

Historically, the most popular approach to studying the cognitive and behavioural phenotypes of genetic syndromes or neurodevelopmental disorders has been the matching approach. This approach is characterised by a design that controls for age. When utilising a matching approach researchers recruit participants with the syndrome/disorder of interest and ask these participants to complete a test that measures a given construct e.g. receptive language. The researchers usually compare the performance of the syndrome/disorder group to a control group of TD individuals matched for chronological age, and a second group of TD individuals matched for mental age (Thomas et al., 2009).

Thomas et al. (2009) note that there are three types of conclusions that researchers can draw from this type of approach: the domain of interest is preserved, delayed or deviant in individuals with the syndrome/disorder. For example, if individuals in the syndrome/disorder group were found to have poorer receptive language than a chronologically age matched control group, but not a mental age matched group, it might be concluded that receptive language was delayed in individuals with the syndrome/disorder. However, if receptive language was poorer than both the chronologically age matched control group and the mental age matched control group the researchers would conclude that receptive language is deviant in the syndrome/disorder group (Thomas et al., 2009).

The matching approach is often utilised by cognitive neuropsychologists to study impaired and preserved cognitive domains in adult populations (Thomas et al., 2009). This approach can be utilised for cross syndrome descriptions of task performance or behaviour, and has been influential in describing behavioural phenotypes and endophenotypes of disorder groups (O'Brien & Yule, 1995). Despite this, the approach has several limitations especially when utilised to study rare genetic syndromes and neurodevelopmental disorders. One limitation is that at any one time point the matching approach can only be applied adequately to a studying a group with a narrow age and ability range. Most rare genetic syndromes include individuals with a wide range of ages and ability levels, but studies that have employed the matching approach have often focused a particular age or ability level within a syndrome group whilst ignoring other ages and abilities. Alternatively when the sample size of a syndrome group is small, the matching approach is often applied, grouping many individuals of varied ability together. Grouping individuals masks within syndrome variability and this 'snapshot' approach limits the generalisability of findings from these studies (Thomas at al., 2009).

Karmiloff-Smith (1998, 1999) argued that when the matching approach is used in a 'snapshot' manner it ignores the developmental profile of a syndrome group and treats individuals with a given syndrome/disorder as developmentally static. A single snapshot of an adult population of individuals within a syndrome group is too simplistic because it only considers the end state of development and fails to consider how this end state is arrived at. Individuals with developmental disorders are just as liable as TD individuals to change and develop over time (Karmiloff-Smith, 1997, 1998; Scerif & Karmiloff Smith, 2005). This is not to say that a snapshot approach could not be used at several stages of development for a given syndrome group to map developmental changes. However, it can be argued that this is a developmental approach that employs a matched control group as opposed to a matching approach per se.

Recently, the developmental trajectory approach to studying cognition and behaviour in rare genetic syndromes has become a popular alternative to the matching approach. The developmental trajectory approach has long been adopted by developmental psychologists to study how cognition and behaviour relate to mental and chronological age in TD children. Scerif & Karmiloff-Smith (2005) argue that the developmental trajectory approach fits with rare genetic syndromes because these syndromes are 'developmental disorders' that cannot be divorced from the influence of development.

Thomas et al. (2009) describe how the application of the developmental trajectory approach involves recruiting individuals from a syndrome group of various ages and abilities. Their performance on a test is measured and plotted as a function of mental age or chronological age. The generated trajectory is then compared to the trajectory for TD children. Given that a function is derived linking performance to age for the syndrome group and the disorder group, individuals from the disorder group do not have to be matched directly with TD individuals.

Furthermore, the trajectory approach can be applied to diverse groups (i.e. with a range ages and abilities). It is ideal for studying rare genetic syndromes with small sample sizes (Thomas et al., 2009; Karmiloff-Smith et al, 2004).

The trajectory approach provides richer data by depicting how a syndrome group's performance on a given task converges or diverges with that of a TD comparison group across development. For example, unlike the matching approach, a developmental trajectory may distinguish between a delayed onset of an ability that develops at the same rate as in TD children and a delayed onset of an ability that develops at a slower rate than in TD children. Furthermore, by viewing trajectories it is possible to detect a premature asymptote and non-linear trajectories (Thomas et al. 2009).

Paterson, Brown, Gsödl, Johnson and Karmiloff-Smith (1999) have demonstrated the importance of studying developmental trajectories in their work on vocabulary learning in children with Williams syndrome (WS). Preschoolers with WS have difficulty with vocabulary learning that is comparable to individuals with Down syndrome (DS). However, by late adolescence/early adulthood the language ability of individuals with WS far exceeds that of individuals with DS. The opposite pattern is found for number ability whereby younger individuals with WS exceed the performance of individuals with DS, however, by adulthood this pattern has reversed. A 'snapshot' approach to studying WS and DS might have masked these important developmental changes.

Although the developmental trajectory approach has many advantages over the matching approach it is limited in a number of ways. It provides a large amount of descriptive data that may not be appropriate if the purpose of the study is to provide an overview of group differences. When using this approach it is also desirable to avoid floor and ceiling effects by using a test that is sensitive to changes across development. However, an appropriate test may not always be available when working with a very diverse group of individuals. If ceiling effects do occur, one way to deal with this is to select part of the trajectory that is linear and analyse the rate of progression to ceiling. However, some abilities may develop rapidly within a developmental window so that a linear proportion of a trajectory cannot be isolated. Under these circumstances a 'pure' trajectory approach may not be appropriate.

1.6.2 Interim summary

This review of the developmental and matching approaches has outlined the strengths and weaknesses of each approach. Where it may be preferable to use a developmental trajectory approach to gather rich detailed data, there are times when group level 'snapshot' perspective can provide a quick and concise overview of a syndrome and lead to further research questions. While both approaches are adopted within this thesis, emphasis is placed on understanding cognition and behaviour developmentally.

1.7 Chapter Summary and Thesis Outline

Disorder groups can be contrasted to study behaviour, for example, by comparing and contrasting repetitive behaviour profiles across disorders. It has been acknowledged that for these contrasts to be most informative a fine-grained approach to studying behaviours may be necessary. Fine grained approaches have been used to gain insight into the heterogeneous repetitive behaviour profiles in a number of genetic syndromes.

Individuals with RTS were introduced in this chapter and the phenotypic repetitive behaviours observed in this syndrome were described. To date, very little is known about how repetitive behaviours in RTS compare to those displayed in other disorder groups, or about the mechanisms that give rise to these behaviours. Anecdotal reports also suggest individuals with RTS are motivated by social interaction. The presence of repetitive behaviour alongside social inclination points towards a dissociation of the triad of impairments associated with ASD. A comparison of the repetitive behaviour profile of RTS and ASD would further our understanding of the extent to which the repetitive behaviour profiles of these syndromes are comparable.

In addition, cognitive endophenotypes were introduced in this chapter and it was argued that specific endophenotypes may underpin specific phenotypic behaviours. The executive dysfunction hypothesis of repetitive behaviour was introduced, which offers an alternative to numerous theories of repetitive behaviour. The theory is adept to explain variation in repetitive behaviour because EF consists of a number of dissociable components. Therefore, specific deficits or delays to EFs could give rise to specific types of repetitive behaviour.

Finally, developmental trajectories were discussed and it was argued a developmental approach to studying EFs may be valuable. The developmental trajectory approach is appropriate for studying a disorder group with a low N that contains individuals with varying degrees of ability. It was argued, however, that matching approaches are also valuable for gaining an overview of behaviour in a disorder group.

In the following chapter of this thesis the current knowledge of repetitive behaviour in RTS is extended using a group design and the questionnaire methodology developed by Moss et al. (2009). RTS is central to chapter two while Autism Spectrum Disorder, Fragile X syndrome and Down syndrome are introduced as comparison groups. In addition, the triad of impairments is explored in this chapter, and in particular, whether RTS can inform our understanding of autistic phenomenology. In chapter 3 the development of an EF battery for people with intellectual disabilities is described. This battery is based on tasks from the TD literature. It was developed for use within a developmental trajectory framework, and to aid description of the development of EFs in RTS. In chapter 4 the performance of individuals with RTS on the newly developed battery is described. This chapter is concerned entirely with the EFs and the merits of exploring their development within a syndrome group. The development of EFs in people with RTS is compared to the development of EFs in TD children. Finally, in chapter 5 the relationship between EFs and repetitive behaviour is explored in RTS by comparing performance on the EF battery to parental reports of EF and repetitive behaviour.

At the end of this thesis a number of methodological approaches will have been employed to demonstrate that the profile of repetitive behaviour in RTS is dissociated from the social/communication impairments typically observed in ASD, that the development of EFs is atypical in RTS, and that a link can be made between cognition and behaviour in this syndrome group.

CHAPTER 2

The Repetitive Behaviour Profiles of Autism Spectrum Disorder, Rubinstein-Taybi, Fragile-X and Down Syndromes

2.1 Introduction

As noted in section 1.3.3 repetitive behaviour is purported to be a phenotypic characteristic of Rubinstein-Taybi syndrome (RTS) and a number of other neurodevelopmental disorders (Udwin & Dennis, 1995). Little is known about the phenotypic repetitive behaviour profile of RTS; however, it is well established that repetitive behaviour forms part the triad of impairments in Autism Spectrum Disorder; a disorder defined by its behavioural characteristics (ASD) (Lewis & Bodfish, 1998). Thus, in this chapter the repetitive behaviour profile of ASD provides a benchmark against which the repetitive behaviour profile of RTS can be measured. ASD is also of interest as a comparison group because anecdotal reports suggest that individuals RTS may not have the social/communication impairments associated with the other aspects of the triad of impairments. Fragile-X (FXS) and Down (DS) syndromes were also included as comparison groups in this chapter. FXS and DS are genetic syndromes that are not defined by behavioural characteristics. They are relevant comparison groups because they have been argued to have high and low levels of repetitive behaviour respectively, as well as differing social characteristics.

Individuals with ASD engage in repetitive behaviour at a higher frequency and intensity than controls matched for age and ability (Bodfish, Symons, Parker and Lewis, 2000; Hermelin & O'Conner, 1963; Lord, 1995; Lord & Pickles, 1996; Richler, Bishop, Kleinke & Lord, 2007; Watt, Welnerby, Barber & Morgan, 2008). In addition, Bodfish et al. (2000) found that individuals with ASD engaged in a larger number of topographies of repetitive behaviour than a heterogeneous control group. This is in agreement with Turner (1995) who assessed individuals with ASD on the repetitive behaviour interview (RBI; cited in Turner, 1997). Overall the ASD group engaged in almost all of the 11 classes of repetitive behaviour captured by this assessment. Furthermore, Turner noted that 98% of individuals with ASD displayed repetitive behaviour in three or more of the eleven classes of repetitive behaviour whilst the comparable figure was 17% for a heterogeneous intellectual disability control group.

A high frequency and intensity of repetitive behaviour forms one component of the ‘triad of impairments’ that characterises ASD. The other components are social interaction deficits and communication deficits. For an individual to be diagnosed with Autism they must have characteristics from all three components of the triad (DSM-IV, APA, 1994; ICD-10, WHO, 1993). This diagnostic emphasis on the triad of impairments has led researchers in search of one underlying mechanism of Autism. However, in recent years a number of research studies have been conducted that suggest the social and non-social elements of the triad might be fractionated and have different aetiology (for a review see Happe & Ronald, 2008).

Evidence to support the dissociation of the triad of impairments may come from cross syndrome comparisons. The repetitive behaviours demonstrated in many syndromes and disorders appear to be similar in form to the repetitive behaviours noted in ASD; for example, resistance to change and body stereotypy reported in people with RTS (Udwin & Dennis, 1995; Stevens, Carey & Blackburn, 1990). As noted in section 1.3.3 Rubinstein-Taybi syndrome is of interest because anecdotal reports suggest that individuals with RTS are motivated to seek social contact, thus suggesting a social impairment might not be pronounced (Stevens et al., 1990). Therefore, whilst some phenotypic behaviours of individuals with RTS may be similar to individuals with ASD (i.e. repetitive behaviour), these reports suggest the social communication profile of these syndromes is not well aligned. If the repetitive behaviour profile of RTS is comparable to that of ASD but individuals with RTS have fewer social/communication deficits, it may lend support to a fractionated triad of impairments.

Although repetitive behaviour has been frequently noted in ASD and individuals with genetic syndromes such as RTS, the study of repetitive behaviour has historically been neglected relative to other characteristics of these disorders. For example in ASD, social and communication deficits have received more attention (Rutter, 1996; Bodfish et al., 2000). One reason for this neglect was the adherence of many researchers to the view that repetitive behaviour is merely related to the severity of a person's intellectual impairment (Lewis and Bodfish, 1998; Turner, 1997). Evidence has gradually accumulated that challenges this view (Bartak & Rutter, 1976; Tantam; 1991; Turner, 1997; Yerys et al., 2009). Bartak and Rutter (1976) explored repetitive behaviours in 19 children with high -functioning Autism in comparison to a low-functioning group. Difficulty adapting to new situations, adherence to routines, ritualistic behaviours and attachment to objects were reported in both groups. A larger proportion of the high functioning children engaged in ritualistic behaviour than the low functioning group, and the prevalence of circumscribed interests was similar in the groups (e.g. obsessions with maps). More recently, Turner (1995, cited in Turner, 1997) provided evidence in line with Bartak and Rutter (1976), demonstrating that high functioning individuals with ASD engaged in clinically relevant repetitive behaviour at a similar frequency to their low functioning counterparts.

Moss, Oliver, Arron, Burbidge & Berg (2009) (section 1.3.2) challenged the notion that repetitive behaviour is simply an index of intellectual disability. Within a single syndrome group it is possible for certain repetitive behaviours to be elevated relative to others (e.g. Prader-Willi syndrome) and profiles are largely heterogeneous across groups. If repetitive behaviour were simply an index of intellectual disability this is unlikely to occur.

The findings of Moss et al. (2009) raise other important considerations regarding the study of phenotypic repetitive behaviour profiles, particularly when comparing these profiles to repetitive behaviour observed in ASD. Although it has been argued that there is a higher intensity and frequency of repetitive behaviour in ASD than mental age matched comparison groups, often these comparison groups were heterogeneous intellectual disability groups, or alternatively one other neurodevelopmental disorder e.g. Down syndrome. Therefore, it is difficult to draw conclusions about how repetitive behaviour in syndromes like RTS compares to repetitive behaviour in ASD. In addition, very few studies of ASD have described how variations in repetitive behaviours at a fine grained level of description converge and diverge in comparison to other neurodevelopmental disorders. For example, it is possible that individuals with RTS may show similar levels of a specific repetitive behaviour in comparison to individuals with ASD, but have lower levels of other repetitive behaviours. A gross level of description might mask these potential differences.

Description of repetitive behaviour profiles is also important for understanding the underlying causes of these behaviours (Turner, 1997). As previously noted in section 1.4.1, an executive dysfunction account of repetitive behaviour has been suggested in ASD and there is also growing evidence that executive dysfunction may underpin repetitive behaviour in a number of other genetic syndromes and neurodevelopmental disorders (for example Prader-Willi syndrome, Woodcock, Oliver and Humphreys, 2009c). If the link between EF deficits and repetitive behaviour is to be fully understood the repetitive behaviour profiles of these disorder groups must first be outlined.

The following chapter is concerned primarily with describing the repetitive behaviour profile of RTS relative to ASD focusing on a fine-grained level of description (as described by Moss et al., 2009). However, Fragile X and Down syndromes are also included as comparison groups – the two most common genetic disorders (Dykens, Hodapp, & Finucane, 2000). These syndromes are of interest because of their varying degrees of social communication deficits and repetitive behaviour relative to RTS and ASD.

As noted in section 1.3.2, it has been suggested that individuals with Fragile X syndrome (FXS) have a generalised heightened specificity for repetitive behaviour (Moss et al., 2009). These behaviours are similar in form to those reported in ASD (Hatton et al., 2006). Individuals with FXS have also been described as having autistic-like social communication deficits (Udwin & Dennis, 1995). For example, Turk & Graham (1997) found that individuals with FXS engaged in more eye contact avoidance than a heterogeneous intellectual disability group and individuals with DS. However, these social communication deficits are not considered as severe as the lack of interest in social interaction often observed in people with ASD (Udwin & Dennis, 1995). Udwin and Dennis (1995) argue that compared to individuals with ASD individuals with FXS are more likely to seek out social contact although they often present as shy and socially anxious.

Individuals with DS are noted for their social competence and empathy (Sigman & Ruskin, 1999; Kasari & Freeman, 2001; Karsari & Sigman, 1996; Hornby, 1995; Joseph & Tager-Flusberg, 1999). Social competence in DS contrasts with the social presentation of many individuals with ASD, but seems qualitatively similar to anecdotal reports of social behaviour in individuals with RTS (Stevens et al., 1990). These reports concur with evidence from studies where typically developing (TD) children have been compared to individuals with DS. Individuals with DS gaze more frequently at a partner's face when working in pairs to complete a task. Individuals with DS also display more positive facial expressions when working on these tasks (Kasari, Freeman, Mundy & Sigman, 1995). Thus, individuals with DS potentially have fewer social deficits than individuals with ASD given the impairment of ASD relative to TD children. There is also evidence that individuals with DS engage in less repetitive behaviour than those with a codiagnosis of ASD (Hepburn & MacLean, 2009).

To summarise, the literature suggests that: ASD is characterised by social-communication impairments and repetitive behaviours; FXS is characterised by some social communication deficits along with repetitive behaviours; DS is characterised by lower levels of repetitive behaviours and fewer social communication deficits than FXS and ASD; and finally, RTS is characterised by an unusual profile of repetitive behaviours coupled with anecdotal reports of sociability. Further delineation of the repetitive behaviour profiles of these syndromes is necessary to confirm these potential differences.

Comparing these syndromes directly is difficult given the varying degrees of intellectual and physical disability across groups. For example, FXS is characterised by mild-moderate intellectual disability, RTS is characterised by moderate ID, and hearing difficulties are common in DS (Udwin & Dennis, 1995). However, matching participants across groups is likely to reduce the likelihood of each syndrome sample representing their population. Therefore, both a total group (total sample) and matching approach (matched sample) were adopted in this chapter.

The aims of this chapter were:

- To adopt a total sample approach (not matched) to compare the topographies of repetitive behaviour across four groups (RTS, ASD, DS and FXS) and the frequency that these groups engage in these behaviours.
- To repeat these analyses with a matched subset of participants to explore whether the pattern of results remains consistent once age, degree of disability, verbal ability, and degree of mobility are controlled.
- To adopt a total sample approach to compare the percentage of participants in each group who have 'clinically significant' repetitive behaviour as defined by an established questionnaire measure.
- To adopt a total sample approach to explore the relationships between repetitive behaviour and ASD phenomenology (communication and social interaction) while controlling for ability level in each syndrome.
- To adopt a total sample approach to explore the relationship between repetitive behaviour and level of ability in each syndrome.

When comparing the repetitive behaviour profiles of these four syndromes one prediction was that in agreement with previous literature the prevalence of repetitive behaviour would be low in the DS group and that this would be fairly consistent across all topographies of repetitive behaviour. Conversely, given that ASD is behaviourally defined by social/communication deficits and high levels of repetitive behaviour the opposite pattern was predicted to DS - high prevalence and frequency across a broad range of topographies. The range of repetitive behaviours in the FXS profile is predicted to be similar to ASD, although, the frequency of repetitive behaviour may be slightly reduced relative to ASD. RTS, however, is of most interest given the syndrome's reported levels of social engagement coupled with the possibility of autistic-like repetitive behaviours. A more variable profile of repetitive behaviours may be observed in this syndrome that mirrors a combination of aspects from the ASD and DS profiles. In line with previous literature, resistance to change and body stereotypy may be pronounced in RTS. If a variable profile of repetitive behaviour were confirmed in RTS this would lend support for adopting a fine-grained approach to repetitive behaviour. A final prediction was that social communication deficits would be related to repetitive behaviour in ASD and FXS, however, this relationship may be less pronounced in RTS given the fewer anecdotal reports of social communication deficits.

2.2 Method

2.2.1 Recruitment

2601 families of individuals with either Autism Spectrum Disorder (ASD), Rubinstein-Taybi, Fragile-X, or Down syndromes were invited to participate as part of an ongoing large scale questionnaire study investigating cognitive and behavioural difference in rare genetic syndromes and neurodevelopmental disorders (Arron, Oliver, Berg, Moss & Burbidge, 2011; Berg, Arron, Burbidge, Moss & Oliver, 2007; Burbidge et al., 2010; Moss et al., 2009; Moss et al, 2008; Oliver, Berg, Burbidge, Arron & Moss, 2011).

Families were invited to participate through their appropriate support groups. 202 families with RTS were invited through the Rubinstein-Taybi Support Group UK, 500 families of individuals with Down syndrome were invited through the Down Syndrome Association, 432 families of individuals with Fragile-X syndrome were invited through the Fragile-X Society, and 1467 families of individuals with ASD were invited through eight branches of the National Autistic Society in the London and West Midlands area.

2.2.2 Participants

748 participants returned questionnaire packs. Eight participants were excluded from the analysis because they had not completed over 75% of questionnaire items. 41 were excluded because they did not have a confirmed diagnosis of a syndrome, six because they did not provide the age of the person they care for, and thirteen because they were under four years of age (the SCQ was inappropriate for children younger than four). One participant was excluded because they had an additional chromosomal abnormality.

For the ASD group the presence of ASD was checked using the Social Communication Questionnaire (SCQ; Berument, Rutter, Lord, Pickles & Bailey, 1999; previously known as the Autism Screening Questionnaire). 23 participants were excluded because they were in the ASD group but did not reach the criteria for Autism Spectrum Disorder on this questionnaire.

Given that participants were recruited as part of an ongoing study that is investigating cognitive and behavioural difference in a wide range of syndrome groups, nine other syndromes and six other questionnaire measures were excluded from these analyses. Moss et al. (2009) has previously published the data depicting the repetitive behaviour profiles for six of these excluded groups. Moss et al. (2009) has also reported the repetitive behaviour profile for the FXS group that was reanalysed within this current chapter as a comparison group[1].

2.2.2.1 Total Sample.

Ability levels could not be controlled statistically because of the non-parametric nature of the data. To maximise the sample size and the likelihood of each sample representing their given population a total sample approach (as opposed to a matching approach) was adopted for the first stage of the analysis. The percentages of individuals diagnosed by each qualified professional and the demographic characteristics of the groups are displayed in table 2.1 and 2.2 (left hand side) respectively.

Table 2.1
The percentage of individuals diagnosed by professionals.

	Group			
	ASD (N = 241)	FXS (N = 196)	RTS (N = 87)	DS (N = 132)
Paediatrician	56.4%	38.8%	49.4%	84.8%
Clinical Geneticist	0.8%	52.6%	43.7%	4.5%
General Practitioner	10.4%	2%	1.1%	4.5%
Psychiatrist	17.4%	1.5%	-	-
Clinical Psychologist	7.9%	0.5%	1.1%	-
Educational Psychologist	5.4%	0.5%	-	-
Other	1.7%	4.1%	4.7%	6.2%

[1] The FXS group contains five more participants than in the study reported by Moss et al. (2009) because a small subset of FXS participants were added to dataset at a later date.

2.2.2.2 Matched Sample

A subset of 168 participants (42 from each group) formed a matched sample. The sample was matched for verbal ability (speech score on the Wessex), self-help score, and age. Self-help score was employed as an indicator of degree of disability. Participants were also matched for mobility, although this was only partially successful due to the severity of mobility problems in FXS. The groups were not matched for vision and hearing because it was not possible to match a large enough subset of participants if these variables were taken into account.

The matched subsets of participants were included in a secondary analysis to explore whether the pattern of results observed in the total sample analysis remained once these variables had been controlled for. The demographic characteristics of the matched subset are displayed in table 2.2 (right-hand side).

Table 2.2

The demographic characteristics of the groups (ASD, FXS, RTS & DS).

		Full Group Analysis								Matched Group Analysis						
		Group														
		A	B	C	D					A	B	C	D			
		ASD	FXS	RTS	DS	df	F/χ^2	*p* value	Post hoc analyses	ASD	FXS	RTS	DS	F/χ^2	*p* value	Post hoc analyses
N[a]		241	196	87	132					42	42	42	42			
Age[b]	Mean	11.91	17.48	19.62	23.52	3	47.39	<.001	D > B > A; C > A	15.58	15.50	15.86	15.90	.03	.993	-
	SD	5.82	8.93	11.45	12.33					8.35	7.02	7.06	7.47			
	Range	4.10-45.84	6.30-47.49	4.24-59.41	4.37-47.77					6.53-45.84	6.31-34.06	6.60-32.80	4.95-34.63			
Gender[c]	% Male	85.5	100	54.0	43.2		180.24	<.001	B > A > D, C	81	100	57.1	38.1	43.23	<.001	B > A, C, D; A > D
Self help[d]	% Partly able/able[e]	89.6	90.8	77.0	93.1	3	15.82	=.001	A, B, D > C	88.1	90.5	83.3	95.2	3.24	.357	-
Mobility[d]	% Mobile[f]	95.0	72.0	78.0	92.4	3	55.19	<.001	D, A > C, B	92.7	71.4	82.9	88.1	7.69	.053	-

[a] N may vary across the analysis due to missing data.

[b] In years

[c] 100% of FXS were male because the syndrome is X-linked.

[d] Data derived from the Wessex Scale (Kushlick et al. 1973).

[e] Those scoring six or above on the total score of the self help subscale (items g-i).

[f] Those scoring six on the total score of the mobility subscale (items e & f).

Note. A letter missing from the post hoc analyses column indicates that this group was not different from other groups.

Table 2.2 continued.

The demographic characteristics of the groups (ASD, FXS, RTS & DS).

		Total Group Analysis								Matched Group Analysis						
		Group A ASD	B FXS	C RTS	D DS	df	F/χ²	*p* value	Post hoc analyses	A ASD	B FXS	C RTS	D DS	F/χ²	*p* value	Post hoc analyses
Vision[a]	% Normal	96.7	88.1	85.1	63.4	3	78.99	<.001	A > B, C > D	97.6	88.1	78.6	61.9	19.42	<.001	*A > D*[b]; A > C
Hearing[a]	% Normal	97.1	97.4	84.1	65.9	3	104.95	<.001	A, B > C > D	97.6	97.6	78.6	61.9	27.67	<.001	A, B > C, D
Speech[a]	% Verbal	92.5	96.3	84.9	96.2	3	14.53	=.002	B, D > C	90.5	95.2	88.1	97.6	3.59	.309	-
SCQ	Mean score	26.38	20.93	17.03	9.79	3	182.83	<001	A > B > C > D	27.82	23.98	17.25	11.37	50.95	<.001	A, B > C
	(SD)	5.47	6.79	5.32	6.97					5.34	5.49	5.39	8.16			

[a] Data derived from the Wessex Scale (Kushlick et al. 1973)

[b] The difference between ASD and DS approached significance at .007

Note. A letter missing from the post hoc analyses column indicates that this group was not different from other groups.

2.2.3 Measures

2.2.3.1 Demographic Questionnaire

The participants' demographic information was collected using a background questionnaire (see Appendix B). This included information on age, gender, mobility, verbal ability (more than 30 words/signs), primary/secondary diagnosis of a genetic syndrome, and when and by whom the diagnosis was made.

2.2.3.2 **Wessex Scale** (Kushlick, Blunden & Cox, 1973)

The Wessex Scale (see Appendix C) is a short disability rating scale that is completed by someone well acquainted with the person with an intellectual disability i.e. a parent or caregiver. The items evaluate the social and physical attributes of the individual forming five subscales: self help, continence, mobility, speech and literacy. The measure has modest reliability (mean Kappa value of .62 and .54 for overall classification and item level reliability respectively) but it has been as argued to be an effective tool for large-scale questionnaire studies (Palmer & Jenkins, 1982).

2.2.3.3 Repetitive Behaviour Questionnaire (RBQ; Moss et al., 2009)[2]

The repetitive behaviour questionnaire (section 1.3.1 & Appendix A) is a 19 item informant questionnaire that has been designed specifically to measure discrete, observable repetitive behaviours rather than measuring repetitive behaviour at a gross level of description. Each repetitive behaviour is operationally defined and examples of each behaviour are provided. Items are presented alongside a five point Likert scale that is used to measure the rate that the behaviour occurred during the last month (ranging from never to more than once a day). These items form five subscales: stereotyped behaviour, restricted preferences, insistence on sameness, compulsive behaviour and repetitive speech. A full scale verbal and non-verbal score can be calculated. Moss et al. (2009) state that the RBQ is applicable “for use with children and adults with a range of intellectual abilities. It is suitable for use with verbal and non-verbal individuals and for individuals who fall within the autistic spectrum” (p. 576-577). Moss et al. (2009) demonstrated that the RBQ has good inter-rater reliability (Spearman’s coefficients range from .46 to .80; 75% > .60) and good test-retest reliability (range from .61-.93; 53% > .60) at item level. The RBQ also has good concurrent and content validity (.6; $p < .001$) with the repetitive behaviour subscale of the Autism Screening Questionnaire (Berument et al., 1999).

Internal consistency is good at subscale level for stereotyped behaviour and compulsive behaviour ($\alpha > 70$). Internal consistency is lower for the restricted preferences ($\alpha = .50$), repetitive speech ($\alpha = .54$) and insistence on sameness ($\alpha = .65$) subscales. However, Moss et

[2] While direct observation of repetitive behaviours is more objective than the use of questionnaire methodology specific repetitive behaviours are likely to be related to environmental contexts. It would not have been possible to observe the range of repetitive behaviours that an individual engages in over a short period of time. Questionnaire methodology allowed for repetitive behaviour to be captured across a larger time window and for parents to highlight behaviours occurring most frequently, which were likely to be the behaviours having the largest impact on the lives of individuals with RTS and those who support them (for further discussion see section 6.5.2 of the General Discussion).

al. (2009) note that this lower internal consistency is not surprising given that the behaviours are categorised together based on their assumed "function rather than their form" (p. 580) and therefore poor agreement might be expected between items in the same subscale (Moss et al., 2009).

In line with Moss et al. (2009), in the current chapter participants engaging in a repetitive behaviour once or more than once a day (scoring 3 or 4 on an item) were deemed to be scoring above the clinical cut-off for that behaviour. Inter-rater reliability (Kappa) for clinical cut off scores ranges from .23 to 1.0 (94% of items above .40), test-retest reliability ranges from .61 to .93 (52.6% of items above .80) (Moss et al., 2009).

2.2.3.4 Social Communication Questionnaire: Lifetime Version (SCQ; Berument, Rutter, Lord, Pickles & Bailey, 1999; previously the Autism Screening Questionnaire).

The SCQ is a 40 item parent report questionnaire that acts as a screen for the presence of Autism Spectrum Disorder in people with intellectual disabilities (see Appendix D). The life time version was used in this chapter, which assesses an individual based on their developmental history. A total score and three subscales can be calculated: communication, repetitive and stereotyped patterns of behaviour, and social interaction. Individuals who score 15 or above on the SCQ meet the screening cutoff for ASD. Berument et al. (1999) validated the SCQ with 200 children sampled from developmental disorder clinics (sensitivity = 0.85; specificity = 0.75). The total score on the SCQ relates strongly to total score on the Autism Diagnostic Interview - Revised even after age, gender, language ability and performance IQ were taken into account (Lord, Rutter & Couteur, 1994), which suggests the measure has high concurrent validity (Berument, Rutter, Lord, Pickles & Bailey, 1999).

The SCQ was included in the current chapter as a measure of ASD phenomenology to explore relationships between social communication deficits and repetitive behaviour. However, it was anticipated that the repetitive and restricted behaviour subscale of the SCQ would correlate significantly with some items of RBQ because the measures asked about the same repetitive behaviours. Therefore, in the current chapter the repetitive and restricted subscale of the SCQ and the RBQ were not compared.

A proportional communication subscale was used in the current chapter. This was calculated by applying a formula to the communication subscale for non-verbal participants who could not score on the verbal items included in this subscale (proportional formula = score on communication subscale / 8 x 13). The number of non-verbal participants varied across the groups so the proportional formula was employed to avoid the mean score being artificially lowered by the non-verbal participants.

2.3 <u>Data Analysis</u>

Data obtained from the Repetitive Behaviour Questionnaire at subscale and item level violated the assumption of normality (Kolmogorov-Smirnov: $p < .05$). These data could not be transformed so non-parametric analyses of variance were used[3]. The groups were compared at full scale, subscale and item level of the RBQ using Kruskall-Wallis non-parametric analyses of variance and pairwise Mann-Whitney U tests. Given the RBQ has

[3] When analyses of variance are conducted in chapter 3 & 4 of this thesis parametric statistics are initially performed and the results are checked with non-parametric tests; however, only non-parametric analyses of variance are reported in the current chapter because: *all* data presented in this chapter was non-parametric as opposed to being formed of a combination of parametric and non-parametric data; the distribution of scores on the RBQ at item and subscale level were *strongly* skewed (at item level of the RBQ only four possible scores could be obtained leading to data clustering together); the large number of statistics reported here would have been overly complicated by reporting parametric statistics alongside non-parametric statistics. It was also desirable to complete the same analysis as Moss et al. (2009) so that the results reported here could be compared directly at a later date.

item level reliability, analyses were carried out for all items for all groups irrespective of group differences at subscale level. This analysis was an exploratory analysis so a conservative alpha level of .005 was used throughout as opposed to .001 to minimise the chances of making at type II error. The above analysis was conducted for the total sample and also for the matched sample of participants (matched for age, self-help score and verbal ability across groups).

For the total sample, Chi Square tests were conducted to examine differences in the proportion of participants falling above the item level clinical cut-offs for repetitive behaviour on the RBQ. In addition, Pearson's partial correlations were conducted to examine associations between scores on the subscales of the RBQ and the social interaction and communication subscales of the SCQ while controlling for self help score (from the Wessex Scale). Although the data was non-Gaussian Pearson Partial Correlations were deemed appropriate at subscale level for the current data set because the sample size was large. Motulsky (2010) notes that Pearson correlations are robust for large non-Gaussian samples due to Central Limit Theorem. In addition, the data from the subscales were skewed but the skew did not exceed 2.0; Kendall and Stuart (1958), note that it is skewness greater than 2.0 that leads to a reduction in the 'true' size of the Pearson correlation coefficient. Scatter plots were examined for outliers that may affect the Pearson correlations.

Spearman Rho correlations were conducted to explore the link between repetitive behaviour and ability level at item level (self help score of the Wessex Questionnaire). This analysis was carried out at item level so that the possible effect of ability level could be discussed in relation to the item level analysis displayed in figure 2.1. Spearman Rho correlations were conducted as opposed to Pearson correlations because at item level several variables were skewed above 2.0, and several over 4.0.

2.4 Results

2.4.1 Total Sample Analysis.

Analyses were conducted to compare the total samples' scores on subscales and items of the Repetitive Behaviour Questionnaire.

2.4.1.1 Full Scale and Subscale Level Analysis.

The results of these analyses are displayed in table 2.3. The analyses revealed that there was a significant main effect of group for the all subscales and for the verbal and non-verbal full-scale scores (ps $<.001$).

The RTS group have significantly higher scores than DS on the stereotyped behaviour, compulsive behaviour, and verbal full scale subscales, however they do not differ from ASD or FXS on these subscales. The ASD and RTS group sit between DS and FXS on the repetitive speech subscale with significantly higher scores than DS but lower scores than FXS. RTS do not differ from any group on the restricted preferences and insistence on sameness subscales although both ASD and FXS score more highly on these subscales than DS.

2.4.1.2 Item Level Analysis

Significant differences were found for 17 out of 19 items ($p <.005$). Significant differences were absent for tidying up (χ^2 (3) = 6.54, p = .088), and organising objects ($\chi^2(3)$ = 7.43, p = .060). The results of the post hoc analysis are displayed in figure 2.1 in the format devised by

Table 2.3

Total Group Analyses. Mean score, standard deviation, statistical analyses and post hoc analyses at subscale and full scale level of the RBQ.

	Group				df	χ^2	*p* value	Post hoc analyses
	A ASD	B FRX	C RTS	D DS				
	Mean (SD)							
Stereotyped behaviour	6.55 (4.15)	6.47 (4.10)	6.21 (4.27)	2.39 (3.63)		97.13	<.001	ABC>D
Compulsive behaviour	8.27 (7.76)	7.03 (6.93)	7.11 (6.48)	4.29 (6.22)	3	38.18	<.001	ABC>D
Restricted preferences[a]	5.22 (3.63)	5.51 (3.71)	4.57 (3.45)	2.76 (3.02)	3	51.20	<.001	AB>D
Insistence on sameness	3.96 (2.77)	4.3 (2.73)	3.46 (3.07)	2.29 (2.78)	3	43.96	<.001	AB>D
Repetitive speech	5.94 (3.98)	7.14 (3.67)	4.67 (3.69)	2.03 (2.84)	3	121.77	<.001	B>AC>D
Verbal total score[a]	29.23 (16.99)	30.08 (15.50)	26.01 (15.56)	13.25 (14.46)	3	94.49	<.001	ABC>D
Nonverbal total score[b]	22.40 (13.61)	21.80 (12.72)	19.34 (11.82)	9.88 (11.51)	3	93.38	< .001	ABC > D

[a] Analysis only includes participants who are verbal

[b] Score calculated using non-verbal items for all participants

Note. Mean scores reported. Median scores are uninformative with too many zeros

Note. A letter missing from the post hoc analyses column indicates that this group was not different from other groups.

Moss et al. (2009). In this figure a plus sign indicates that the group is scoring significantly higher than another group on an item, whereas a minus sign indicates that the group is scoring significantly lower than another group on that item. Visual inspection of figure 2.1 reveals that people with ASD and FXS have higher overall levels of repetitive behaviour than people with RTS and DS, with DS showing the lowest levels of repetitive behaviour (scoring below all three groups on seven items). ASD scored significantly higher on rituals than FXS and and DS while individuals with FXS scored significantly higher on repetitive questioning than the other groups. RTS had more repetitive questioning and body stereotypy than DS and less restricted conversation and repetitive phrases than ASD and FXS.

2.4.1.3 Chi Square Analysis.

A further aim of this chapter was to examine whether there were group differences in the numbers of participants falling above the cut-off for clinical relevance on each item of the RBQ. The results of this analysis are displayed in table 2.4. Significant differences were found at group level for 13 out of 19 items of the RBQ. The Chi square post hoc analyses supported the findings of the Mann-Whitney U tests in that all significant results were in the same direction. Unlike the Mann-Whitney U analysis, there were no significant group differences for just right behaviour, spotless behaviour, lining up objects, and cleaning.

In a similar manner to ASD and FXS, a significantly higher number of individuals with RTS fell above the clinical cut offs for stereotypy in comparison to DS. In agreement with the previous item level analysis there was a dissociation of verbal items in RTS. RTS did not differ significantly from the ASD group on the repetitive questions item but did differ from this group on the restricted conversation and repetitive phrasing/signing items.

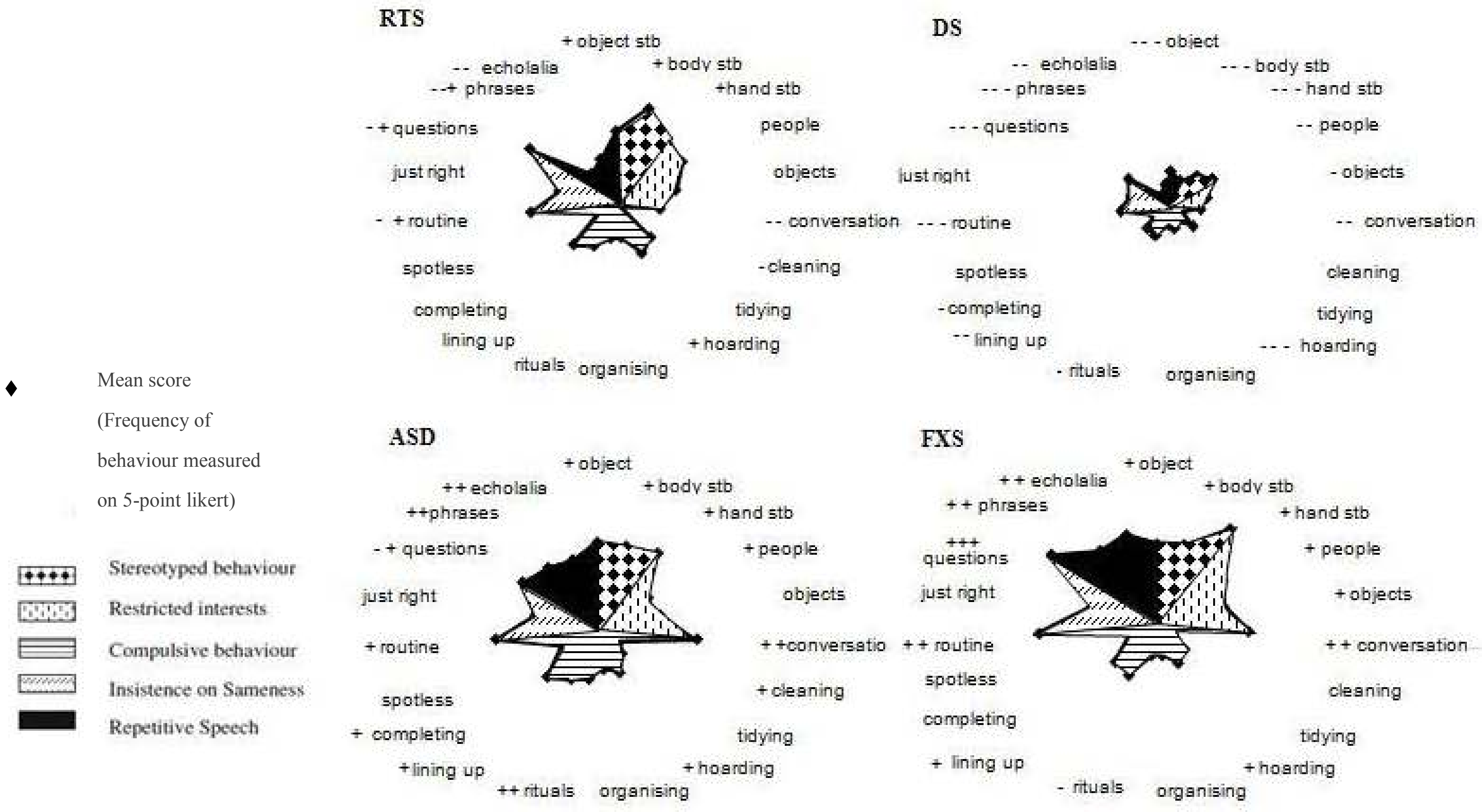

Figure 2.1

The repetitive behaviour profiles of ASD, FXS, RTS and DS at item level. A plus sign indicates that the group had a significantly higher mean score on that item than another group, whereas a minus sign indicates that the group had a significantly lower mean score than another group on that item. *Note.* 5 point likert scale: 0 = never, 1 = once a month, 2 = once a week, 3 = once a day, 4 = more than once a day.

Repetitive Behaviour in ASD, RTS, DS & FXS

Table 2.4

Percentage of participants falling above the cut-off for clinical significance on each item of the RBQ, chi square statistical analyses and post hoc analyses for total participant groups (Autism Spectrum Disorder (ASD), Fragile-X (FXS), Rubinstein-Taybi (RTS) and Down syndromes (DS).

	Group A ASD	B FXS	C RTS	D DS	χ^2	*p* value	Post hoc analyses
		%					
Stereotyped behaviour							
Q1 Object stereotypy	49.4	41.5	40.2	17.8	35.44	<.001	ABC>D
Q2 Body Stereotypy	51.0	46.4	63.2	13.2	68.11	<.001	ABC>D
Q3 Hand stereotypy	54.8	66.7	52.9	23.1	61.12	<.001	ABC>D
Compulsive behaviour							
Q4 Cleaning	13.4	9.2	2.3	6.2	11.41	ns = .010	--
Q5 Tidying	16.7	17.9	25.3	14.6	4.42	ns = .219	--
Q6 Hoarding	23.8	22.1	28.7	9.2	15.27	= .002	ABC > D
Q7 Organising objects	17.6	16.8	18.4	11.5	2.77	ns = .429	--
Q12 Rituals	28.3	17.9	20.7	10.0	18.44	<.001	A > D
Q16 Lining up objects	28.7	29.1	26.4	15.4	9.51	ns = .023	--
Q18 Completing behaviour	39.2	31.3	33.3	16.9	19.49	< .001	AB[b] > D
Q19 Spotless behaviour	20.3	14.8	11.5	10.1	10.46	ns = .106	--
Restricted preferences							
Q8 Attachment to people[a]	28.7	40.6	42.9	22.8	14.82	= .002	BC > D
Q10 Attachment to objects	35.1	39.5	36.8	19.8	14.79	= .002	AB[c] > D
Q13 Restricted conversation[a]	54.3	51.5	25.4	11.4	74.02	< .001	AB>CD
Insistence on sameness							
Q15 Preference for routine	56.2	69.2	49.4	31.0	46.86	<.001	B>A[b]C[c]D
Q17 Just right behaviour	31.4	33.8	34.5	23.8	4.36	ns = .226	--
Repetitive Speech							
Q9 Repetitive questions[a]	47.4	70.9	60.3	25.2	3.39	<.001	B>A>D; C > D
Q11 Repetitive phrases/signing	44.3	51.0	20.0	9.3	78.32	<.001	AB>CD
Q14 Echolalia[a]	43.5	48.3	25.4	11.6	50.62	<.001	B > CD; A > D

[a] Analysis only includes participants who are verbal

[b] The pairwise comparison for ASD and RTS approached significance at .005

[c] The pairwise comparison for RTS and DS approached significance at .006

Note. A letter missing from the post hoc analyses column indicates that this group was not different from other groups.

2.4.1.4 SCQ Analysis

Given that repetitive behaviours have been linked to the social communication deficits associated with autistic phenomenology the relationship between repetitive behaviour and social communication deficits was explored. The results are displayed in table 2.5.

In ASD the SCQ Social Communication Subscale was related to the RBQ Compulsive Behaviour Subscale ($R = .19$, $p =.004$), the RBQ Insistence on Sameness Subscale ($R = .21$, $p =.002$), and Non-Verbal Score ($R = .23$, $p <.001$). The SCQ Social Interaction subscale was related to the RBQ Compulsive Behaviour Subscale ($R = .19$, $p = .004$) and the Non-Verbal Total Score ($R = .21$, $p = .002$). The relationship between the Social Interaction Scale and the RBQ Insistence on Sameness subscale approached significance ($R = .17$, $p = .008$).

In FXS significant relationships were found between the SCQ Communication Subscale and the RBQ Repetitive Use of Language Subscale ($R =.25$, $p = .001$) and the Non Verbal Total Score ($R = .23$, $p = .003$). In FXS highly significant relationships were found between the SCQ Social Interaction Subscale and the RBQ Compulsive Behaviour Subscale ($R = .28$, $p <.001$), the Insistence on Sameness Subscale ($R = .33$, $p <.001$), and RBQ Non Verbal Score ($R = .34$, $p <.001$).

In DS significant relationships were found between the SCQ Communication Subscale and the Stereotyped Behaviour Subscale ($R = .53$, $p <.001$), the Repetitive Use of Language Subscale ($R = .34$ $p =.001$), and the RBQ Non-Verbal Score ($R = .37$, $p < .001$). The relationship between the Communication Subscale with the Compulsive Behaviour Subscale ($R = .27$, $p = .005$), and the Restricted Preferences Subscale ($R = .28$, $p = .006$) approached significance. The Social Interaction Subscale was related to the Stereotyped Behaviour Subscale ($R = .51$, $p < .001$) and the RBQ Non-Verbal Total Score ($R = .30$, $p = .002$).

Table 2.5

Pearson's partial correlations between subscales of the RBQ and the communication and social interaction subscales of the SCQ for total groups (ASD, FXS, RTS & DS). Exploring the relationship between repetitive behaviour and Autistic Phenomenology (controlling for self help score)

Group	Subscales of the Social Communication Questionnaire (SCQ)	RBQ: Stereotyped Behaviour Subscale	RBQ: Compulsive Behaviour Subscale	RBQ: Restricted Preferences Subscale	RBQ: Insistence on Sameness Subscale	RBQ: Repetitive Use of Language Subscale	RBQ Total Non-verbal Score
ASD	SCQ: Communication Subscale	.15	.19**	.10	.21**	.16	.23***
	SCQ: Social Interaction Subscale	.10	.19**	.13	.17*[a]	.09	.21**
FXS	SCQ: Communication Subscale	.14	.17	.13	.17	.25**	.23**
	SCQ: Social Interaction Subscale	.20*[b]	.28***	.19	.33***	.22*[c]	.34***
RTS	SCQ: Communication Subscale	.14	.-.02	.-15	.10	.27	-.03
	SCQ: Social Interaction Subscale	.08	.-.01	.17	.05	-.05	-.05
DS	SCQ: Communication Subscale	.53***	.27*[d]	.28*[e]	.23**	.34**	.37***
	SCQ: Social Interaction Subscale	.51***	.21	.14	.15	.16	.30**

*** Significant at < .001, ** significant at <.005, * significant at <.01

[abcde] = .008, .007, .005, .005 & .006 respectively

While there are relationships between repetitive behaviour and social/communication deficits in ASD, DS and FXS it is notable that in the RTS group no significant relationships were found between the RBQ and the SCQ despite the fact that individuals with RTS engage specific repetitive behaviours at a similar frequency as individuals with ASD.

2.4.1.5 Ability Level and Repetitive Behaviour

Spearman Rho correlations were conducted to explore the relationship between degree of disability (measured by the Wessex Self Help Score) and items from the RBQ. These are displayed in Table 2.6.

In people with ASD ability level was related to object stereotypy, hand stereotypy, body stereotypy, rituals, attachment to objects, repetitive phrase, echolalia and lining up objects. In RTS ability level correlated with object stereotypy and echolalia. In DS object stereotypy, body stereotypy, and attachment to objects, repetitive phrase and echolalia were related to ability level[4]. A similar pattern was observed in FXS whereby object stereotypy, body stereotypy, hand stereotypy repetitive phrase, attachment to people, repetitive questions[5] and echolalia were related to ability level.

Overall it appears that ability level was associated with a wider range of repetitive behaviours in FXS, ASD and DS than in RTS. Stereotypy and repetitive speech items were most frequently associated with ability level; however, there were no relationships between ability level and two repetitive speech items in RTS (repetitive questions and repetitive phrase).

[4] In RTS and DS echolalia and attachment to objects were at $p < .003$ and .001 respectively; all other ps < .001.

[5] In FXS repetitive questions and attachment to people were at $p < .003$ and .001 respectively; all other ps <.001

Table 2.6
Total Group Analyses. Pearson's correlations between the Wessex Self Help Score (measure of degree of disability) and repetitive behaviour at item level of the RBQ.

	Group			
	ASD	FXS	RTS	DS
Stereotyped behaviour				
Q1 Object stereotypy	-.37***	-.33***	-.35**	-.40***
Q2 Body Stereotypy	-.41***	-.38***	-.12	-.32***
Q3 Hand stereotypy	-40***	-.41***	-.26	-.23*[a]
Compulsive behaviour				
Q4 Cleaning	.12	-.08	.13	.18
Q5 Tidying	-.10	-.06	-.10	-.02
Q6 Hoarding	-.04	-.02	.13	.08
Q7 Organising objects	-.11	-.05	-.01	.05
Q12 Rituals	-.22**	-.14	-.00	-.08
Q16 Lining up objects	-.22**	-.10	-.14	.01
Q18 Completing behaviour	-.13	-.07	-.14	-.09
Q19 Spotless behaviour	-.13	.09	-.02	.04
Restricted preferences				
Q8 Attachment to people[a]	-.08	-.25**	.16	-.08
Q10 Attachment to objects	-.26***	-.19*[b]	-.02	-.28**
Q13 Restricted conversation[a]	-.05	-.06	-.12	-.07
Insistence on sameness				
Q15 Preference for routine	-.08	-.12	-.04	.10
Q17 Just right behaviour	-.17	-.06	-.06	-.04
Repetitive Speech				
Q9 Repetitive questions	-.13	-.23**	-.16	-.24*[c]
Q 11 Repetitive phrases/signing	-.19**	-.27***	-.14	-.31***
Q 14 Echolalia	-.32***	-.29***	-.36**	-.28**

*** Significant at <.001** Significant at <.005
* Significant at < .01
[a b c] Significant at.008, .009 & .008 . respectively

There was an absence of relationships across all groups for the insistence of sameness subscale the majority of items from the compulsive behaviour subscale, and the restricted conversation item.

2.4.2 Interim Discussion

The group analyses were conducted to compare the repetitive behaviour profiles of RTS, ASD, FXS and DS. Further aims were to explore whether dissociations between different repetitive behaviour items would be observed within the groups, to explore the relationship between repetitive behaviour and the social and communication deficits associated with ASD, and to explore the association between degree of disability and the repetitive behaviour observed in each group. A total sample approach was adopted for these analyses whereby the groups were not matched to control for age and ability. This approach was adopted to capture the nature of repetitive behaviour in each group in its entirety, rather than for a subset of individuals.

One prediction was there would be heightened general specificity for repetitive behaviour in ASD relative to other syndrome groups. In relation to RTS and DS this prediction was confirmed, however, repetitive speech (in particular repetitive questioning) seems particularly pronounced in FXS with this syndrome engaging in heightened amounts of questioning relative DS and ASD. Furthermore, a large proportion of the FXS group fall above the clinical cut-off for this behaviour relative to the other groups. Despite generally lower levels of repetitive behaviour in RTS, repetitive questioning is also pronounced in RTS who have a similar level of questioning as ASD. The RTS profile is of interest because whilst the repetitive questioning item is pronounced in this syndrome, other verbal behaviours such as restricted conversation, repetitive phrase and echolalia are lower than FXS and ASD indicating a dissociation within the subclass of verbal repetitive behaviour. Body stereotypy is also high in RTS in comparison to DS and people with RTS seem to show comparable body stereotypy to that observed in ASD.

Although these analyses capture the entire profile of repetitive behaviour in the groups, it is not certain whether variation in repetitive behaviour across the groups arises because of differences in the groups' demographic characteristics. For example, DS is the oldest and most able group, and this may underpin the observed low levels of repetitive behaviour. In contrast, ASD are the youngest group and RTS are the least able group, which may be exaggerating repetitive behaviours. Poor verbal ability in RTS may lead to repetitive questions rather than repetitive phrase or conversation because questions require less developed verbal skills. In addition, a number of relationships have been demonstrated between age/ability and stereotypy. Therefore, the lower level of ability in the RTS group may be leading to more stereotypy in this group. In FXS, mobility problems may underpin heightened repetitive behaviours, particularly if the repetitive behaviours were functional, i.e. using repetitive questions to elicit social interaction with caregivers. In order to address this problem, secondary analyses were conducted with matched groups of participants.

2.4.3 Matched Sample Analysis

2.4.3.1 Full Scale and Subscale Level Analysis.

The results of the full scale and subscale analysis between participant groups are displayed in table 2.7. The results indicated that there was an overall significant difference for all five subscales of the RBQ and for the total verbal score ($p < .001$).

2.4.3.2 Item Level Analysis.

The results of the item level analysis are displayed in table 2.8. There were significant differences between groups for body and hand stereotypy, restricted conversation, preference for routine, repetitive phrases or signing ($ps < .001$), and echolalia ($p = .002$). Differences between groups for object stereotypy and repetitive questions were approaching significant at $p= .005$ so post hoc analyses were also conducted on these items.

Post hoc analyses revealed that Down syndrome had significantly lower scores on stereotypy items in comparison to the other groups. ASD had a higher score than DS on body and object stereotypy, FXS scored more highly on hand and body stereotypy, and RTS scored more highly on body stereotypy than DS. ASD, FXS and RTS did not differ in their levels of stereotypy. ASD and FXS had significantly higher scores on items measuring repetitive phrase than RTS and DS, and higher scores for echolalia and preference for routine than DS.

Table 2.7

Matched Sample Analyses. Mean score, standard deviation, statistical analyses and post hoc analyses at subscale and full scale level of the RBQ.

	Group A ASD	B FRX	C RTS	D DS	df	χ^2	*p* value	Post hoc analyses
	Mean (SD)							
Stereotyped behaviour	7.65 (4.09)	6.95 (4.17)	5.97 (4.20)	3.07 (3.98)		25.66	<.001	A, B, C > D
Compulsive behaviour	8.16 (6.78)	7.99 (7.25)	7.26 (6.48)	3.39 (4.95)	3	17.12	=.001	A, B, C >D
Restricted preferences[a]	6.11 (2.77)	5.51 (3.71)	4.48 (3.20)	3.28 (3.29)	3	15.50	=.001	A, B > D
Insistence on sameness	4.41 (2.77)	4.49 (2.67)	3.30 (3.23)	1.88 (2.63)	3	20.23	<.001	A, B >D
Repetitive speech	6.80 (3.32)	7.58 (3.21)	4.81 (3.45)	2.76 (2.72)	3	32.84	<.001	A, B > D; B > C
Verbal total score[a]	33.46 (15.46)	31.35 (14.52)	25.87 (15.09)	13.87 (13.87)	3	32.25	<.001	A, B > D
Nonverbal total score[b]	24.25 (12.46)	23.44 (13.17)	18.85 (12.14)	9.78 (10.47)	3	33.94	<.001	A, B, C > D

[a] Analysis only includes participants who are verbal

[b] Score calculated from non-verbal items for all participants

Note. Mean scores reported. Median scores are uninformative with too many zeros

Note. A letter missing from the post hoc analyses column indicates that this group was not different from other groups.

Table 2.8 *Matched Sample Analyses. Mean score, standard deviation, statistical analyses and post hoc analyses at item level of the RBQ.*

	Group A ASD	B FXS	C RTS	D DS	χ^2	*p* value	Post hoc analyses
Stereotyped behaviour							
Q1 Object stereotypy	2.63 (1.63)	1.86 (1.72)	1.67 (1.78)	1.24 (1.72)	12.86	.005	A > D
Q2 Body Stereotypy	2.38 (1.78)	2.29 (1.72)	2.45 (1.88)	0.86 (1.54)	21.56	<.001	A, B > D; C > D
Q3 Hand stereotypy	2.64 (1.69)	2.81 (1.58)	1.86 (1.88)	0.98 (1.60)	25.84	<.001	A, B > D
Compulsive behaviour							
Q4 Cleaning	0.74 (1.45)	0.62 (1.27)	.02 (.15)	0.28 (0.97)	11.92	ns. .008	-
Q5 Tidying	0.80 (1.27)	0.88 (1.29)	1.05 (1.48)	.43 (1.13)	6.60	ns. .086	-
Q6 Hoarding	0.88 (1.45)	0.79 (1.39)	1.21 (1.68)	.31 (.98)	9.61	ns. .022	-
Q7 Organising objects	.83 (1.41)	0.86 (1.44)	0.93 (1.49)	.60 (1.23)	1.11	ns. .774	-
Q12 Rituals	1.26 (1.70)	0.81 (1.55)	0.86 (1.52)	.39 (1.07)	7.40	ns. .060	-
Q16 Lining up objects	1.31 (1.64)	1.42 (1.70)	1.43 (1.70)	.78 (1.35)	4.13	ns. .248	-
Q18 Completing behaviour	1.52 (1.67)	1.60 (1.75)	1.36 (1.68)	.68 (1.39)	7.76	ns. .051	-
Q19 Spotless behaviour	0.81 (1.42)	1.02 (1.63)	.40 (1.04)	.27 (.90)	7.47	ns. .058	-
Restricted preferences							
Q8 Attachment to people[a]	1.54 (1.72)	1.82 (1.63)	1.77 (1.56)	1.38 (1.57)	1.54	ns. .674	-
Q10 Attachment to objects	1.81 (1.86)	1.51 (1.81)	1.48 (1.80)	1.19 (1.63)	2.78	ns. .427	-
Q13 Restricted conversation[a]	2.63 (1.65)	2.64 (1.60)	1.23 (1.65)	0.79 (1.42)	30.74	<.001	A, B > C, D
Insistence on sameness							
Q15 Preference for routine	2.69 (1.65)	2.78 (1.59)	1.97 (1.80)	1.05 (1.56)	22.61	< .001	A, B > D
Q17 Just right behaviour	1.66 (1.64)	1.67 (1.56)	1.33 (1.76)	0.83 (1.39)	8.10	ns. .044	-
Repetitive Speech							
Q9 Repetitive questions[a]	2.60 (1.71)	3.27 (1.23)	2.61 (1.70)	1.87 (1.67)	12.44	.005	B > D
Q11 Repetitive phrases/signing	2.09 (1.76)	2.43 (1.71)	.58 (1.16)	0.24 (0.89)	49.52	<.001	A, B > C, D
Q14 Echolalia[a]	1.91 (1.72)	2.12 (1.62)	1.55 (1.80)	0.68 (1.32)	15.37	.002	A, B > D

[a] Analysis only includes participants who are verbal.

Significant differences were only found between FXS and DS for the final verbal item, repetitive questioning, with FXS having significantly higher scores on this item. Inspection of the means suggests that RTS has comparable levels of repetitive questioning to ASD as seen in the group analysis.

2.5 Discussion

In this chapter the profile of repetitive behaviour for Rubinstein-Taybi syndrome was explored in relation to the profiles of Autism Spectrum Disorder, Fragile-X and Down syndromes. It was hypothesised that repetitive behaviour profiles would be heterogeneous and that ASD and FXS would have high levels of repetitive behaviour, particularly in comparison to the DS. It was also hypothesised that specific repetitive behaviours would be pronounced in specific syndrome groups and that this would lend support for studying repetitive behaviour at a fine-grained level of description. It was predicted that high levels of body stereotypy and resistance to change would be observed in RTS in agreement with previous reports (Stevens et al., 1990). Finally, relationships between repetitive behaviour and social/communication deficits associated with ASD, and repetitive behaviour and ability level were explored. A descriptive summary of the key findings is displayed in table 2.9.

Table 2.9
Descriptive summary of the key findings for ASD, FXS, RTS & DS

	Group			
	ASD	FXS	RTS	DS
Degree of repetitive behaviour	High	High	Moderate	Low
Degree of social/communication deficit (SCQ Score)	High	High	Moderate	Low
Relationship between repetitive behaviour and social/communication deficits	Present	Present	Absent	Present

Analyses were conducted initially with the total sample. Individuals with ASD were found to engage in more repetitive behaviour than Down syndrome at subscale and item level. At item level ASD also engage in more restricted conversation, repetitive phrase and echolalia than RTS. However, ASD do not have significantly higher levels of repetitive behaviour than FXS at subscale or item level except for the ritualistic behaviour item. Conversely, FXS engage in higher rates of repetitive questions than ASD and there is a significantly higher proportion of individuals with FXS falling above the clinical cut off for repetitive questioning and preference for routine than individuals with ASD.

There were no differences between ASD and FXS when this analysis was repeated with the matched sample; however, ASD and FXS still had significantly higher scores than DS on more than six repetitive behaviour items and higher scores than RTS on two items (repetitive phrase and restricted conversation). This is in agreement with reports that repetitive behaviour occurs frequently in ASD, but suggests it might not be heightened above that observed in certain disorders groups (i.e. FXS).

The disappearance of significant differences between FXS and ASD in the matched sample analyses may have occurred because the original differences were a product of differing age and mobility levels across the groups, or alternatively, these differences may have been lost due to lack of power once the sample size was reduced. However, the findings from the total sample analyses have the most external validity given the total sample is more likely to represent the characteristics of individuals with these syndromes in the wider population. Thus, individuals with FXS in the wider population may engage in more repetitive questioning than individuals with ASD.

It was predicted that the DS group would have lower scores on repetitive behaviours items overall and this was confirmed. The repetitive behaviour profile for DS is in stark contrast to the ASD and FXS in all analyses. Individuals with DS in the total sample engaged in a range of repetitive behaviours less frequently than at least two other groups. In the matched sample the DS group remained significantly lower on body, hand and object stereotypy, restricted conversation, preference for routine, repetitive phrase and echolalia compared to at least two other groups. This is despite the fact the DS group had poorer vision and hearing, a factor that is a known risk marker for repetitive behaviour (Tröster, Brambring & Beelman, 1991; Murdoch, 1996; Bachara & Phelan, 1980). Although, it is arguable that echolalia and repetitive phrase are less likely if an individual cannot hear phrases in order to repeat them.

It was also predicted that there would be specificity within the syndrome groups, particularly in RTS where heightened resistance to change and body stereotypy were anticipated. An uneven profile of repetitive behaviours was found for RTS. The total RTS sample engaged in body stereotypy and repetitive questioning at a similar level to that observed in the ASD sample. This was irrespective of the RTS group scoring below ASD on the SCQ total score and the absence of relationships between repetitive behaviour and the communication/social impairments associated with ASD. RTS also had heightened scores on the adherence to routine item relative to DS, which is in agreement with anecdotal reports of resistance to change in RTS. However, other behaviours such as restricted conversation, repetitive phrase and echolalia occur far less frequently in RTS and did not differ significantly from DS. The pattern of results observed in RTS suggests that repetitive behaviours can be dissociated at a fine grained level of description. If repetitive vocalisations had been grouped together it would have obscured this pattern in RTS.

The matched group analyses revealed that even when age, intellectual disability and verbal ability were controlled RTS had comparable levels of body stereotypy to ASD (significantly more than in DS). The RTS group engage in restricted conversation and repetitive phrase less frequently than both ASD and FXS, and although scores on the repetitive questioning item were no longer significantly heightened in comparison to DS the scores are not significantly lower than ASD and FXS either. Inspection of the mean score on the repetitive behaviour item reveals that RTS have almost exactly the same mean and standard deviation on this item as ASD. Taken together these results continue to support the dissociation of repetitive behaviours within groups, along with varying generalised levels of repetitive behaviour across groups.

The relationship between repetitive behaviours and the social communication deficits associated with ASD were also explored. It was surprising that the strongest relationships between social/communication deficits and repetitive behaviour were found for FXS and DS and not for the ASD group. However, this pattern is likely to be a product of the wider range of scores obtained in the FXS and DS groups on the SCQ. The range of scores suggest there are more individuals obtaining low scores on the RBQ and low scores on SCQ in these groups, and this may have given rise to a stronger, more linear relationship between the measures.

Repetitive behaviour in RTS did not correlate with the social/communication deficits measured by the SCQ. This was in line with the prediction and is consistent with anecdotal reports of RTS as "sociable" (Goots & Liemohn, 1977; Baxter & Beer, 1992; Stevens et al., 1990). This pattern of results supports the possibility of dissociation to the triad of impairments because, despite the absence of relationships between repetitive behaviour and social communication deficits in RTS, individuals with RTS engaged in topographies of repetitive behaviours similar to those observed in ASD. Furthermore, there is evidence that some of these behaviours occur at a similar frequency to those observed ASD (e.g. repetitive questions and body stereotypy). While RTS has highly specific heightened repetitive behaviours the syndrome appears to sit between disorder groups because RTS also shares characteristics of the repetitive behaviour and social profile of DS including low frequency occurrences of specific repetitive behaviour and fewer social/communication deficits.

The implications of a fractionated triad of impairments have been discussed by Happe and Ronald (2008). In particular, a fractionated triad indicates the likelihood of different underlying causes for each part of the triad and the importance of assessing the components of the triad separately (see section 6.3.1 of general discussion for expanded discussion). The current results further highlight the importance of assessing the triad in a range of clinical groups. Furthermore, because specific repetitive behaviours were found to occur at a similar frequency in ASD and other rare genetic syndromes, it is possible that the mechanisms that underpin these repetitive behaviours are not distinct to ASD.

Finally, it was found that some repetitive behaviours, namely, stereotypy, repetitive phrases/signing and echolalia may be partly related to degree of intellectual disability. However, it is worth noting these behaviours are unlikely be related solely to ability level given the variation found in repetitive behaviour in the matched sample. For example, there were significant differences between the matched samples for stereotypy. There is also some variation across syndrome groups in respect to the degree to which repetitive behaviours correlate with ability level (only object stereotypy and echolalia are related to ability level in RTS). Furthermore, a large number of repetitive behaviours do not correlate with age or ability in any of the groups although they relationships are in the anticipated direction.

It can be concluded that repetitive behaviour varies across disorders and that specific repetitive behaviours may be associated with specific disorders. While some repetitive behaviours correlate with age, others do not. This supports the possibility of differing underlying aetiology and developmental trajectories for specific repetitive behaviours. It is too simplistic to argue that all repetitive behaviours decrease with age, nor is it the case that if a person has one repetitive behaviour they are guaranteed to have the others. These findings converge with those of Moss et al. (2009) who demonstrated the heterogeneous nature of repetitive behaviour profiles. These findings also lend support to Turner (1997) who argued that grouping behaviours together serves to mask subtle differences that need to be observed if the underlying mechanisms of these behaviours are to be understood. Finally, there is evidence to support a relationship between social/communication deficits and repetitive behaviour in ASD, FXS & DS. This relationship was absent in RTS, indicating that these behaviours may be distinct from ASD phenomenology. In ASD, the relationship between social/communication and repetitive behaviour was weaker than expected; however, both repetitive behaviours and social communication deficits were high in ASD.

A caveat of this study is the low response rate from families of individuals with ASD and DS. This is likely to have occurred because these syndrome groups are more likely to be with invited to participate in studies like the one reported in this chapter. It may be that families of individuals with less severe difficulties had fewer care-giving demands and more time to respond, thus reducing the differences between FXS and ASD and increasing the chances of finding significantly less behaviour in DS. This seems unlikely for DS as the results presented in this chapter concur with the previous reports of DS (Hepburn & MacLean, 2009). In addition, it could be argued that the opposite pattern of responding should be expected from families of individuals with ASD in that families with the greatest need are more likely to be motivated to respond.

A final caveat is that while behaviour appears to occur at a similar frequency in ASD and FXS it may be that differences would emerge if severity of the behaviour was measured or if the scale on the RBQ was expanded to allow for more frequent behaviour to be reported (i.e. more than once a hour). Despite this there still appears to be a good range of scores on the RBQ scale suggesting the measure is capturing the differences between the groups.

In this chapter it was demonstrated that RTS have a dissociated repetitive behaviour profile relative to ASD, FXS and DS. The repetitive behaviour observed in RTS was not found to be related to ASD phenomenology and ability level was not related to the majority of behaviours observed in this group. This suggests that an alternative explanation for repetitive behaviour is warranted. In the chapter five of this thesis the repetitive behaviour profile of RTS is revisited and the links between these behaviours and executive function are explored. Prior to chapter five, the development of an executive function battery is described (chapter three) and the developmental trajectories of the executive functions are examined (chapter four).

CHAPTER 3

Development of an Executive Function Battery for Individuals with Intellectual Disabilities

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3.1 <u>Preface</u>

In chapter 1 the constructs repetitive behaviour and executive function (EF) were described and evidence for the executive dysfunction hypothesis of repetitive behaviour was presented. It was argued that EFs develop throughout childhood and a developmental trajectory approach to studying cognition in rare genetic syndromes would supplement a traditional matching approach. In chapter 2, a total group and matching approach were utilised to explore the repetitive behaviour profile of Rubinstein-Taybi syndrome (RTS) relative to Autism Spectrum Disorder and two other genetic syndromes (Down & Fragile-X syndromes). It was found that RTS have an uneven profile of repetitive behaviour with a clear dissociation between repetitive speech items. Repetitive behaviour was heightened in ASD and FXS relative to DS, and the RTS profile aligned with elements of both the DS and ASD profiles. The RTS profile was not related to social and communication deficits characteristic of ASD. In the following chapter the focus changes from repetitive behaviour to the development of the EFs. A description of how an EF battery was compiled and modified for use with an intellectual disability (ID) population is provided. The developmental literature is drawn upon in this chapter to justify the selection of tests that measure developmental changes in EF.

3.2 Introduction

To date, there are very few batteries of tests that are suitable for studying the development of executive function (EF) across the range of intellectual disability (ID). In the current chapter the limitations of existing batteries are discussed and literature on EF tests is reviewed. The development of an EF test battery for individuals with ID is then described, alongside pilot studies that were conducted to ascertain whether modifications to the tests altered their difficulty. Although the battery developed for this thesis is suitable for individuals with ID generally, it was designed with Rubinstein-Taybi syndrome (RTS) in mind so that associations between EF and repetitive behaviour in this syndrome could be explored later.

An appropriate battery for studying the development of EF in individuals with RTS needed to have a low floor, span the ability level of this population, and measure clearly defined executive constructs (i.e. working memory, inhibition and task shifting). The batteries that are often used to assess EF in children are displayed in table 3.1 along with the limitations of these batteries. A number of these batteries are not suitable for individuals with a range of abilities because they do not cater for younger children (e.g. D-KEFS and TeACH). Those batteries that do have lower floors are limited because they either use parental report rather than direct assessment, measure EF as a global construct rather than breaking it into individual components, miss out key components of EF such as working memory, or simply do not include enough tests of an EF component to cater for participants with a wide range of abilities. Given these observations a new battery of tests needed to be compiled and developed that would be suitable for measuring inhibition, working memory and task shifting in an ID population.

There are two types of tests that can be used to measure EF: computerised tests and live tests. At the time when the battery for this thesis was developed, a number of computerised batteries were being developed for typically developing (TD) preschoolers and older children (A. Diamond, personal communication, April, 2, 2008). However, computerised tests are less likely to be suitable for very young children or those who have a severe ID because the tests have a large number of trials, and more crucially, may be less engaging than interacting directly with a researcher[1]. Furthermore, robust normative data had not been collected for these computerised tests at the time of the battery development. Live tests were employed to overcome a number of the difficulties with computerised tests. It was felt that these tests would be more engaging for people with RTS because they involve interaction with an experimenter, are usually short in duration and do not require a large number of repetitive trials. They are also frequently cited within the literature. Indeed, because live tests are published throughout literature, dissemination of results obtained from these tests will reach a wide audience in a format that is easily comparable to previous studies conducted with TD children.

As noted in section 1.6.1, a key aim of this thesis was to employ a developmental trajectory approach to studying the development of the EFs in RTS; however, one difficulty of utilising live tests when following this approach is that it is preferable that one test would be used to measure a particular construct across all ages and abilities (Thomas et al., 2009). There are very few live EF tests, particularly for inhibition, that span a wide range of ability levels in younger children. Indeed, live tests of inhibition are usually only appropriate for discrete

[1] These difficulties were confirmed after informally piloting a subsection of computerised tests (provided by A. Diamond, personal communication, April, 2, 2008) with several children and adults with RTS.

Table 3.1

Age range, EFs measured and limitations of existing EF batteries for children.

Battery	Age Range	EFs Measured	Limitations
The Test of Everyday Attention for Children TEA-Ch (Manly, Robertson, Anderson, & Nimmo-Smith; 1999)	6-16 years	Shifting and Inhibition	Cannot be used to test EF below a mental age of 6 years. Does not contain a test of working memory.
CANTAB (Cambridge Cognition Ltd; 2006)	4yrs +	Shifting, spatial working memory, planning, inhibition,	Computerised battery that may not motivate young children with ID. Not suitable for participants with a mental age below 4 years.
NEPSY-II (Korkman, Kirk & Kemp (2007)	3-16 years	Global EF, inhibition subset, planning subset	Gives a global measure of EF rather than breaking the components down. Only has an inhibition subtest. Limited number of inhibition tests for younger children.
Behaviour Rating Inventory of Executive Functuon (Preschool Version) (BRIEF-P; Gioia, Espy, Isquith, 2002)	2-5 years	Inhibition, planning, working memory, emotional regulation and shifting.	Parental rating form rather than direct assessment may be subject to bias.
EF battery for 3 year olds (Willoughby, Blair, Wirth & Greenberg; (2010)	3 years	Inhibition, working memory and planning.	Battery not available at the time of testing. Contains just five tests of EF which are suitable for young children but the battery does not cater for older children.
Delis-Kaplan Executive Function Scale (D-KEFS; Delis, Kaplan & Kramer, 2001)	8-89 years	Assesses inhibition, problem solving, planning, impulse control, concept formation, abstract thinking and creativity.	Does not contain a separate measure of working memory. Is not suitable for participants with a mental age below eight years.

developmental age bands (Carlson, 2005). Therefore, for this thesis it was necessary to select a number of tests that span a range of developmental ages to ensure that the battery was suitable for as many participants as possible.

While it is particularly important to keep the floor of a test battery as low as possible, ceiling effects should also be avoided. However, it was decided that if a number of older participants or participants with mild ID were at ceiling on the battery, the age at which individuals with RTS reach ceiling on these tasks could be compared to TD children and still yield worthwhile findings. Hence, it was decided that the battery should cover a mental age range of at least 2.5 years to 5 years because generally a moderate degree of ID is reported in RTS syndrome and it was anticipated that a large proportion of the sample would fall in this mental age range (Hennekam, 2006). Furthermore, tasks that cover the mental age band of 3-5 years are of interest because it is during this age bracket that rapid development of EFs is observed in TD children (Simpson & Riggs, 2005).

As previously discussed, a final limitation of live EF tests is that it is very difficult to get a pure task that measures one EF, even for micro level EFs. EF tests are concerned with higher level processes and often a test of one EF component will make secondary demands on another EF (Rabbitt, 1997). For example, when an individual is required to hold the rules in mind for an inhibition task they will employ working memory. However, individual tasks are still predominantly associated with the measurement of one component of EF in the literature. By compiling a large battery of tests it was anticipated that relationships between EFs could be explored in later chapters of this thesis so that underlying causes of task failure could be extrapolated.

The final criteria for tests included in a battery were:

- The battery should be suitable for individuals with a severe to a mild ID, some of who will have very young mental ages.
- Tasks should be included with a view to reducing floor/ceiling effects.
- The developmental period of 2.5 - 5 years (mental age) should be covered sufficiently.
- Tasks should be suitable for individuals with RTS, many of whom are motivated by social contact.
- Instructions need to be simplified and there should be minimal demands on verbal responses as expressive language may be compromised.
- Tests need to be quick to administer so that a large range of tasks can be included in the battery.

In the following section of this chapter a review is presented of tests that have been utilised (primarily by developmental psychologists) to study EFs in TD children. These will be referred to as tasks from this point forward in line with the TD literature. This review was conducted to identity tasks that could be incorporated within a developmental trajectory framework to measure EFs in individuals with RTS. The main focus of this review is inhibition, working memory and shifting, although emotional regulation will also be discussed in relation to inhibition, the reasons for which are also discussed below.

3.3 <u>Review of Executive Function Tasks</u>

3.3.1 Inhibition Tasks

Two types of inhibition are frequently cited within the developmental literature: conflict inhibition and delay inhibition (Carlson, 2005; Garon, Bryson & Smith, 2008). Tasks that measure these two types of inhibition have been categorised as simple or complex inhibition tasks depending on their working memory demands (Garon, et al. 2008).

Garon, et al. (2008) argued that delay inhibition tasks are simple response inhibition tasks because they put minimal demands on working memory. In delay inhibition tasks children are asked to withhold a prepotent response over a delay. For example, in the Gift Delay task a child is left alone with a gift bag and asked not to touch it while the experimenter searches outside the room for a bow (Kochanska, Murray & Harlan, 2000). Peeking into the bag and touching the gift are coded. Carlson (2005) demonstrated that the majority of TD children are able to refrain from peeking into the bag or touching the gift at 24 months (approximately 72% of children). However, many five year old children cannot pass a harder version of this task, in which children are told not to peek at the experimenter whilst she wraps a present noisily behind them. Despite this task being classified as a simple inhibition task (low working memory demands), there is still a memory component because children have to remember not to look at or touch the gift.

Conflict inhibition tasks differ from delay inhibition tasks because they require participants to *produce* a counter-intuitive response rather than simply *withhold* a response over a given period of time (Garon et al. 2008). For example, one of the simplest tests of conflict inhibition (low working memory demands) for infants is the Object Retrieval task whereby a child sees an object inside a clear container and must detour their hand to an opening in the side of the container in order to retrieve the toy (Diamond, 1990; Diamond, 1991). Direct reaching (the prepotent response) results in the child's hand touching the barrier in front of the object and it has been argued that failure on this task is due to poor inhibitory motor control (Diamond, 1990). 12 month-olds pass this task.

At 24 months tasks such as the Shape Stroop, Tower and Reverse Categorisation have been suggested to be the most appropriate conflict inhibition tasks (Carlson, 2005; Kochanska, et al. 2000; Carlson, Mandell & Williams 2004; Kochanska, Murray, Jacques, Koenig & Vandegeest, 1996). In the Shape Stroop the experimenter calls out names of fruits and children are required to point to corresponding 'small' pictures of these fruits and to avoid pointing to larger (more salient) pictures of these fruits, on which the small fruits are superimposed. During the Tower task children take turns with the experimenter to place blocks to build a tower. Children must inhibit the desire to place the next block when the experimenter hesitates on their turn. When completing the Reverse Categorisation children are required to sort big blocks into a small bucket and little blocks into a big bucket[2]. Of these tasks the Shape Stroop is a simple inhibition task because it does not require participants to hold complex task rules in mind, however, the Tower task and Reverse Categorisation are classified as complex inhibition tasks because the participant is required to remember the rules of the task (simple working memory demands).

[2] *The Reverse Categorisation task has been administered in the literature in a format that arguably adds a shifting component (for example in Carlson, Mandell & Williams, 2004). This is because the participant is first required to sort objects into their congruent buckets (big and small objects into corresponding big and small buckets) before they sort the big and small objects into the incongruent buckets. Thus, to be successful participants must shift from the previously reinforced set to the incongruent way of sorting.*

The majority of children pass the Shape Stroop and Reverse Categorisation when they are three years old so tasks such as the Grass-Snow task are more appropriate (Carlson & Moses, 2001). In the Grass-Snow task children are required to point to a green card when the experimenter says snow and a white card when the experimenter says grass. Other tasks that are appropriate for children aged 3-6 include the Bear-Dragon (a simplified version of the children's game 'Simon Says'), the Black-White Stroop (say black when the experimenter shows a white card and vice versa), and Luria's hand game (make a fist when the experimenter points and point when the experimenter makes a fist) (Reed, Pien & Rothbart, 1984; Simpson & Riggs, 2005; Luria, Pribram & Homskaya, 1964). Garon et al. (2008) categorised all conflict inhibition tasks for older children as complex inhibition tasks, because participants are required to hold the rules of the task in mind.

3.3.2 Working Memory Tasks

As noted in section 1.4.2 working memory is often divided into two slave systems: the visuo-spatial sketchpad that stores visual information and a phonological loop that stores verbal information. The separation of these two slave systems is supported by studies that demonstrate that these systems have different developmental pathways (Gathercole, 1998).

A further distinction is frequently made between simply holding information in working memory, and the more complex ability of monitoring and updating the information that is being held. This distinction is supported by neuroimaging studies that suggest different areas of the brain are activated when individuals complete tasks that require them to simply hold information in mind or monitor and update that information (Smith & Jonides, 1998). It is often debated whether working memory tasks that simply involve holding information in mind should be classified as short term memory tasks (for example, Engle, Laughlin, Tuholski & Conway, 1999). This is largely a matter of definition and, in line with Garon et al. (2008), in the current thesis the distinction is adopted between 'simple' working memory tasks (not requiring manipulation of information) such as span tasks, and 'complex' working memory tasks that do require manipulation of information.

The ability to hold an object in mind develops before children are six months old (see Palphrey et al., 2004) and tasks have been developed to measure working memory in infants. Garon (2008) notes that the task used most frequently to assess infants' working memory is the delayed reaching task. In this task the infant watches as an item is hidden in one of two locations. After a delay the child is encouraged to retrieve the item. If they can retrieve the item on three consecutive trials the length of the delay between observing the object being hidden and retrieving the object is increased. Infants' working memory improves between six and twelve months on this task (Diamond & Doar, 1989). For example, Pelphrey et al. (2004) tested a large sample of infants aged 5-12 months and varied the delay between presentation and search, as well as the number of hiding locations. The authors demonstrated that whilst there was very little improvement between 5-8 months, the percentage of correct reaches increased between 8-12 months.

At two years of age some of the most frequently used phonological and visuo-spatial working memory tests for measuring simply how much an individual can hold in mind are span tasks. Span tasks are usually digit or word span tasks (to measure phonological working memory) and or box-tapping tasks such as the Corsi Blocks task (to measure visuo-spatial working memory) (Carlson, Moses, & Breton, 2002; Pickering, Gathercole & Peaker, 1998). In the verbal span tasks the experimenter says a string of words and the participant has to hold these words in mind and then repeat them back to the experimenter. Span length can be measured by increasing the lengths of the strings of words until the participant can no longer successfully recall them. The Corsi Blocks task follows a similar format other than that the participant watches as the experimenter taps a sequence of blocks on a block board. Participants respond by tapping the same sequence.

Studies have demonstrated that children not only improve on span tasks between the ages of three and five years, but also after the preschool years (Dempster, 1981). Span tasks are useful because they are quick and easy to administer and, because the length of the string of information can be indefinitely increased, they are suitable for young children through to adults. These tasks allow for improvements to be tracked throughout development.

A variation of these span tasks that require monitoring and updating are backward span tasks. In these tasks the participant is required to repeat the string of words or actions to the researcher backwards. Whilst these tasks have been useful for studying monitoring and updating in TD children it is likely that the instructions for backward span tasks may be too complex for most individuals with RTS to understand (L. Collis, 2008, personal communication, Spring, 2008).

One of the most simple monitoring and updating tasks that has been developed for young children (from 15 months) is the Scrambled Boxes task (Griffith, Pennington, Wehner & Rogers, 1999; Diamond, Prevor, Callender & Druin, 1997). In the Scrambled Boxes task a child observes the experimenter hide a star in each of six individually decorated boxes. The child then has to retrieve all six stars without returning to an empty box. The boxes are hidden between searches and their location is scrambled so that the child has to remember the picture on the top of each box to be successful on the task. This task requires children to update the information being held in working memory; hence it is a complex working memory task (Diamond et al., 1997). Improvements on this task have been noted from 15 months to 7 years (Diamond et al., 1997).

3.3.3 Shifting Tasks

As noted previously (section 1.4.2) shifting involves modifying behaviour in response to new information. This new information is often in conflict with previous information meaning a deliberate and purposeful mental shift is required. A distinction is often made between different types of shifting (or shift type). Garon, Bryson & Smith (2008) note that shift type is defined by whether the shift occurs at the perceptual or response stage. When the task requires a participant to attend to a different aspect of the stimulus, it is called attentional shifting, and when the task requires a selection of a different motor response, it is called response shifting.

There are tests of response shifting for children as young as 12 months, for example, the Multi-location Search task (Zelazo, Reznick & Spinazolla, 1998; Carlson, Mansell & Williams, 2004) and the Spatial Reversal task (McEvoy, Rogers & Pennington, 1993). Both of these tasks involve hiding an object at one location until it has been retrieved by the participant correctly on several consecutive trials and then shifting the hiding location. Continuing to search at the original location is indicative of an inability to switch response set. A similar task to the Spatial Reversal task is the A not B task (Diamond, 1985). This task is administered in a similar manner to the Spatial Reversal task other than the participant watches as the experimenter hides the object and a short delay is imposed before the individual is allowed to search. Despite having watched the object move location, very young children perseverate on the original location.

Attentional shifting is more difficult to measure in young children because often the tasks have more complex rules. Despite this, the separated dimensions version of the dimensional change card sort game (DCCS) has been shown to be an appropriate test of attentional flexibility in children as young as 2.5 years (Diamond, Carlson & Beck, 2005). The dimensional change card sort task is a card game that requires children to sort cards into two piles based on the colour of the object on the card, and then switch to sorting the cards by shape. However, the two sorting dimensions conflict with one another so that the child has to inhibit the pervious sorting dimension. More complex versions of the dimensional change card sort task have been developed that are appropriate for children up six years of age (Zelazo, 2006).

3.3.4 Emotional Regulation Tasks

The inhibition tasks previously discussed have been defined as 'cool' inhibition tasks (Wang & Carlson, 2007). To complete these tasks participants must suppress a response; however, the task does not have an affective (hot) component requiring a participant to regulate or suppress their emotions. The ability to regulate emotions has been shown to improve between the ages of 3-5 years alongside inhibitory control (Saarni, 1984), and Zelazo and Müller (2002) have argued while inhibition and emotional regulation are associated with different parts of the prefrontal cortex they are components of a single coordinated system. Recently, Carlson & Wang (2007) demonstrated that inhibition is related to emotional regulation in preschool children. They argued that this was because both inhibition and emotional regulation require an individual to suppress a response and do the opposite of what is expected. Despite the convergence of inhibition and emotional regulation in the TD literature, it may be that problems with hot and cool EFs could manifest themselves differently in terms of behavioural outcomes. Therefore, a measure of emotional regulation was included in the current battery so to not rule out exploring this possibility.

There are very few behavioural measures of emotional regulation in childhood and most studies have relied on parent report methods (Carlson & Wang, 2007). However, Carlson and Wang (2007) used two behavioural measures of emotional regulation, the Disappointing Gift paradigm (originally developed by Saarni, 1984), and the Secret Keeping task. In the Disappointing Gift paradigm the child is given an attractively wrapped gift that is actually just a woodchip. The child's ability to suppress a negative emotion (disappointment) is taken as the measure of emotional regulation. In the Secret Keeping task the child has to suppress a positive emotion; they must not reveal that a gold fish in the room can talk. Both of these tasks are ethically dubious when working with participants with ID because it may not be easy to dispel the disappointment caused by the Disappointing Gift task, and lying to a participant about the communicative abilities of a goldfish and then revealing the truth may also cause a great deal of disappointment and confusion, especially if the participant struggles to make sense of the situation in which this has arisen. The Secret Gift task was developed for this thesis based on these two tasks (see section 3.4.2.4.3). During this task the participant is still required to keep an exciting secret (that they and their carer/parent are about to receive a present) but the secret is true and plays out as the participant would expect.

Carlson and Wang (2007) argued that emotional regulation tasks such as the Disappointing Gift or Secret Keeping tasks were not developmentally appropriate for children younger than 4 years of age. Therefore, it was envisaged that the Secret Keeping task would only be appropriate for participants who have a milder ID or who are older.

3.4 Task Development and Pilot Studies

In the next section of this chapter a description is provided of the tasks that were included at the initial stage of the battery development. A summary of the subsequent pilot studies that were conducted to develop this battery are also described. Over the course of the pilot studies, tasks were added to or removed from the battery, and others were adapted to lower the battery floor or to make the battery more appropriate for people with ID. Some tasks were added in the final stages of the battery development because after piloting it was apparent that more standardised measures of an EF construct should be included (e.g. DCCS). Figures 3.1., 3.2. and 3.3. help illustrate how the test battery evolved. For clarity, separate flow charts have been constructed for each component of the EF battery and the bottom row of each chart represents the final battery. The method and key results from each pilot study, which informed decisions about battery development, are summarised with reference to these flow diagrams.

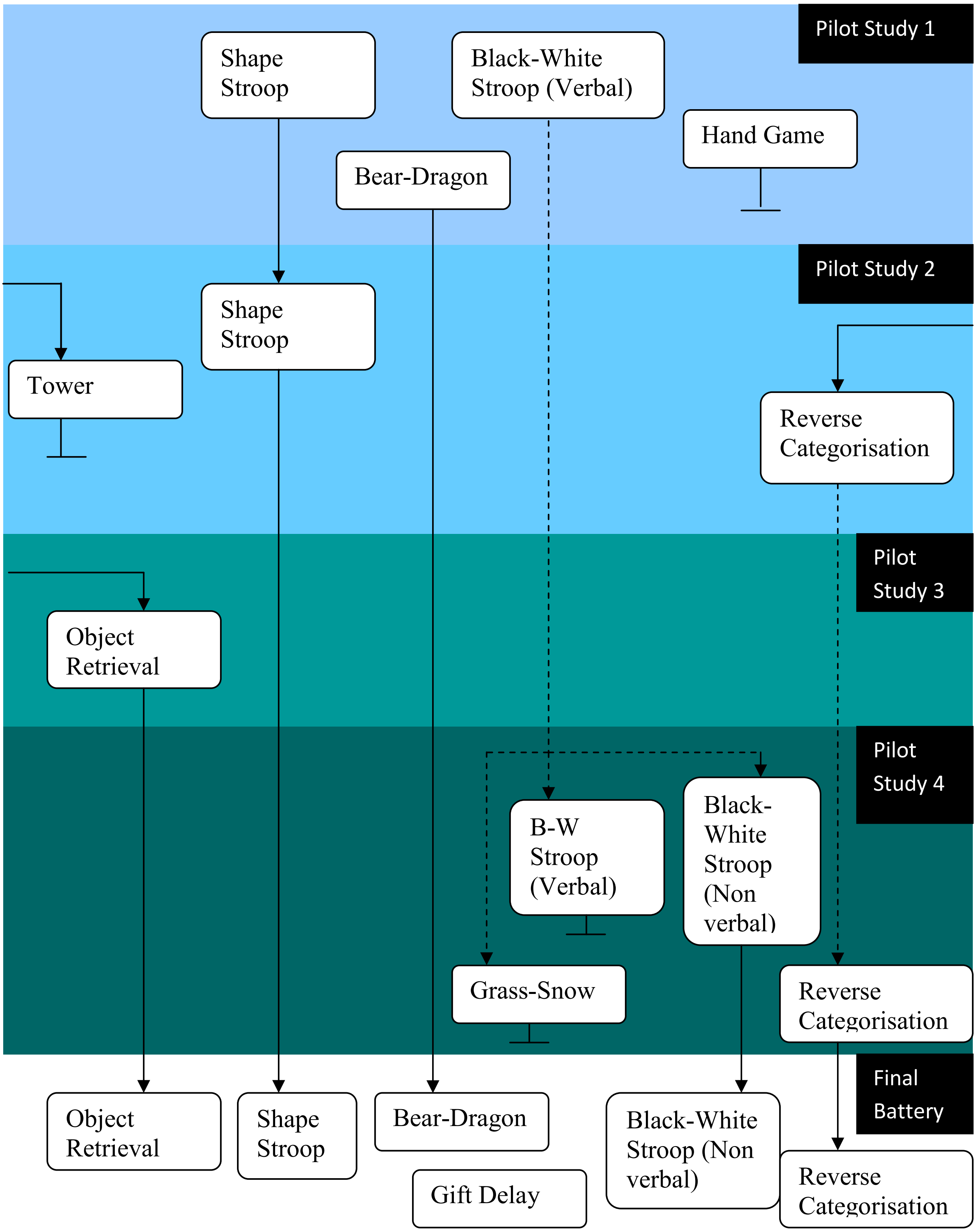

Figure 3.1 *The development of the inhibition battery.*
Note. Some tasks (e.g. Bear-Dragon) proceeded directly to the final battery, some were excluded after pilot study one (hand game), some were piloted in later studies and then omitted (Tower), some went through a process of development (Black-White Stroop), and tasks such of as the Gift Delay were not piloted due to setting constraints.
Note. Broken lines indicate a change to a task.

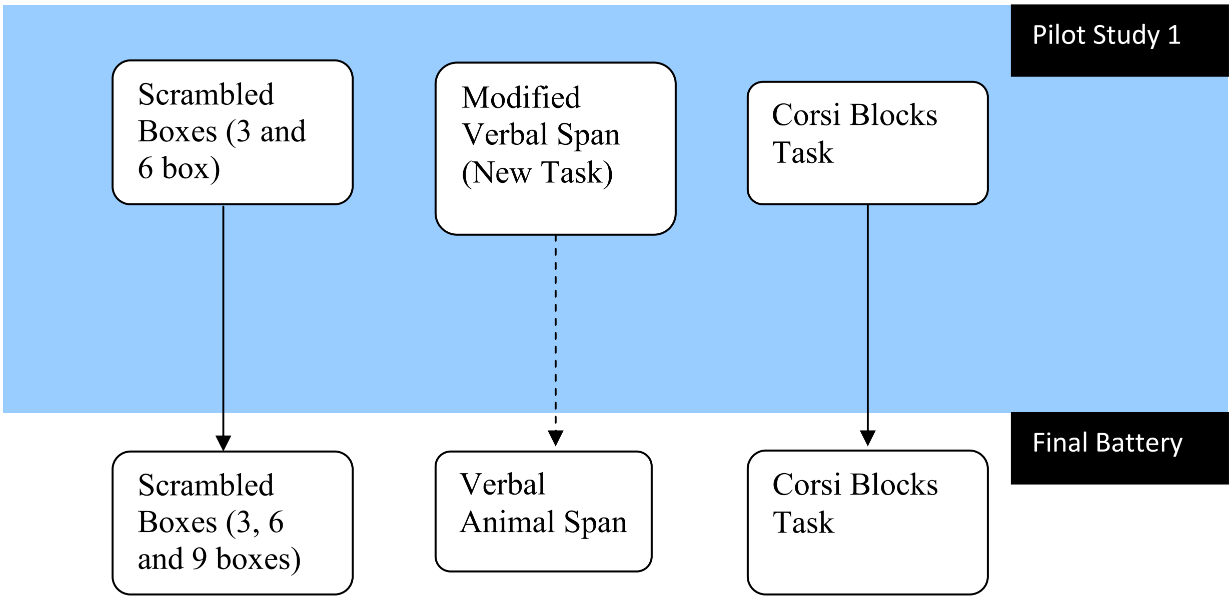

Figure 3.2 *The development of the working memory battery.*
Note. The Scrambled Boxes and Corsi Blocks tasks proceeded immediately to the final battery. The non-verbal phonological loop task was modified.
Note. Broken lines indicate a change to a task.

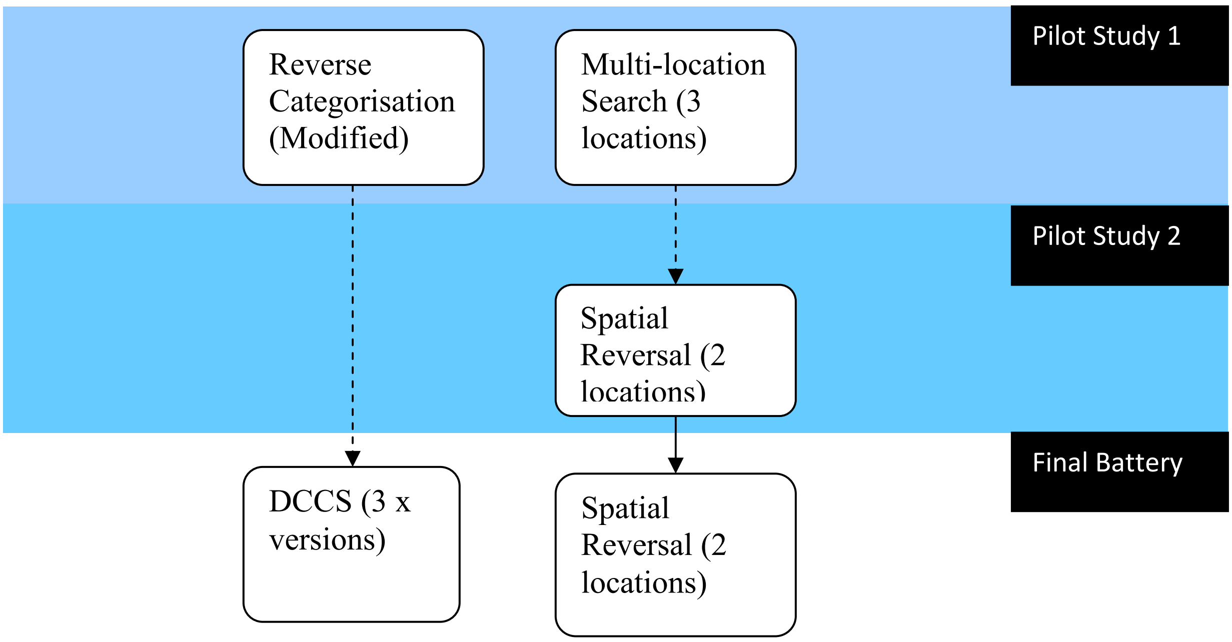

Figure 3.3 *The development of the shifting battery.*
Note. Reverse Categorisation was modified for the inhibition battery and the DCCS was included as a robust measure of attention shifting in preschoolers. The Multi-location Search was replaced by the Spatial Reversal after pilot study 1; a similar task but with fewer search locations.
Note. Broken lines indicate a change to a task

3.4.1 Introduction to Pilot Study 1

The tasks described in this pilot study formed the first battery of tests and were selected from the developmental literature because they met most of the criteria for inclusion (described in section 1.3.2) and were good examples of the tests available for measuring EFs across a variety of abilities and ages. The floor of this first battery was 22 months.

The battery was piloted with TD children aged 3-4 years. The purpose of this initial pilot study was to: a) rank the inhibition tasks in order of difficulty to confirm these tests covered the required range of development, b) to ascertain that the other EF tasks were appropriate for individuals with a mental age of 3 to 4 years (i.e. the children were not at floor or ceiling on the tasks and children obtained a range of scores on these tasks). 3 to 4 year-olds were chosen for this pilot study because the initial battery catered for individuals with a mental age of 22 months to 5 years and the 3-4 year olds represented the median age. The Gift Delay and Secret Gift task are described in this method because they formed part of the initial battery; however, it was not possible to pilot the Gift Delay and Secret Gift tasks because of the constraints of testing in schools.

3.4.2 Method

3.4.2.1 Participants

38 children (19 boys) from a nursery in Birmingham, UK, took part in the study. The mean age for the total sample was 47 months (range = 42-53). 71% of the children were Caucasian, 11% were Black, 18% were Asian. The children were all competent English speakers. 14 of the children (5 boys) whose mean age was 48 months (range = 43-54 months) completed four inhibition tasks. 12 children (7 boys) whose mean age was 47 months (range 53-52 months)

completed three working memory tasks. 12 children (7 boys) whose mean age was 48 months (range 43-52 months) completed two response shifting tasks[3] [4].

3.4.2.2 Inhibition Tasks

3.4.2.2.1 **Hand Game** (Luria et al., 1964)

Participants were asked to make a fist (F) if the experimenter pointed, and point (P) if the experimenter made a fist. Two practice trials (one for a point and one for a fist) were followed by feedback. There were 16 predetermined pseudorandomized conflict trials (F,F,P,F,P,P,P,F,F,P,FP,F,F,P,P). Feedback was not given after individual trials, but the rules were repeated after 8 trials. The maximum score was 16.

3.4.2.2.2 **Black-White Stroop** (Beck, Riggs & Gorniak, 2009; Simpson & Riggs, 2005).

Eight black (B) and eight white (W) 10 x 8 cm cards were used in this task. During a warm up phase participants were asked to identify a black and white card to check they knew these colours. In the experimental phase, participants were required to say "black" when the experimenter presented a white card and say "white" when the experimenter presented a black card. Two practice trials (one for a "white" card, and one for a "black" card) were followed by feedback. Practice trials were repeated once if necessary. There were 16 predetermined pseudorandomised experimental trials (B,W,B,W,W,B,B,W,B,W,W,B,W,B,B,W). Feedback

[3] For all pilot studies children were tested in a quiet area away from distractions.

[4] For all studies reported in this thesis ethical approval was granted from the University Ethics Committee. Ethical approval for the research conducted in the chapter 2, 4 & 5 was approved by the Coventry Research Ethics Committee. For pilot studies, head teachers and nursery managers provided consent for testing in schools and nurseries and were given 'opt out' consent forms for parents (Appendix E). Data collected in schools was anonymised using identifier numbers.

was not given after individual trials but the task rules were repeated after eight trials. Participants' first responses on each trial were coded, so an error followed by a correction was coded as an error.

3.4.2.2.3 Shape Stroop (adapted from Kochanska, Murray & Harlan, 2000**).**

Three small and three large pictures of fruits (2 x apple, 2 x orange, 2x banana) and two 29.7 x 42 cm laminated cards were used in this task. The first laminated card depicted a large orange (diameter 16 cm) with a small 3.5 cm x 3.5 cm apple superimposed on top of it (warm up card). The second laminated card depicted three large fruits (apple, banana & orange) with a conflicting small fruit superimposed on top of them (experimental card). In a warm up phase, participants were shown the six pictures of big and little fruits and asked to identify each in turn. This served to check that participants understood the concept of 'big' and 'little' and knew the names of the fruits. Participants were then shown the warm-up card and were asked to point to the big orange and the little apple. The experimenter then presented the experimental card and asked the participant to point to the fruits in turn. There were six predetermined pseudorandomised experimental trials: three points to big (B) fruits and three points to little (L) fruits: (B, L, L, B, L, B). The inhibition (small fruit) and non-inhibition trials were coded separately. The maximum score for each type of trial was three with one point lost for each incorrect point. The participants' first responses were coded.

3.4.2.2.4 Bear-Dragon (Reed, Pien & Rothbart, 1984).

A bear hand puppet and a dragon hand puppet were used in this task. The experimenter sat opposite participants and during a warm up phase participants were asked to do nine actions commanded by the experimenter e.g. "touch your head." This was to check participants understood and could execute the commands. Participants were then introduced to the 'nice bear' puppet and the 'naughty dragon' puppet and instructed to do the actions the 'nice bear' commanded but not the actions the 'naughty dragon' commanded. There were two practice trials after which feedback was given. Practice trials were repeated once if necessary. Participants proceeded to the experimental trials irrespective of performance on practice trials; however, the experimenter asked a check question, "who don't we listen to?" to check if the participant had understood the inhibition rule. There were then sixteen predetermined pseudorandomised bear (B) and dragon (D) trials (B,D,B,B,D,D,D,B,D,B,D,B,D,D,B,D). Participants were reminded of the rules after eight trials. The bear and dragon trials were coded separately. The maximum score for each type of trial was eight with one point lost for each incorrect action. The participants' first responses were coded.

3.4.2.2.5 Gift Delay (Delay Inhibition Task; Kochanska, Murray & Harlan, 2002; G. Kochanska, personal communication, May 7, 2008)

A large 33 x 27 cm gift bag, a present, wrapping paper, clear tape and a gift bow were used in this task. The task had two parts the 'gift wrap' and the 'gift bow'. In the gift wrap phase the experimenter announced that she needed to wrap a present for participants. The experimenter then moved behind participants, asked them not to peek whilst she wrapped the present and then wrapped the present noisily for one minute. If participants turned around, the experimenter reminded them not to peek, however, if participants turned around a second time, the experimenter no longer reminded them. In the gift bow phase the experimenter put the wrapped present inside the gift bag and positioned it on the table in easy reach of participants. The experimenter declared that she had forgotten to put the gift bow on the present and asked participants to stay seated and not touch the present until she had found the gift bow. The experimenter then moved as far away as possible from participants but stayed in view, turned away from them and looked through her bag for the bow for one minute. A second experimenter pretended to read a magazine while monitoring that the participant was safe.

This task was scored using guidelines provided from Kochanska (personal communication, May 7, 2008). In the wrap phase participants received a peek score (turns around but does not return fully forward = 1, turns around but turns back around = 2, peeks over shoulder far enough to see wrapping = 3, turns head to the side but less than 90 degrees = 4, does not try to peek = 5). In the bow stage participants received a touch score (opens gift = 1, lifts/picks gift up = 2, touches gift but does not lift it up = 3, never touches gift = 4), and a seat score (is in seat for less than 30 seconds = 1, is in seat for 30 seconds or more but less than one minute = 2, is in seat for 1 minute = 3).

3.4.2.3 Working Memory Tasks

3.4.2.3.1 Scrambled Boxes (3 and 6 box versions) (Griffith, Pennington, Wehner & Rodgers, 1999).

Two versions of this task were included in the first test battery: Three Scrambled Boxes and Six Scrambled Boxes. The apparatus were nine round wooden boxes (diameter = 7cm) each decorated with a shape, nine foam stars, a cardboard treasure chest, a 29.7 x 42cm cardboard screen and two cardboard baseboards that indicated where the boxes should be positioned in each task. The boxes were positioned 5 cm and 8 cm apart for the three and Six Scrambled Boxes task respectively. In both versions of the task, participants watched as the experimenter put a star in each box and closed them. Participants' were asked to find the stars and put them in their treasure chest. Once a box was selected and the star removed, the empty box was returned, the boxes were hidden behind the screen and the positions of the boxes were scrambled by the experimenter. The boxes were scrambled for five and ten seconds in the Three and Six Scrambled Box task respectively. Participants were then allowed to search again. The maximum scores for the Three and Six Scrambled Boxes tasks were four and seven respectively, with one point lost for each incorrect reach. The task was terminated if the participant lost all their points.

3.4.2.3.2 Modified Verbal Span (adapted from Dempster, 1981).

The participant was given a laminated card with six coloured squares on it (red, blue, green, yellow, purple and orange). On each trial the experimenter read a sequence of colours starting with sequences of just two colours. The participant was required to respond by touching the same sequence of colours on their laminated card. There were two practice trials of two colour sequences after which feedback was given. Experimental trials were administered after practice trials irrespective of performance. Every three experimental trials the number of colours in a sequence increased by one. The task was terminated when participants got three consecutive trials incorrect. Participants were given one point for each correct sequence produced.

> ***Modifications to this task*****:** In the original version of this task reported by Dempster (1981) the experimenter read out a string of words or digits and the participant repeated them back to the experimenter. In this study, laminated cards were used to try to make this task appropriate for non-verbal participants with ID who have good receptive language. Colours were used because these are easy to depict visually.

3.4.2.3.3 Corsi Blocks (Pickering, Gathercole & Peaker, 1998).

The apparatus for this task was a 20 x 25cm white block board on which ten 3.4 x 3.4cm blue blocks were mounted irregularly. The experimenter sat opposite the participant. The procedure for this task was similar to the modified verbal span other than that on each trial the experimenter tapped out a sequence on the blocks and the participant was asked to copy these sequences. The experimenter tapped each individual block no more than once per sequence. Participants were given one point for each correct sequence produced[5].

[5] A pairs coding scheme was adopted in later chapters of this thesis for span tasks such as the Corsi Blocks task. This coding scheme is described in section 3.6.4 of this chapter in the description of the Verbal Animal Span task and is justified in section 4.3.2.3.1 of chapter 4 in relation to the RTS sample.

3.4.2.4 Shifting Tasks

3.4.2.4.1 Modified Reverse Categorisation (adapted from Carlson et al., 2004).

Two equal sized black buckets and 16 blue or red triangles and squares were used. Participants were asked to sort all the objects into the buckets by colour (pre-switch condition). Participants were then asked to sort the objects by the same dimension (colour) but into the opposite buckets (response shifting condition). Participants were then asked to sort the objects by shape rather than colour (attention shifting condition). There were two practice trials before the first condition but none for consecutive conditions to maximize the effectiveness of the shift component of the task. Participants passed a condition if they sorted 75% and over of the objects correctly.

> ***Modifications to this task*****:** In the original version of this task described by Carlson (2004) children were required to sort big blocks into a big bucket and small blocks into a small bucket. They were then required to sort the objects into the opposite buckets. A prepotent response exists naturally in this task (big things go together) so failure to sort correctly after the switch phase may be underpinned by problems with shifting, inhibition, or both. The adapted version of this task reduced the prepotent response and included response shifting and attentional shifting trial.

3.4.2.4.2 Modified Multi-location Search (Zelazo, Reznick & Spinazolla, 1998).

The experimenter presented a set of three cardboard drawers connected side by side. Each drawer was a different colour. Participants were shown how open a drawer and told that a sticker would be hidden inside a drawer and that it was the participant's job to find the sticker. On the first trial a sticker was hidden in each drawer so that the participant was correct, while on consecutive trials a sticker was only hidden at the location where the participant had previously looked. This was repeated until the participant had retrieved the sticker correctly on four consecutive searches at this location; the hiding location was then switched to a different coloured drawer before inviting participants to get the reward. If the participant had not attained or reversed set after 10 trials the experiment was terminated. The maximum score on this task in each condition was seven with one point lost for each incorrect reach.

> ***Modifications to this task:*** In the version of this task reported by Zelazo et al. (1998) symbols were attached with strings to the drawers as opposed to the drawers being different colours. Snacks were hidden as opposed to stars and participants pulled the strings to obtain the snacks. Snacks were not used in the current pilot study because it was deemed undesirable to reinforce children with food and coloured drawers were used as opposed to symbols attached with strings because strings made the drawers difficult to open.

3.4.2.4.3 **Secret Gift** (New emotional regulation task)

Participants and the experimenter were alone at the start of this task. The experimenter talked to participants about birthdays and how lovely it is to receive presents. The experimenter then told participants that they have brought them a present to say thank you for doing all the tasks, and that they have also brought their parent/carer a present to say thank you for letting the experimenter visit their house. The experimenter stated that this was a secret, announced that she was going to fetch the presents from the car and asked the participant not to say anything to their parent/carer about the present because it was a 'big surprise'. The experimenter then left the participant and their carer/parent entered the room for two minutes. Performance on this task is categorised as pass or fail depending on whether the participant revealed the secret to their parent/carer. Latency to reveal the secret is also recorded.

3.4.3 Pilot Study 1 Results and Discussion

The aim of this pilot study was to compare the difficulty of the tasks (inhibition battery only) and to ascertain whether the tasks were suitable for individuals with a mental age of 3-4 years.

3.4.3.1 Inhibition Task Results and Discussion

The mean scores for each task, Pearson's corrections[6] and partial correlations between the tasks are shown in figure 3.4 and table 3.2.

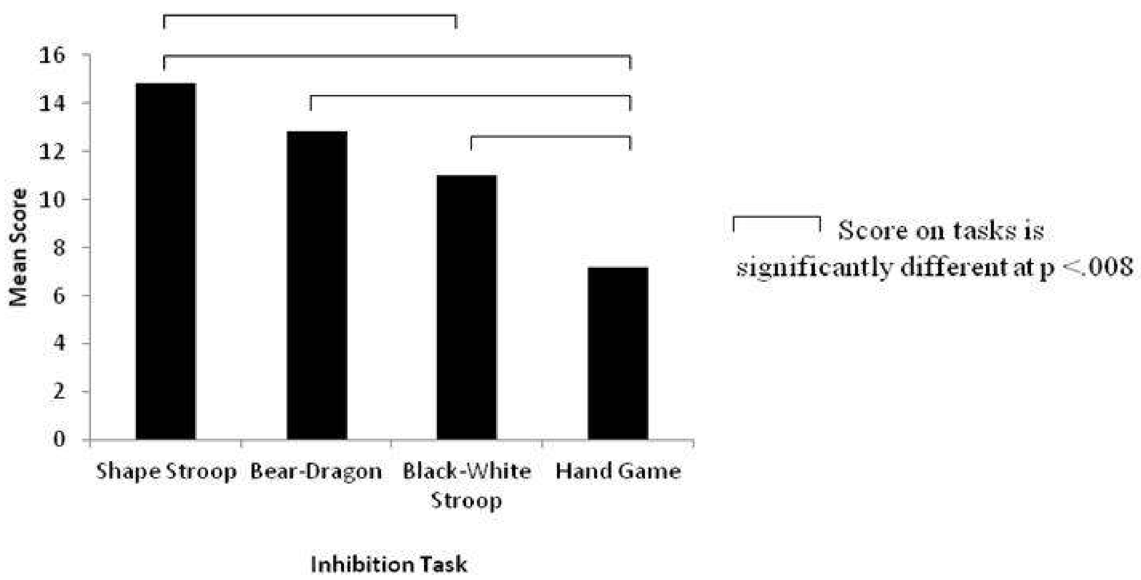

Figure 3.4 Preschoolers mean scores from the four inhibition tasks (N = 14)
Note. Maximum score = 16.

[6] Pearson's correlations were conducted because the majority of the data was parametric. Correlations are reported at less stringent associated probability levels than in chapters 1 and 5 of this thesis due to a smaller number of correlations being conducted and because of the exploratory nature of the pilot studies.

Table 3.2

Pearson's correlations and partial correlations between inhibition tasks from pilot study 1.

	Shape Stroop	Bear-Dragon	Black-White Stroop	Hand Game	Age
Shape Stroop	1.00	.52	.47	.30	.14
Bear-Dragon	.52[a]	1.00	.42	.47	.05
Black-White Stroop	.47	.42	1.00	.67**	.02
Hand Game	.41	.55	.75***	1.00	.30

* $p < 0.05$ ** $p < 0.01$ *** $p < .005$

[a]*The correlation between the Bear-Dragon task and the Shape Stroop approached significance (p = .058).*

Note. Partial correlations are displayed in lower half of table.

A repeated measures ANOVA was carried out on the raw scores. There were significant differences between the tasks (F= 14.21, DF = 3.39; $p < .001$).

Paired sample t-tests were carried out between the measures using a Bonferroni correction with an associated probability level of .008 to correct for multiple comparisons (.05 divided by the number of tests). The hand game was significantly more difficult than the Black-White Stroop (t(13) = 3.70, $p = .003$, $d = 0.92$), the Bear-Dragon (t(13) = 3.85, $p = .002$, $d = 1.06$) and the Shape Stroop (t(13) = 5.90, $p < .001$, $d = 2.05$). The Black-White Stroop was significantly more difficult than the Shape Stroop (t(13) = 5.67, $p < .001$, $d = 1.71$) but not the Bear-Dragon (t(13) = 1.37, $p = .193$, $d = 0.42$). The Bear-Dragon was not significantly different from the Shape Stroop (t(13), 1.51, $p = .155$, $d = 0.50$). There was a significant correlation between the Black-White Stroop and the hand game in both the bivariate (R = .67, $p = .009$), and the partial correlations (R = .75, $p = .003$) (see table 3.2).

Data for the Shape Stroop and the Bear-Dragon violated assumptions of normality (Kolomogorov-Smirnov < .001.) Non-parametric tests (Friedman two-way analysis, Wilcoxon signed ranks tests and Spearman's correlations) were also carried out on these data and the above findings held true.

Luria's Hand Game was excluded from the inhibition battery after this pilot study because it was felt that this task would be too difficult for many individuals with RTS. Furthermore, it was difficult to interpret the children's hand gestures during this task and anecdotally, this task appeared the least engaging of the four inhibition tasks. This decision was also supported by the strong positive correlation between this measure and the Black-White Stroop that suggests that the two tasks are measuring the same construct and that the Black-White Stroop would serve as an appropriate alternative.

The Black-White Stroop appeared to be an appropriate test of inhibition for this age group (range of scores = 7-16) but it was decided a non-verbal version of this task may be more appropriate for individuals with RTS. Therefore, although this task was not excluded from the test battery, changes were made to it in a later pilot study (see pilot study 4 for details). Most children were at ceiling on the Shape Stroop (figure 3.4). However, this was expected because the task is more suitable for younger children. Therefore, this task proceeded to the next stage of piloting with a younger age group (pilot study 2; figure 3.1).

The Bear-Dragon was kept in the battery because it was more difficult than the Shape Stroop. Furthermore, while the Bear-Dragon did not differ from the Black-White Stroop in this pilot study, Carlson (2005) found that preschoolers performed significantly better on the Bear-Dragon task than the Black-White Stroop when these tasks were administered to a larger sample of children. Therefore, the Bear-Dragon task may fit between the Shape-Stroop and Black-White Stroop in terms of developmental progression. Anecdotally, this task appeared to thoroughly engage children during the pilot study.

3.4.3.2 Working Memory Results and Discussion

Table 3.3
Mean, standard deviation and range for each working memory task from pilot study 1.

Measures and variables	M	SD	Range
3 Boxes Scrambled			
Total score (out of 4)	3.75	0.62	2-4
6 Boxes Scrambled			
Total score (out of 7)	5.0	1.71	2-7
Verbal word span	2.55	0.94	0-4
Corsi Blocks task	3.08	0.29	2-4

Note. A non-parametric Spearman Rho correlation revealed a significant relationship between the Three and Six Scrambled Boxes tests ($R = .63$, $p < .05$). No other relationships were significant or approached significance.

It can be seen in table 3.3 that most children scored higher on the Scrambled Boxes task than the Corsi Blocks task. One possibility is that the process of actively engaging with the task to open the boxes improved the children's memory span. These tasks were included in the final battery (figure 3.2) because all children understood the task instructions and attained an adequate range of scores on these tasks. The Adapted Verbal Span task was excluded from the test battery after this pilot study. It was felt that the discrepancy between a verbal input and a non-verbal output (use of the response card) on this task was difficult for the children. For example, on some occasions the children scanned the response card for some time looking for the red square to point at, by which time they may have forgotten the next item in the sequence. Therefore, this task might not have been representative of verbal working memory in our sample. A verbal span task (word span for animals) was used in the final battery for verbal participants (described in section 3.6.4).

3.4.3.3 Shifting Results and Discussion

The descriptive statistics for the shifting tasks are displayed in table 3.4.

Table 3.4

Mean, standard deviation and range for each shifting task from pilot study 1.

Measures and variables	M	SD	Range
Multi-location Search			
% attaining set in preswitch trials	58.3%	-	-
% attaining set in postswitch trials	57.1%	-	-
Average score (preswitch) (Out of 7)	0.58	0.51	0-1
Average score (postswitch) (Out of 7)	2.43	2.82	0-6
Reverse Categorisation	Ceiling	Ceiling	Ceiling

42% of the children failed to attain set in the preswitch stage in the Multi-location Search task so did not progress to the post-switch (reversal) stage. It may be that children failed to attain set because they were excited and tended to search randomly for the reward. A decision was made to include a reversal task that had two search locations (the Spatial Reversal task; see section 3.4.5.2.3) as opposed to three search locations (the Multi-location Search task). It was anticipated that fewer search locations may make the 'hiding rule' more obvious to the children and help them attain set in the preswitch trial.

The adapted version of the Reverse Categorisation task was difficult to interpret because all the children were at ceiling on this task. It was removed from the battery and a more standardised measure of attentional shifting, the Dimensional Change Card Sorting task was included (described in section 3.6.1) (Zelazo, 2006).

3.4.4 Introduction to Pilot Study 2

Figure 3.1 illustrates that the Tower task was added to the test battery in the second pilot study. At the time of this pilot study being conducted, Kochanska (personal communiation, May 2008) was using the Tower task as a measure inhibition in children aged 24 months. This task was piloted as a possible alternative to the Shape Stroop. This pilot study also included a modified Reverse Categorisation. Although, the Reverse Categorisation task was previously rejected as a shifting task a modified version of this task still had potential as an inhibition task for toddlers aged 24 months. Finally, the Spatial Reversal task was piloted as an alternative to the Multi-location Search.

3.4.5 Method

3.4.5.1 Participants

11 toddlers (5 boys) from a nursery in North Staffordshire, UK, took part in the study. The mean age for the total sample was 38 months (range = 31-49 months). All of the children were Caucasian and were competent English speakers. Each child completed all the tasks in this pilot study.

3.4.5.2 Test Battery

The Shape Stroop task was administered as previously described in section 3.4.2.2.3.

3.4.5.2.1 **Tower** (Kochanska et al., 1996)

13 3.5 x 3.5 cm building blocks were used in this task. The experimenter explained to participants that they would take turns to build a tower. The blocks were split between the experimenter and participants and the experimenter placed the first block and encouraged participants to place their block. When it was the experimenter's turn to place a block on future turns she hesitated for two seconds to make the participants wait. Placing a block on the experimenter's turn was taken as a measure of poor inhibition. A score was calculated using the following formula provided by Kochanska (personal communication, May 7, 2008): total number of blocks placed x 10/number of blocks the child places. In line with Kochanska (personal communication, May, 7, 2008) toddlers built two towers during the task and an average score was taken.

3.4.5.2.2 Modified Reverse Categorisation (Inhibition Version)

The apparatus used in this task were a standard sized red bucket and a blue bucket, and 14 coloured balls (seven red, seven blue). The buckets were positioned in front of participants who were instructed to sort the blue balls into the red bucket and the red balls into the blue bucket. This was demonstrated by the experimenter followed by two practice trials after which feedback was given. Practice trials were repeated once if necessary. There were twelve predetermined randomised experimental trials of red (R) and blue (B) balls (B,R,B,R,R,B,B,R,B,R,R,B). The rules were repeated after six balls had been sorted. The maximum score on this task was 12 points, with one point lost for each incorrect ball sort. Children were asked to sort the balls into the congruent buckets after the task to "help put the balls away" to check they could match the colours correctly.

Modifications: To make sure that this task was a measure of inhibition as opposed to a shifting task, the children were not asked to sort the balls into the congruent buckets (i.e. red balls into red buckets) before they sorted them into the incongruent buckets. Colour was chosen as the sorting dimension rather than size (the sorting dimension from the original task) because, for children who have learnt to match colours, putting red things in a red bucket is likely to be more salient than putting big toys in a big bucket and vice versa (i.e. prepotent response in the colour version seems more obvious).

3.4.5.2.3 Spatial Reversal (McEvoy Rogers & Pennington, 1993)

Two plastic cups, a cardboard baseboard that indicated where the cups should be placed, a 29.7 x 42cm cardboard screen and several small toys/objects were used in this task. The cups were placed on the board 20 cm apart. On the first trial the cups were hidden behind the screen and the experimenter hid a toy under each cup. The experimenter removed the screen and asked the participant to lift one of the cups to try and find the toy. The participant was always correct on the first trial. The experimenter repeated the process, hiding a toy/object under the same cup that the participant selected on the first trial until the participant had retrieved the toy/object correctly on four consecutive trials. The side of hiding was then reversed. There were twelve attainment and twelve reversal trials. If the participant failed to either attain set in twelve trials or reverse set after twelve trials, the task was discontinued. The maximum score on this task was nine with one point being lost for every incorrect reach.

3.4.6 Pilot Study 2 Results and Discussion

3.4.6.1 Inhibition Tasks Results and Discussion

The descriptive statistics for these tasks and Pearson's correlations between them are displayed in tables 3.5 and 3.6.

Table 3.5
Descriptive statistics for the inhibition tasks from pilot study 2.

Task	Mean (SD)	Range
Reverse Categorisation (max score = 12)	8.82 (2.44)	6-12
Tower (min score = 10, max score = 20)	15.44 (2.94)	12-20
Shape Stroop (max score = 3)	2.63 (0.50)	2-3

Table 3.6
Pearson's correlations and partial correlations between inhibition measures from pilot study 2.

	Tower	Reverse Categorisation	Shape Stroop	Age
Tower	1.00	.73***	.07	.73***
Reverse Categorisation	.69***	1.00	-.46	.57*
Shape Stroop	.06	-.58*	1.00	-.06

* $p < 0.05$ ** $p < 0.01$ *** $p < .005$

Note. Partial correlations are displayed in the lower half of the table.
Note. Data for the Shape Stroop violated assumption of normality (Kolmogorov-Smirnov = $p < .001$). Spearman Rho correlations were conducted. The results remained significant and consistent with those reported above.

It can be seen in table 3.5 that there was a good range of scores on the Reverse Categorisation task (6-12 balls sorted correctly). Observation of the children during this task revealed all children sorted the balls correctly on at least one trial before shifting to the prepotent response. Therefore, it was clear that even the youngest children understood the sorting rule at the start of the task, but were often unable to suppress the dominant response.

The mean score on the Shape Stroop was 11 (range 10-12) indicating that even the youngest children found this task exceptionally easy. This was not surprising as Carlson (2005) demonstrated that 59% of 24 month olds passed the Shape Stroop and the youngest participant in this study was 30 months.

There appeared to be a good range of scores on the Tower task (12-20). As two towers were built any discrepancy between scores could be examined. This task did not seem very reliable because performance differed by as much as 10.89 points between the first and second trials. Furthermore, success on this task appears to be highly dependent on social understanding and co-operation. Since some children and adults with ID may also have difficulties with social understanding one concern was that the delay imposed by the researcher before placing her block may lead to confusion and confound this task.

3.4.6.2 Shifting Task

Table 3.7

Descriptive statistics for the Spatial Reversal task from pilot study 2

Measures and variables	M	SD	Range
Spatial Reversal			
% attaining set in preswitch trials	88.89	-	-
% attaining set in postswitch trials	66.67	-	-
Average score (preswitch) (Out of 7)	3.22	2.53	0-7
Average score (postswitch) (Out of 7)	4.14	2.04	0-6

88.89% of children attained set in the preswitch trial of the Spatial Reversal (table 3.7). 66.67% attained set after the reversal but some of the children scored zero on the reversal task perseverating on the preswitch location. It was concluded that the Spatial Reversal task was an appropriate replacement for the Multi-location Search.

3.4.7 Introduction to Pilot Study 3

In order to lower the floor of the battery to less than 22 months one new task was introduced (the Object Retrieval task) and piloted on five infants (two boys) from a nursery in Birmingham, UK. The infants were aged between 14-16 months. Four infants were Caucasian and one was black.

3.4.7.1 The Object Retrieval Task (Diamond, 1990; 1991).

The equipment for this task was a transparent 19 x 18 x 10cm box and an opaque box of the same size, each of which had an entrance on one side. Either the transparent or the opaque box was positioned in front of the participant within their reach. The participant observed as an object was placed inside the box, through the opening. The participant was asked to retrieve the object. The experimenter held the box to stop the participant from tipping it over or dragging it towards them. There were five trials with the opaque box followed by five with the transparent box during which the position of the entrance and object was varied (opening at front, opening left, opening right, opening at the top of the box with object at back of box, opening at the top of the box with object at front of box). Reaching to retrieve the object was coded as: 0 = tries to reach through box, 1 = looks through the opening and reaches, 3 = looks then reaches, 4 = reaches without looking through the opening.

It was not possible to use the video recording equipment necessary to code these data, but in terms of task procedure, all the children were able to comprehend the task instructions and carry out the necessary actions to retrieve the toys. Therefore, this task was included in the battery for any individuals who had a severe ID.

3.4.8 Introduction to Pilot Study 4

The purpose of this final pilot study was to compare the various versions of the Stroop tasks in the battery to check that the modifications made to the Reverse Categorisation (colour instead of size) had not made the task more difficult and hence comparable to the Black-White Stroop. A comparison was also made between the verbal Black-White Stroop to a new non-verbal version of the Black-White Stroop that was developed for this study. This new non-verbal version of the Black-White Stroop was based on the Grass-Snow task except for the colours of the cards (Carlson & Moses, 2001). This modified version of the Black-White Stroop was developed rather than using an alternative non-verbal Stroop task, such as the

Grass-Snow task, because it was felt that individuals with ID were more likely to understand the terms Black-White than Grass-Snow.

3.4.9 Method

3.4.9.1 Participants

27 children (16 boys) from a nursery in North Staffordshire, UK took part in the study. The mean age was 50.31 months (range 46-58 months). All children were competent English speakers. 59% of the children were Caucasian, 19% were Black, 22% were Asian. Two children were excluded from the analysis due to failure to cooperate during all four tasks.

3.4.9.2 Task Battery

Each child was tested in two separate sessions and received two tasks in each session. The order of the tasks was counterbalanced so that the Black-White Stroop (verbal) and Black-White Stroop (non-verbal) versions never immediately followed one another. The Reverse Categorisation and Verbal Black-White Stroop were administered as described previously in sections 3.4.5.2.2 and 3.4.2.2.2.

3.4.9.2.1 Modified Black-White Stroop (Pointing):

This task was administered in a similar manner to the Verbal Black White Stroop. The apparatus used were a 40 x 60cm board on which black and white cards (20cm x 20cm) were mounted horizontally. Below each card was a felt hand print and the participant was asked to place their hands on these hand prints between trials. The participant was shown the board and asked to identify the black and white cards. The experimenter explained that in this task the participant was required to point to the black (B) card when the experimenter said 'white' and to the white (W) card when the experimenter said 'black'. The experimenter demonstrated this to the participant.

3.4.9.2.2 Grass-Snow (Carlson & Moses, 2001)

This task was administered in a similar manner as the Black-White Stroop (pointing). However, the experimenter explained that in this task the participant was required to point to the green card when the experimenter said 'snow' and to the white card when the experimenter said 'grass'. The experimenter demonstrated this to the participant.

3.4.10 Pilot Study 4 Results and Discussion

It can been seen in table 3.8 that children made the least errors on the Reverse Categorisation, and that the mean scores for the Grass-Snow, Black-White Stroop (verbal) and Black-White Stroop (pointing) appear similar. A repeated measures ANOVA was carried out on these data. Results showed that there were differences between tasks (F = 9.36, DF = 3,78; $p <$ .001).

Table 3.8

Descriptive statistics for inhibition tasks from pilot study 4.

Task	Mean (SD)	Range
Reverse Categorisation	13.70 (2.49)	9-16
Black-White Stroop (verbal)	9.56 (4.11)	0-16
Black-White Stroop (pointing)	10.04 (5.11)	0-16
Grass-Snow (pointing)	10.96 (4.55)	0-16

Table 3.9

Pearson's correlations and partial correlations between inhibition tasks from pilot study 4.

	Reverse Categorisation	Black-White Stroop (Verbal)	Black-White Stroop (Pointing)	Grass-Snow	Age
Reverse Categorisation	1.00	.46*	.39*	.36	.31
Black-White Stroop (Verbal)	.46*	1.00	.51**	.43	.07
Black-White Stroop (Pointing)	.40*	.50**	1.00	.56***	.05
Grass-Snow	.37	.42	.56***	1.00	.04

* $p < 0.05$ ** $p < 0.01$ *** $p < .005$

Note. Partial correlations are displayed in lower half of table.

Note. Data from the Reverse Categorisation was not normally distributed (Kolmogorov-Smirnov = .001). Spearman Rho correlations were conducted. The relationships between the Reverse Categorisation and the

Black-White Stroop (pointing) (R = .34, p = .084), the Black-White Stroop (verbal) (R = .35, p = .070) and the Grass-Snow (R = .33, p = .089) were no longer significant; however, the trend was in the same direction.

Paired sample t-tests were carried out between the measures using an associated Alpha level of .008. The Reverse Categorisation was significantly easier than the Black-White Stroop (verbal) (t (26) = 5.83, p < .001, d = 1.22) the Black-White pointing (t(26) = 4.03 (26) p < .001, d = 0.91) and the Grass-Snow (t(26) = 3.29, p < .001, d = 0.74). This confirmed that the reverse categorization was likely to be a suitable test of inhibition for less able individuals with ID.

As expected the modified Stroop task, the Black-White Stroop (pointing), did not differ significantly from the Black-White Stroop (verbal) (t(26) = .54, p = .597, d = 0.10) and the Grass-Snow (t(26) = 1.06, p = .299, d = 0.19). The Black-White Stroop (pointing) and Black-White Stroop (verbal) were also significantly positively correlated (R = .51, p = .007), suggesting that the two tasks measure the same component of EF. This correlation remains significant even after controlling for age using partial correlations (R = .50, p = .009). Therefore, the Black-White Stroop (pointing) replaced the Black-White Stroop (verbal) in the final battery. Finally, the Black-White Stroop (verbal) did not differ from the Grass-Snow (t(26) = 1.57, p = .129, d = 0.32). Non-parametric tests (Friedman two-way analysis, Wilcoxon signed ranks tests and Spearman's correlations) were also carried out on these data and the above findings held true.

3.5 Final Executive Function Battery

The final battery included the Shape Stroop, modified reverse categorization (inhibition version), Bear-Dragon, Black-White Stroop (pointing version), Corsi Blocks task, Three and Six Scrambled Boxes and the Spatial Reversal task. Three versions of the Dimensional Change Card Sort Task (DCCS) were included as measures of attentional shifting as opposed to the modified reverse categorization task, which was not suitable as a shifting task. The DCCS has been extensively administered to preschool children and thus was a logical alternative (Zelazo, 2006). A Nine Scrambled Boxes task was included because a number of children were at ceiling on the Six Scrambled Boxes task in the pilot study. A modification of a traditional digit span, the Verbal Animal Span, was included. Animal names were used as opposed to numbers to attempt to make this task more engaging for participants and because we anticipated that animals would be a concrete semantic class that individuals with ID were more likely to understand. The A not B task was included as a simplified shifting task for participants who might not attain set on the Spatial Reversal task. Finally, the Gift Delay task (delay inhibition) and a new emotional regulation task (Secret Gift Task) were included so that these constructs could be measured alongside conflict inhibition (a summary of the final battery is displayed in table 3.10). It was not anticipated that individuals with RTS would complete all of these measures because this would make the battery lengthy and impractical. The details of the administration of this battery to individuals with RTS are described in section 4.3.2.3.1 in chapter 4 of this thesis and full task protocols are provided in Appendix F. The descriptions of the tasks that were included in the battery but have not been previously described are provided below.

3.6 Additional Tasks

3.6.1 Dimensional Change Card Sort Tasks

DCCS Standard Version (Zelazo, 2006)

14 cards were used in this task. Six depicted red rabbits and six depicted blue boats. There were two target cards, a red boat and a blue rabbit that were mounted above two sorting trays. Participants were asked to sort the cards by colour so that all the blue cards were under the blue rabbit target card and all the red cards were under the red boat target card. Participants had one practice trial (sorting a red rabbit card) after which feedback was provided. Participants then sorted six cards and no feedback was provided. After six trials the rule was changed and participants were asked to sort the cards by shape, e.g. all boats (B) go under the boat. The participant sorted another six cards and no feedback was given on these trials. The cards were presented to the participant in a predetermined randomised order (Pre-switch: R, R, B, R, B, R; Post-Switch: R, R, B, R, B, B). The total score was the number of cards sorted correctly in the post-switch phase. The task was terminated after the pre-switch phase if the participant failed to attain set.

DCCS Separated Dimensions (Diamond et al., 2005)

The separated dimensions DCCS was similar to the standard version except that the two sorting dimensions were separated on the cards. The cards depicted grey rabbits (R) on red backgrounds and grey boats (B) on blue backgrounds (Pre-switch: R, R, B, R, B, R; Post-Switch: R, R, B, R, B, B).

DCCS Border Version (Zelazo, 2006) The border version uses seven of the original 14 cards from the standard version and six extra cards: four red rabbits with black borders around them (Rbr), and four blue boats with black borders around them (Bbr). When the card has a border participants are instructed to sort the cards by colour, but when the cards do not have a border participants are instructed to sort the cards by shape. There are 12 predetermined randomised trials (Rbr, B, Bbr, R, B, Bbr, R, Rbr, Bbr, R, Rbr, B). The rules are repeated to the participant on every trial.

3.6.2 Nine Scrambled Boxes (adapted from Diamond, 1997)

This task has the same protocol as the Six Scrambled Boxes (section 3.4.2.3.1) but uses nine boxes.

3.6.3 A not B Task (Diamond, 1985)

This task was administered using a similar protocol as the Spatial Reversal task but the participant watched the object being hidden. After the object was hidden there was a delay of 10 seconds before the participant was allowed to search during which the experimenter ensured the participant was not fixating on the location of the object. The task was terminated if the participant had not attained or reversed set after 10 trials. The maximum score for this task for each condition was 7 with one point lost for each incorrect reach.

3.6.4 Verbal Animal Span (adapted from digit span, Bull, Epsy & Senn, 2004)

This task followed the same format as the Corsi Blocks task and the Adapted Verbal Span (sections 3.4.2.3.2 & 3.4.2.3.3) except participants repeated strings of animal names (one syllable in length) verbally. An adapted version of a one point per pair coding scheme was adopted for this task (D.A Devenny, personal communication, April 14, 2008; Fudala, Kunze & Ross, 1974; Marcell & Weeks, 1988). For example, if the sequence is dog-horse-rat-cow and the response given is dog-horse-rat-cow then the paired item score would be 3 (i.e. dog-horse, horse-rat and rat-cow). If the response was dog-horse-cow-rat the paired score would be 1.

3.7 A comment on Alpha Levels

At this point in this thesis a further methodological issue will be discussed, namely, the Alpha levels within this thesis. As highlighted previously in sections 2.3 and 3.4.3.1, Alpha levels adopted within this thesis vary across the chapters depending on the analysis. P-values presented in this thesis are all two-tailed and Alpha levels were adjusted according to the following criteria:

- When conducting ANOVAs or T-tests the standard Alpha level (.05) for the analyses was divided by the number of tests conducted within that subsection. However, when this calculation produced an Alpha level smaller than .005 the Alpha level was set at .005 rather than adopting the more stringent value. This was to avoid making a type II error, particularly because the majority of this thesis was an exploratory analysis with a novel syndrome group in which rarity restricts sample numbers. It was decided that an inclusive approach was preferable to overlooking potentially important results.

- When Spearman Rho and Pearson's correlations were conducted three associated Alpha levels were used throughout. In chapters two and five a large number of correlations were conducted together so these levels were more stringent (.01, .005, .001). In this chapter and the following chapter, three less stringent values were used (.05, .01, .005) because the analyses were broken into subsections and fewer correlations were conducted within these subsections in comparison to chapters two and five. These values are not as stringent using a Bonferroni correction, but a Bonferroni correction would have required p-values so small that it was unlikely that relationships would have been found, which would have rendered the results uninformative.

3.8 Chapter 3 Summary

The chapter has outlined the rationale for compiling a new battery of tasks to measure the development of EF in RTS syndrome. This battery was developed because of the dearth of suitable batteries that measure working memory, inhibition, and task shifting in sufficient detail. A review of the EF literature revealed a number of suitable tasks for measuring EF from 2.5 years, and tasks were selected that covered the developmental window during which EF is known to develop rapidly in TD children (3-5 yrs). These tasks were chosen because it was anticipated that they would be appropriate for individuals with ID. Pilot studies were reported in which the battery development was described as well as the changes that were made to tasks based on the performance of TD children. Hence, the final battery is a combination of tasks taken directly from the developmental literature and modified tasks.

Table 3.10.

A summary of the EF tasks included in the test battery developed for the current thesis. This information is presented in a format used by Garon et al. (2008.)

Task	***Description***	***Age range (MA)***
	Simple response inhibition tasks	
	Inhibition tasks where participants are not required to remember complex rules	
Object Retrieval	An object was placed in a transparent box. The participant must reach around the box to obtain the object through an opening. DV: the type of the reach (i.e. whether the participant can detour their reach to obtain the object).	6-12 months
Gift Delay (wrap and bow)	The participant was required to wait while a gift is wrapped for them and the experimenter searches for a bow to go on the gift. DV: whether the participant can wait.	22 months upwards
	Complex response inhibition tasks	
	Inhibition tasks with working memory demands (i.e. holding a rule in mind)	
Shape Stroop	The participant must point to small pictures of fruit superimposed in larger pictures of fruits. DV: the number of fruits correctly pointed to.	22-36 months
Reverse Categorisation	The participant sorts red balls into a blue bucket and blue balls into a red bucket. DV: number of balls correctly sorted.	24-42 months
Bear-Dragon	The participant does all the actions commanded by the bear and suppresses the actions commanded by the dragon. DV: number of correct dragon trials.	3+ years
Black-White Pointing	The participant points to a black card when the experimenter says white and a white card when the experimenter says black. DV: number of correct points.	3+ years
	Response shifting:	
	Shifting from to a new way of responding (does not contain an attention shift)	
A not B (Diamond,	The participant watched as an object was hidden under a cup and then was allowed to search for it after a delay. The side of hiding was reversed once the participant had obtained the item correctly on four consecutive trials. DV: number of erroneous reaches in the reversal stage	

Spatial Reversal	The participant searched for an object hidden under a cup. The side of hiding was reversed once the participant had obtained the item correctly on four consecutive trials. DV: number of erroneous reaches in the reversal stage	24 months and up

Table 3.10 continued.

A summary of the EF tasks included in the test battery developed for the current thesis. This information is presented in a format used by Garon et al. (2008.)

Task	***Description***	***Age Range (MA)***
	Attention shifting	
	Attending to a new aspect of the same stimulus in order to respond correctly	
DCCS (standard, border and separated dimensions version)	The participant sorted cards according to one dimension (shape) and then switched to sort cards by an alternative dimension (colour). DV: the number of cards sorted correctly in the post switch phase.	2.5 years and up
	Simple working memory tasks	
	Remembering information for a task at hand (does not require updating or monitoring)	
Corsi Blocks Task	The participant was asked to copy a sequence of taps on a block board. Sequences increased in length as the task progressed. DV: The number of correct pairs of box taps.	2 years and up
Verbal Animal Span	The participant was asked to repeat a list of animals or words. Sequences increase in length as the task progresses. DV: The number of correct pairs of animals.	2 years and up
	Complex working memory tasks	
	Remembering information for a task at hand and updating the information as the task progresses	
Scrambled Boxes	The participant searched for stars hidden within decorated boxes. The positions of the boxes were scrambled between searches. DV: the number of correct searches.	15 months and up
	Emotional Regulation	
	Suppressing a response that has a 'hot' affective component	
Secret Gift Task	The participant had to suppress an exciting secret that they and their parent/carer would receive a present from the experimenter. DV: whether the participant revealed the secret, latency to reveal the secret.	4 years and up

CHAPTER 4

Developmental Trajectories of the Executive Functions in Rubinstein-Taybi Syndrome

4.1 Preface

In chapter 3 a battery of tests was compiled for measuring the executive functions (EFs) in individuals who have intellectual disabilities in the moderate disability range. Tasks were selected from the literature that primarily measure inhibition, working memory, shifting and emotional regulation. Several pilot studies were conducted to explore whether the tasks were developmentally appropriate for individuals with a mental age of 2-5 years and modifications made to the tasks did not change their difficulty. In the following chapter the utility of this battery is demonstrated using a cross sectional developmental trajectory design. The battery was administered to individuals with Rubinstein-Taybi syndrome (RTS) with range of ages and ability levels and to typically developing (TD) children. The merit of mapping the developmental trajectories of the EFs is discussed in the introduction, not only in terms of linking the EFs to repetitive behaviour, but in terms of gaining a wider understanding of cognition in RTS relative to TD children.

4.2 Introduction

The executive functions (EFs) are perhaps one of the most extensively researched cognitive constructs in genetic syndromes. As discussed previously in section 1.5, EFs are often studied in rare genetic syndromes because of their hypothesised links with particular behaviours, for example, the executive dysfunction account of repetitive behaviour (Turner, 1997; Lopez, Lincoln, Ozonoff & Lai, 2005). However, EF profiles have also been studied in isolation from specific observable behaviour in rare genetic syndromes because delayed executive development or dissociations between EFs may have far reaching implications for a syndrome group across a number of environmental settings. For example, Jarrold et al. (1999) found that individuals with William syndrome have weaknesses with visuo-spatial working memory compared to relative strengths in phonological working memory, however, the opposite pattern was found in individuals with Down syndrome. One implication of this dissociation is that individuals from these syndrome groups may benefit from different educational strategies. This is particularly likely given working memory has been linked to educational achievement in individuals intellectual disabilities (Alloway & Temple, 2007; Henry & MacLean, 2003; Numminen et al., 2000) in a similar manner to that seen in typically developing (TD) children (Mazzocco & Kover, 2007; Gathercole, Tiffany, Briscoe, Thorn et al., 2005; Bull, Epsy & Wiebe, 2008).

A comparison of EF profiles of individuals with genetic syndromes to TD children may also lead to further research questions about the development of other cognitive skills and behaviour in these groups. It is probable that the relationships observed between EFs and cognitive processes in TD children may generalise to individuals with genetic disorders. In TD children, the development of the EFs have been related the development of a range of abilities including theory of mind, attention, rule use, counterfactual thinking and behavioural regulation (Hughes, 1998; Hughes & Ensor, 2007; Carlson, Moses and Breton, 2002, Diamond & Taylor; 1996; Lyon & Krashegor, 1996; Beck, Riggs, & Gorniak, 2009; Carlson, Mandell & Williams, 2004). For example, Beck, Riggs and Gorniak (2009) found that preschoolers' ability to consider how things could have been if events had occurred differently was related to inhibitory control (i.e. suppressing the knowledge of how things are now). Counterfactual thinking may also impact on the experience of regret and the ability to learn from experience (Gilovich & Medvec, 1995; Roese, 1997). Exploring the development of EFs in RTS will lead to deliberation about the relationship between EF development and other abilities in this syndrome, potentially opening up new avenues for research.

The development of the EFs is complex and in TD children different developmental trajectories for inhibition, working memory and shifting have been proposed (Davidson, Amso, Anderson & Diamond, 2006). Evidence that EFs may develop at different rates and be linked to the development of other cognitive processes supports Karmiloff-Smith's argument that it is questionable whether data collected at one stage of development has utility outside of that developmental window (see section 1.6.1; Karmiloff-Smith, 1998; Thomas, et al., 2009). Recently, authors have found that EFs in rare genetic syndromes may have syndrome specific trajectories. For example, a decline in the EFs has been found in older individuals with Down syndrome and successfully linked to the onset of dementia in this syndrome (Ball, Holland, Hon, Huppert, Treppner & Watson, 2006). Furthermore, Cornish, Scerif and Karmiloff-Smith at al., (2007) have demonstrated syndrome specific developmental trajectories for inhibition and attention in Fragile-X and Down syndromes that are not simply underpinned by generalised intellectual disability.

These descriptions of executive development are invaluable for informing strategies of how to best support individuals in different contexts and at different stages of their lives. There is growing evidence that cognitive training programs may be useful for individuals with EF problems. Klingberg, Forssberg and Westerberg (2002) have demonstrated that working memory can be trained successfully in people with Attention Deficit Hyperactivity Disorder (ADHD) using a computerised training program administered everyday for 25 minutes. Furthermore, this training program was effective for adults without a diagnosis of ADHD. In a randomised control trial Klingberg et al. (2005) found that children's working memory improved on these training programs alongside inhibition and complex reasoning. After training, parents reported that their children were less inattentive and hyperactive/impulsive at a three month follow-up.

Cognitive training and instruction in the use of rehearsal strategies has also been successful in increasing the amount of information individuals with learning disabilities can retain in working memory (Brown, Campione, Bray & Wilcox, 1973; Butterfield, Wambold & Belmont, 1973; Broadley & MacDonald, 1993; Conners, Rosenquist, Arnett, Moore & Hume, 2008; Van der Molen, Van Luit, Van der Molen, Klugkist & Jongmans, 2010). While some of these effects are small and are not always retained without practice, they have been shown to generalise to secondary tasks e.g. story telling (Conners et al. 2008; Laws, Macdonald, Buckley & Broadley, 1995). Furthermore, Conners et al. (2008) found that individuals with Down syndrome developed a phonological similarity effect during training, which they argued may indicate changes in the cognitive mechanism underpinning performance as opposed to individuals simply learning to apply a more effective memory strategy.

Despite the merit of studying EFs in rare genetic syndromes there is still a dearth of research detailing the development of the EFs in a wide range of disorder groups (Karmiloff-Smith, 1998; Paterson, Brown, Gsödl, Johnson & Karmiloff-Smith, 1999; Scerif and Karmiloff-Smith, 2005). For example, very little is currently known about the EF profile of Rubinstein-Taybi syndrome (RTS). The research focus in RTS has largely been on the syndrome's genetic markers, including the (CREB)-binding protein (CBP), and how this impacts on long-term memory in RTS. This has led to the suggestion that intellectual disability in RTS is linked to difficulties in the retention and retrieval of long-term memories (Oike et al., 1999; Wood et al., 2005). While this is clearly a key area of research in RTS, the syndrome is also characterised by dissociations in the profile of repetitive behaviours, which may indicate underlying EF problems (see section 2.4.1.2 for discussion). Furthermore, the CREB binding protein is associated with the hippocampal regions that project to the frontal lobes, thus these mutations may indirectly impact on the development of EFs (Petrij et al., 1995; Wood et al, 2005; Dégenètais et al., 2003).

Thomas et al. (2009, 2010) have described how trajectory methods can be applied to help understand cognitive development in disorder groups; hence the application of this methodology may be useful for understanding EFs in RTS (described in section 1.6.1). Thus, the principle aim of this chapter was to employ developmental trajectory methodology to study the development of EFs in RTS relative to TD children. This was to inform understanding of the EFs in RTS by exploring whether EF development is delayed or deviant. A secondary aim was to demonstrate proof of principle of this approach when studying EF development. It was hoped that the results would lend support for further research exploring EF development in disorder groups. In particular, it was hoped that findings displayed in this chapter would demonstrate how tasks that had been selected and adapted from the TD literature can fit with a developmental approach in disorder groups. As this is a relatively new area of research two methodological issues will also be addressed in this chapter. Firstly, psychometric tests and adaptive assessments were used to estimate mental age (MA) in an RTS sample so that developmental trajectories could be constructed. Given that interpretation of the trajectories depends largely on the accuracy of these mental age estimates a further aim was to explore the convergent validity of these estimates across assessments and to plot the developmental trajectory of mental age as a function of chronological age (CA) age in RTS. The second methodological issue relates to the task impurity problem. In RTS, the influence of working memory on inhibition task performance was explored to confirm that individuals were not failing inhibition tasks because of an inability to hold the rules of the tasks in mind; poor working memory is often observed in people with intellectual disabilities (Numminen et al., 2000).

To summarise, in this chapter these aims were addressed in the following order:

- The convergent validity of the MA assessments was explored, and the developmental trajectories of MA relative to CA were plotted.
- The performance of individuals with RTS on EF tasks was explored using a developmental trajectory approach.
- The influence of working memory on inhibition task performance was explored the RTS.

Given the repetitive behaviour profile of RTS and the emerging evidence linking repetitive behaviour to the EFs (see sections 2.4 & 1.5) it was predicted that individuals with RTS would have delays or deficits in some domains of EF relative to MA.

4.3 Methods

4.3.1 Participants

4.3.1.1 Rubinstein-Taybi Syndrome.

32 participants with RTS took part in the study (16 males; mean chronological age: 222 months; age range: 45-533m; SD: 121.03). 27 participants were recruited from a database held by the Cerebra Centre for Neurodevelopmental Disorders at the University of Birmingham, and five were recruited via the RTS Support Group[1]. All participants with RTS were White-Caucasian ethnic origin. Participants were included if they were at least 36 months old, were mobile, lived in the UK and had a confirmed clinical diagnosis based on the physical characteristics of the syndrome. Few participants had a genetically confirmed diagnosis, partly due to genetic abnormalities typically being found in only 55% of cases (Hennekam, 2006); however, few behavioural and cognitive differences have been identified between those with and without a genetically confirmed diagnosis (Bartsch et al., 1999).

All 32 participants were included in an analysis of convergent validity between MAs obtained from the psychometric assessments (MSEL-WASI-II combination) and Vineland Adaptive Behavior Scales. Seven participants were excluded from the EF trajectory analysis because they did not comprehend the instructions for over 75% of the test battery due to their young age or the severity of their intellectual disability. Practical constraints of testing in schools meant that normative data could not be collected below 39 months of age. Therefore, it was not possible to compare the youngest individuals with RTS to TD children. Of the seven excluded individuals, six had MAs below 39 months, so would not have been included in the

[1] The 27 participants who were recruited through the cross syndrome database formed part of the sample from chapter 2. In addition, all 32 participants are included in chapter 5. See Appendix G and H for recruitment packs for current study.

analysis even if they met the first exclusion criterion. The mean chronological age of the remaining 25 participants was 251 months (12 males; age range 81-533m; SD: 118.53).

Of the 25 participants included in the EF trajectory analysis, one individual did not complete the Black-White Stroop and the Shape Stroop, and two participants did not complete the Dimensional Change Card Sort (DCCS), Spatial Reversal and Verbal Animal Span, due to fatigue or lack of interest.

4.3.1.2 Typically Developing Children.

207 TD children[2] with a mean CA of 59 months (range: 30-89 m; SD: 14.80) were recruited from schools in the West Midlands to form a comparison group. TD children were recruited after it was ascertained that the majority of individuals with RTS in the sample had MAs between 39 and 90 months. 62.6% of TD participants were White-Caucasian ethic origin, 19.0% were Asian and 18.4% were Black. Participants were included in the analyses if they were between 36-90 months old and were not identified by their class teacher as having a developmental disability. Due to time constraints of testing in schools each TD child completed either the inhibition (N = 72), working memory (N = 90) or shifting subdomains of the EF battery (N = 91) and none of the children completed an assessment of cognitive ability. 20 children were excluded from the reversal stage of the Spatial Reversal task because they failed to attain set in the attainment stage prior to the shift.

To plot TD trajectories data was collected from an equal number of TD children (between 8 and 10 children) on each subdomain of the EF battery across 6 month age bands from 3 to 7 years. However, in this chapter where age bands are used they were collapsed into 12 month

[2] Two MRes students tested the typically developing children under the supervision of the chief investigator.

bands. This was to increase the number of participants with RTS in each age band. The number of TD children and participants with RTS in each age band for each subsection of the EF battery is displayed in table 4.1. In table 4.1 individuals with RTS were grouped into age brackets on the basis of their MA derived from the psychometric assessments described below, while the TD group were grouped in terms of the CA. Although MA was not measured in the TD group there is no reason to expect that MA did not equal CA in this group.

TD data for the inhibition tasks, the Spatial Reversal and Scrambled Boxes tasks were not collected beyond 78m because children were approaching ceiling on the majority of these tasks at this age. TD data were collected up to 90m for the working memory span tasks and the DCCS tasks (group sizes are displayed in table 4.1).

Table 4.1
N of RTS and TD participants in each 12 month age band

Task	Group	Age Band (TD = CA; RTS = MA) 3yr 0 m – 3 yr 11 m	4 yr 0 m – 4 yr 11 m	5 yr 0 m – 5 year 11 m	6 yr 0 m – 6 year 11 m	7 yr 0 m – 7 year 11 m	8 yr 0 m – 8 yr 11 m	9 yr 0 m – 12 yr 11 m	Total Number of Participants < 6.5 years[a] or < 7.5 years[b]
Inhibition Analysis									
Shape Stroop	RTS	3	7	6	3	1	0	4	17
	TD	19	23	20	10	0	0	0	72
Reverse Categorisation	RTS	4	7	6	3	1	0	4	18
	TD	19	23	20	10	0	0	0	72
Bear-Dragon	RTS	4	7	6	3	1	0	4	18
	TD	19	23	20	10	0	0	0	72
Black-White Stroop	RTS	3	7	6	3	1	0	4	17
	TD	19	23	20	10	0	0	0	72
Inhibition Composite	RTS	-	-	-	-	-	-	-	17
	TD	-	-	-	-	-	-	-	72
Working Memory Analysis									
Animal Span	RTS	3	7	6	3	1	-	-	20
	TD	17	22	20	21	9	-	-	89
Corsi Span	RTS	4	7	6	3	1	-	-	21
	TD	17	22	20	21	9	-	-	89
Three Scrambled Boxes	RTS	4	7	6	3	1	0	4	21
	TD	17	22	21	8	0	0	0	88
Six Scrambled Boxes	RTS	4	7	6	3	1	0	4	21
	TD	18	22	21	9	0	0	0	90
Nine Scrambled Boxes	RTS	4	7	6	3	1	0	4	21
	TD	17	22	21	8	0	0	0	90
Scrambled Boxes Composite	RTS	-	-	-	-	-	-	-	21
	TD	-	-	-	-	-	-	-	88

[ab] Only individuals below the ages of 78 (6.5 years) were included in the between groups comparison of performance on the inhibition tasks using ANOVA, and below the ages of 90m (7.5 years) for the shifting and working memory tasks. This was because typically developing data were not collected beyond this point.

Table 4.1 continued.
N of RTS and TD participants in each 12 month age band.

Task	Group	Age Band (TD = CA; RTS = MA)							Total Number of Participants < 6.5 years[a] or < 7.5[b] years
		3yr 0 m – 3 yr 11 m	4 yr 0 m – 4 yr 11 m	5 yr 0 m – 5 year 11 m	6 yr 0 m – 6 year 11 m	7 yr 0 m – 7 year 11 m	8 yr 0 m – 8 yr 11 m	9 yr 0 m – 12 yr 11 m	
Shifting Analysis									
DCCS (all versions)	RTS	3	7	5	3	1	0	4	19
	TD	21	21	20	22	7	-	-	91
Spatial Reversal (Reversal Stage)	RTS	-	-	-	-	-	-	-	17
	TD	-	-	-	-	-	-	-	71
Spatial Reversal (Attainment Stage)	RTS	-	-	-	-	-	-	-	12
	TD	-	-	-	-	-	-	-	71

[ab] Only individuals below the ages of 78 (6.5 years) were included in the between groups comparison of performance on the inhibition tasks using ANOVA, and below the ages of 90m (7.5 years) for the shifting and working memory tasks. This was because typically developing data were not collected beyond this point.

4.3.2 Measures

4.3.2.1 Mental age assessment using psychometric tests

Participants with RTS completed either the Mullen Scales of Early Learning (MSEL: Mullen, 1995), which is suitable for individuals from birth to a MA of 5:8 years, or the Wechsler Abbreviated Scales of Intelligence – Second Edition (WASI-II: Wechsler, 1999), which is suitable for individuals with a MA of 6:0 – 89:0 years. To obtain a global MA or full scale IQ score on these assessments raw scores on the subscales are first converted into t-scores based on the participant's CA. T-scores give a more accurate estimate of IQ than raw scores because they are calculated based on CA. However, t-scores could not be calculated for the MSEL in the current study because 94% of participants were older than 68 months and normative data are not provided past this age in the assessment manual. A global MA could not be generated for participants using the WASI-II protocols because none of the participants scored high enough on all four subscales for it to be calculated. Therefore, global MAs were generated for the current study using the method reported by Richler, Bishop, Kleinke and Lord (2007), in which MAs for each subscale of a given assessment were obtained from the raw score tables and a mean was taken. MA in months was derived from the MSEL by averaging MAs for the receptive language, expressive language, visual reception and fine motor domains. The gross motor subscale was not included because the highest MA attainable on this subscale was 33 months and its inclusion would have lowered the mean MA. MA was calculated for the Wechsler Abbreviated Scales of Intelligence (WASI-II), by averaging the MAs for all four subdomains of this battery. The MAs obtained from these two assessments formed a scale for the analyses and is referred to henceforth as the MSEL-WASI-II combination.

4.3.2.2 Adaptive ability assessment

The Vineland Adaptive Behavior Scales – Second Edition (VABS-II; Sparrow, Cicchetti & Balla, 2005) were included as an alternative measure of MA based on parent report rather than direct assessment. There are no guidelines for computing a global MA for the VABS. In the same manner as for the psychometric assessments, a global MA was calculated for the current study by taking an average across the nine primary domains of this assessment. This assessment was included so that it could be used in an analysis of convergent validity with the MA assessment.

4.3.2.3 Battery of Executive Functions for People with Intellectual Disabilities (BEF-ID)

The EF test battery described in chapter 3 was employed. This battery will henceforth be referred to as the Battery of Executive Functions for People with Intellectual Disabilities (BEF-ID). The BEF-ID includes tests of conflict inhibition, working memory and attention/response shifting. The battery also includes a test of emotional regulation (the Secret Gift task) and delay inhibition (the Gift Delay task); however, these tasks were omitted from this analysis because TD data could not be collected for these tasks due to constraints of testing in schools. The RTS data from these omitted tasks will be used in the correlational analysis in chapter 5 that examines associations between performance on the EF measures and repetitive behaviour. The Object Retrieval task and A not B task were also omitted because all participants who completed them were at ceiling on these tests. The final test battery included tests that were suitable for individuals with a range of MAs (24-72 months) (Carlson, 2005). There were five inhibition tasks (Shape Stroop, Reverse Categorisation, Bear-Dragon and Black-White Stroop), three working memory tasks (Verbal Animal Span, Corsi Blocks task, and three, six and nine Scrambled Boxes), and two shifting tasks (Spatial Reversal, and the separated dimensions, standard and border versions of the DCCS).

Heald (2010) analysed the reliability and validity of the BEF-ID when administered to TD children (excluding the Gift Delay and Secret Gift tasks). The inhibition tasks, working memory span tasks and the DCCS[3] have good internal validity (Cronbach's alpha & split-half reliability > .80). The convergent validity for the inhibition tasks was measured using Pearson's partial correlations (controlling for age). There were moderate significant correlations between all inhibition tasks, apart from between the Shape Stroop and Reverse

[3] The Spatial Reversal and Scrambled Boxes tasks did not have a set number of trials so split-half reliability could not be calculated (Heald, 2010).

Categorisation, indicating good convergent validity. There were no significant correlations between the working memory tasks (Verbal Animal Span, Corsi Blocks and Scrambled Boxes) or between shifting tasks (DCCS and Spatial Reversal), however, this was taken as an indicator of good divergent validity in line with Baddeley's model of working memory in which working memory is divided into visuo-spatial and phonological components (Baddeley & Hitch, 1974). The set-shifting tasks can be divided in a similar manner into attention and response shifting tasks (see Garon et al. (2008) for a review).

4.3.2.3.1 Administration and coding of the BEF-ID.

The BEF-ID, along with the other measures, was administered to participants with RTS in their homes. Each measure took approximately five minutes to administer. An overarching focus of this research was on individual differences (i.e. to associate performance on EF tasks with the degree of repetitive behaviour in chapter 5), so when possible the battery was administered in a predetermined set order as depicted in figure 4.1. As noted previously, while there were three versions of the Scrambled Boxes test and DCCS in the battery each individual only completed two of them. If the participant had completed all the tasks they may have experienced fatigue, have become bored if the task was too easy, or upset if the task was too hard.

On the Six Scrambled Boxes task, if a participant retrieved all six stars without error the task was repeated using nine boxes. However, if an error was made the task was repeated with three boxes. So that all participants could be included in the analysis for each version of the scrambled box task and for a composite score to be calculated across the tasks, participants who did not complete the Three Scrambled Boxes task were assigned a full score for this task and those who did not complete the Nine Scrambled Boxes task were assigned a score of 0 for the task. A composite score was calculated by summing scores from the three tasks.

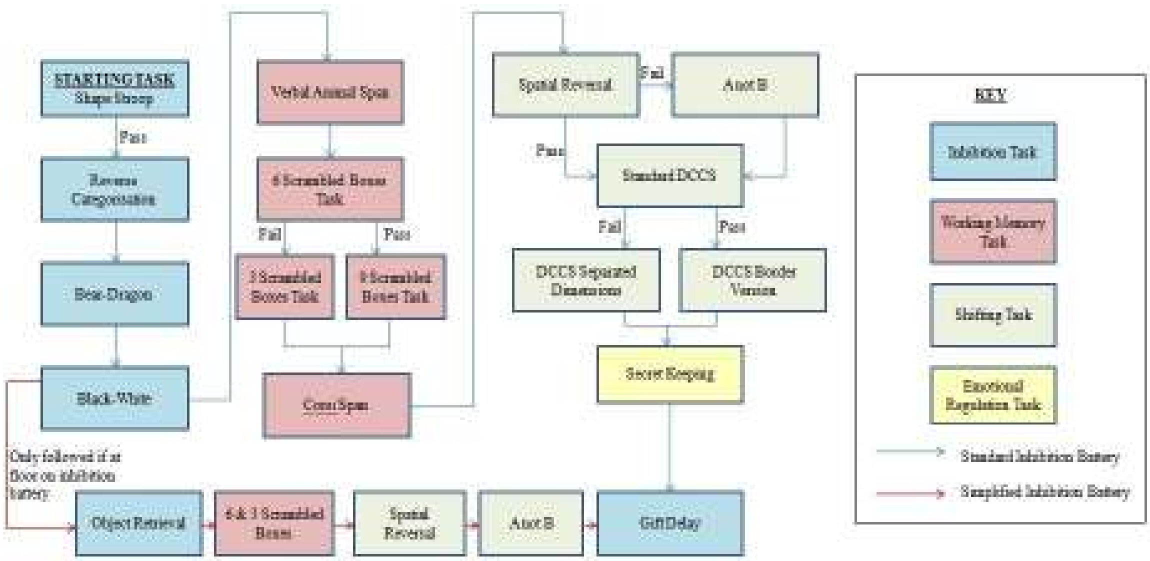

Figure 4.1
The order of administration of the BEF-ID in the current study.
Note. There are two potential routes that can be followed on this battery. All participants who are included in this chapter followed the route depicted in the top half of the diagram.

On the DCCS, all participants completed the standard version first and depending on their performance they either completed the border version (after errorless performance on the standard version) or completed the separated dimension version (if they made an error on the standard version). All versions of the DCCS were re-coded out of 12 so that the scores from each version of the DCCS would contribute equally to a composite score. So that a composite score could be calculated for every participant, participants who did not complete the Border version of the DCCS were assigned a score of 0 and those who did not complete the separated dimensions version the task were assigned a full score (12 out of 12) on the task. The composite DCCS score was computed by summing performance across the three tasks.

Tasks from the inhibition battery were also re-coded out of 16 prior to computing a composite inhibition score. Additional check questions were introduced for the RTS group at the end of the Bear-Dragon task ("who don't we listen to?"), Reverse Categorisation task ("see this bucket, what colour ball?") and the black white Stroop ("When do you point to this card?") to check the participant had retained the rules of the task. All other tasks were administered and coded in accordance with the descriptions in chapter 3.[4]

Breaks were given between each subdomain of EF battery (i.e. after the inhibition tests, and working memory tests) and between each subdomain of the IQ assessment. It was not always possible to administer the tests in the predetermined set order. Due to engagement difficulties, six participants received the working memory tasks first. One concern was that fatigue effects may impact on later performance. Mann-Whitney U tests were conducted to explore whether the performance of those individuals who had the working memory tasks prior to the inhibition tasks differed to those who had received the inhibition tasks first. No differences were found (all *p*s > .05; see Appendix I for a breakdown of these results).

[4] A number of different coding schemes were compared prior to this analysis for the RTS group. For the inhibition tasks this involved increasing the range of possible scores by coding hesitant responses and response corrections separately from immediate incorrect or correct responses. The coding schemes did not change the results so the most parsimonious coding scheme was adopted. For the working memory tasks, three alternative coding schemes were compared including one point per correct item plus one point per correct position. The different schemes did not alter the RTS span task trajectories or results reported later in this in this thesis. The pairs coding scheme was adopted for the span tasks after a preliminary analysis of the RTS data was conducted with a subset of participants for a conference. There appeared to be a slightly stronger trend between the Corsi Blocks Span and the Six Scrambled Boxes task (the other visuo-spatial measure) when the pairs coding scheme was used. It had been anticipated that these visuo-spatial working memory measures would measure of the same construct so the pairs coding scheme was chosen because of this trend. This trend later disappeared as more participants were added to the data set. The pairs coding scheme was chosen for in the final analyses for consistency with previous analyses.

4.3.2.3.2 Inter-rater reliability for coding of BEF-ID.

All coding was conducted initially by a first coder using video recordings. The coding largely relied on objective judgements about clearly definable behaviour (i.e. pointing to a black card in the Black-White Stroop). Interrater reliability was obtained using a second coder for five participants for each task in the battery. These participants were selected by the second coder and where possible participants were selected who were neither at floor nor ceiling on the given test. There was perfect agreement (Kappa = 1) for the all shifting tasks, the Scrambled Boxes tasks, the Reverse Categorisation, Bear-Dragon and Black-White Stroop. There was also perfect agreement between coders for the Corsi Blocks task (Interclass coefficient = 1). Perfect agreement was absent for the Shape Stroop (Kappa = .84) and the Verbal Animal Span (Interclass coefficient = .84).

On the Shape Stroop the coders disagreed about what constituted a participant hesitating on a response (i.e. hand wavering tentatively over one response option) and a definite answer. It was agreed that if the participant appeared to complete their motor movement (e.g. a point) then this was classed as a definite response. A wavering hand movement towards the incorrect response option followed by a correct adjustment was coded as correct. For the Verbal Animal Span the coders disagreed as to whether a participant was saying ‘cat’ or ‘cow’. A third rater was consulted to resolve this issue. The tasks were re-coded based on these observations and perfect agreement was obtained.

4.3 <u>Overview of data analyses and results sections</u>

To recap, the aims of this chapter were to describe the convergent validity of the MA assessments used in the construction of the developmental trajectories; to compare the development of the EFs in individuals with RTS to TD children; and to examine overlapping executive demands in the test battery. The data analyses and results sections address each of these aims in turn. The EF analyses are conducted for each individual subdomain of the EF battery. The details of the specific data analyses are provided in each subsection of the results to aid interpretation given the large number of analyses conducted within this chapter. Alpha levels were set as outlined in section 3.7 of this thesis.

4.4 Results

4.4.1 Convergent validity between mental ages derived from the cognitive and adaptive assessments

An analysis was conducted to examine whether MAs derived from the MSEL-WASI-II combination had convergent validity with MAs derived from and VABS in the RTS group. Prior to this analysis a square root transformation was applied to the data because inspection of the data revealed that the MAs derived from the VABS, and the CAs of the RTS participants, were positively skewed. Parametric correlations were then employed to explore the relationship between these measures and an intraclass correlation coefficient was calculated, which is a general measure of agreement.

The mean, range and standard deviation for the MAs obtained for the RTS participants from the psychometric assessments (MSEL-WASI-II combination) and the adaptive assessment (VABS) are displayed in table 4.2 without the square root transformation. Pearson's correlations between the square roots of CA and the MAs obtained from the assessments are displayed in table 4.3.

Table 4.2

Means, ranges and standard deviations of mental ages from the psychometric and adaptive assessments.

	Mean (SD)	Range
MSEL-WASI-II combination	61.83 (34.20)	14.50-146.70
Mental age from VABS	65.89 (37.16)	17.89-164.78

Note. Statistics are presented without the square root transformation

Table 4.3

Pearson's correlations between the mental ages derived from the cognitive and adaptive assessments (Sq Roots)

	Mental age from MSEL-WASI-II combination (Sq Root)	Mental age from VABS (Sq Root)
Chronological Age (Sq Root)	.65***	.71***
Mental age from MSEL-WASI-II combination (Sq Root)		.91***

***. Correlation is significant at the .001 level (2-tailed).

There was a strong positive relationship between the MAs derived from the psychometric assessments (MSEL-WASI-II combination) and the adaptive assessment (VABS) (R = .91, $p < .001$). The intraclass reliability coefficient between MAs derived from the VABS and psychometric assessments (MSEL-WASI-II combination) was .91 (95% CI: Lower = .82, Upper = .96, (df: 30, 30), F = 21.41, $p < .001$).

4.4.2 Data analysis: Trajectory analysis of mental age measures using linear methods

In the RTS group the relationship between MA equivalent scores derived from the psychometric assessments (MSEL-WASI-II combination) and adaptive assessment (VABS) were explored using a linear trajectory analysis (as described by Thomas et al., 2009, 2010). Linear trajectory analysis compares the onset and slope of trajectories that are plotted as a function of age, to ascertain whether the developmental trajectories differ. SPSS does not have a direct way of comparing trajectories so Thomas et al. (2009, 2010) recommends an adaption to the Analysis of Covariance function within General Linear Model (ANCOVA).

This analysis consisted of three steps. Firstly, a linear regression was conducted to generate the intercept and gradient of the MSEL-WASI-II and VABS trajectories as functions of CA. To aid interpretation CA was rescaled so that the difference between the intercepts of the two trajectories would indicate the difference in MA generated by the assessments at the youngest age of measurement in RTS. The gradient indicated the rate of development for each trajectory.

Secondly, to explore the *overall* differences between the MAs generated by the two assessments the analysis was employed without the covariate (CA). This was essentially a repeated-measures ANOVA with two levels (assessment). Finally, this latter step was repeated adding in CA as a covariate (ANCOVA). The between subjects effects were examined for an overall effect of CA on performance on the assessments. The within subject contrasts were then examined for an interaction between age and task that would indicate the trajectories for the two assessments were different in RTS.

All assumptions for this analysis were met: curve fit analysis and visual inspection of these data revealed the two relationships were sufficiently linear for trajectory analysis. Cook's distance (Cook's D) was conducted and none of the values exceeded 0.2 (values > 1 are potential outliers).

4.4.2.1 Results: Trajectory analysis of mental age measures using linear methods

Figure 4.2 depicts the two developmental trajectories: one for the relationship between Sq roots of MAs that were calculated using the psychometric assessments (MSEL-WASI-II combination) and the Sq roots of CAs, and one for the relationship between Sq roots of MAs that were calculated using the Vineland Adaptive Behavior Scales and Sq roots of CAs.

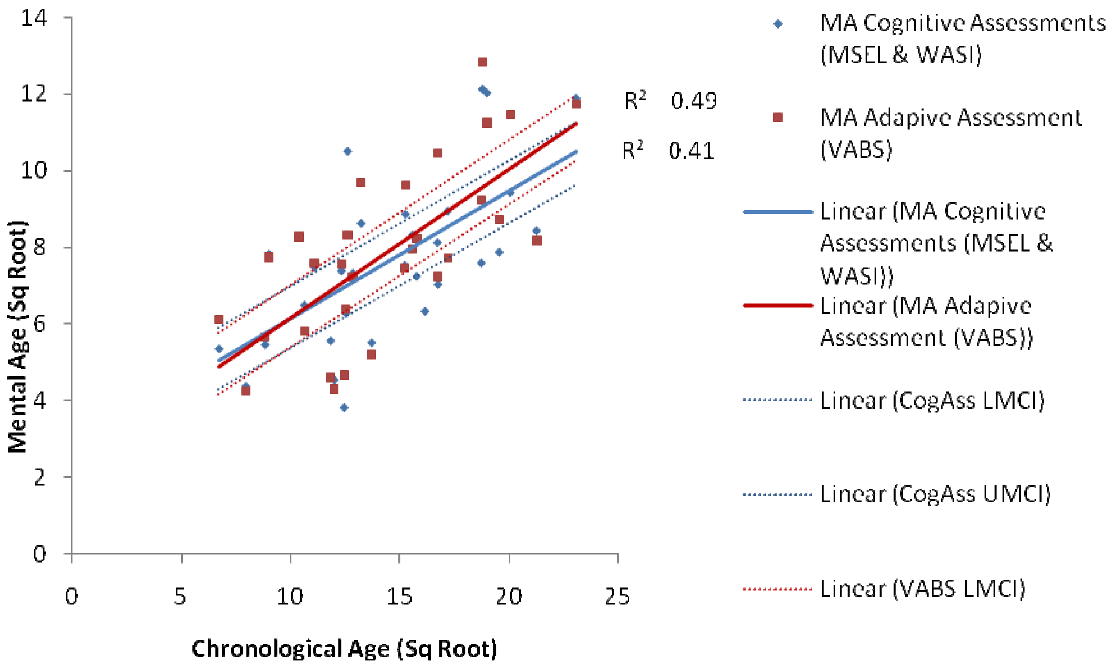

Figure 4.2.
The relationship between the square roots of CA and MA as derived from the psychometric assessments (MSEL-WASI-II combination) and the adaptive assessment (VABS)
Note. This relationship is displayed without the transformation in Appendix J.

A straight line was a reliable fit for the data derived from the MSEL-WASI-II combination (R^2 = .41, F(1, 30) = 20.50, p<.001) with an intercept (constant) of 4.18 and a gradient of 0.27; 95% CI: 2.23 to 5.83. These results indicate that for every chronological month (Sq root), mental age (Sq root) is 0.27 months higher in the RTS sample. A straight line was also a reliable fit to the data derived from the VABS (R^2 = .49, F(1, 29) = 26.73, p<.001) with an the intercept (constant) of 3.89 and the gradient of 0.32; 95% CI: 2.23 to 5.56.

The repeated measures ANOVA revealed no significant differences for the RTS group's overall performance on the MSEL-WASI-II combination when compared to the VABS (F(1, 30)=1.19, *p* = .284 η^2= 0.04). The results obtained from the ANCOVA indicated that overall performance significantly improved with age (F(1,29)=26.16, *p* < .001, η^2 = 0.04) but that there is no significant interaction between age and assessment (F (1,29) = 1.12, *p* =.299, η^2 =

0.37) suggesting that the RTS group did not improve at different rates on these two assessments.

The two developmental trajectories for MAs derived from the psychometric assessments (MSEL-WASI-II combination) and the adaptive assessment (VABS) were well aligned. The convergence between the two measures suggests that they are likely to represent a robust estimate of MA relative to CA. For the remainder of this analysis the MAs derived from the combination of the psychometric assessments will be used (MSEL-WASI-II combination) because the psychometric assessments were a direct assessment of participants' abilities rather than the VABS which is a parental report method.

4.5 <u>Executive function results</u>

4.5.1 The development of the executive functions

The second aim in this chapter was to describe the development of the EFs in RTS relative to TD children. An overview of the analyses that were applied to the EF battery will be presented first followed by the results of each subdomain of the battery. A more specific description of the analyses applied for each subdomain is provided alongside these results.

4.5.2 Overview of executive function data analysis

The analyses of the EF tasks followed a systematic format throughout. Analyses were conducted for each EF component measured by the battery. Descriptive statistics were produced and Spearman-Rho correlations were conducted to explore the relationships between scores on each task[5], composite score, CA and MA in RTS. Spearman Rho correlations were used throughout due to the small sample size and non-parametric nature of the majority of the data.

Following this, an attempt was made to isolate a linear portion of a trajectory for performance on each task for the RTS and TD groups. If a linear portion of a trajectory was established, analysis using linear methods was employed as described by Thomas et al. (2009, 2010). If a linear portion of the trajectory could not be isolated, between groups and repeated-measures ANOVAs were conducted to explore performance on the tasks within and across groups as opposed to conducting a complete trajectory analysis. Visual depiction of these data in 12 month age bands supplements analyses of variances.

4.5.2.1 Upper age limits of analysis.

As previously noted TD data were collected up to 78m for the inhibition tasks, the Scrambled Boxes tasks and Spatial Reversal task, and up to 90m for the working memory span tasks and DCCS. When between group ANOVAs were conducted to compare the RTS and TD groups, only RTS participants up to these ages were included in the analyses. This meant that a small number of more able participants were excluded, but it ensured that the two groups well matched. This decision was further supported for the inhibition battery and DCCS tasks (standard & separated versions) because the majority of participants in both groups were at ceiling on these tasks by these ages. For some tasks, only between group analyses were

[5] Analyses have been conducted throughout for individual tasks as well as for the composite scores. This is because the composite score is a new and arbitrary way of compiling the data and it was considered important to explore relationships at individual task level alongside the composite analyses.

conducted so the descriptive statistics presented in these subsections are for the individuals included in the analyses not the entire group.

All RTS participants were included in the correlational analyses for the inhibition, Scrambled Boxes and shifting tasks. These correlational analyses were largely exploratory and were conducted to: a) inform a decision as to whether to focus on CA or MA trajectories b) describe overall relationship between CA, MA and task performance in the group. Excluding participants would have reduced power to detect these relationships.

An exception to this general rule occurs in the working memory span subsection where both descriptive statistics and correlations are reported for just the individuals with a MA below 90 months. This is because only developmental trajectory analyses using linear methods were applied to these data (not ANOVA). It was not possible to infer how RTS participants with a MA greater than 90 months were performing relative to the comparison group because the data were continuous (no ceiling effects). Thus, it was decided that the four participants with MA above 90 would be excluded prior to span task analyses so that the trajectories that would be compared would be for the age range where TD data were available. The four participants were excluded from the correlations and descriptive statistics for consistency and to aid interpretation of the results. The implications of their exclusion are discussed alongside these results.

4.5.2.2 Outliers

When trajectory analysis using linear methods was conducted these data were examined for outliers using Cook's D. No data points had a Cook's D value above 0.3 so no outliers were found for these analyses. When between subjects and repeated-measures ANOVAs were used, in agreement with Thomas et al. (2009, 2010), it was decided that outliers would not be excluded from the RTS group unless there was prior reason to believe that their performance was atypical. A large variation in scores within a syndrome group is not uncommon and is often due to the varying degrees of intellectual disability within a syndrome group. Outliers were not excluded from the TD data for consistency. Where parametric statistics have been conducted, the equivalent non-parametric statistics have also been employed to reduce the effects of any potential outliers or violations of normality as it was not possible to transform the data from the inhibition tasks, the Scrambled Boxes tasks and the shifting tasks which were skewed.

4.5.3 Results for the inhibition tasks

4.5.3.1 Inhibition descriptive statistics and correlations

The descriptive statistics for each inhibition task and the results of the non-parametric correlations for the inhibition tasks with MA and CA are displayed in tables 4.4 and 4.5.

As MA increased people with RTS performed better on the Shape Stroop ($R = .67$, $p < .001$), the Reverse Categorisation ($R = .64$, $p = .001$) and the Bear-Dragon tasks ($R = .73$, $p < .001$). There was an overall positive relationship between MA and the composite inhibition score ($R = .82$, $p < .001$). However, the relationship between performance on the Black-White Stroop and MA only approached significance ($R = .48$, $p = .017$). Given that there were no significant relationships between CA and the inhibition tasks, the following inhibition analysis focuses solely on the relationship between MA and task performance.

Table 4.4
Mean, range and standard deviation for the inhibition tasks and the Inhibition Composite Score

	Total Sample RTS N = 25; TD N = 72				Sample <77m N = 17 - 18	
	TD		RTS		RTS	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Shape Stroop	15.33 (2.52)	0-16	13.11 (4.71)	0-16	11.92 (5.17)	0-16
Reverse Categorisation	14.56 (2.64)	1.33-16	12.91 (4.52)	2.67-16	11.85 (4.92)	2.67-16
Bear Dragon	12.36 (6.44)	0-16	7.28 (7.48)	0-16	3.89 (5.96)	0-16
Black-White Stroop	11.49 (5.52)	0-16	10.79 (4.19)	1-16	10.06 (3.98)	1-16
Inhibition Composite Score	53.74 (13.56)	18.67-67	44.38 (15.14)	20-64	37.86 (12.92)	20-64

Table 4.5
Correlations between chronological age, mental age, inhibition tasks and composite inhibition score in RTS.

	Mental Age (m)	Shape Stroop	Reverse Catego-risation	Bear-Dragon	Black-White Stroop	Inhibition Composite Score
Chronological Age (months)	.50*	.31	.40	.22	-.00	.26
Mental Age (months)		.67***	.64***	.73***	.48*	.82***
Shape Stroop			.58***	.56*	.26	.76***
Reverse Categorisation				.45*	.38	.71***
Bear Dragon					.45*	.80***
Black-white Stroop						.68***

* Correlation is significant at the .05 level (2-tailed).
** Correlation is significant at the .01 level (2-tailed).
*** Correlation is significant at the .005 level (2-tailed).
RTS N = 25

4.5.3.2 Trajectory analysis using linear regression methods

The possibility of plotting a linear trajectory as a function of MA was assessed for the inhibition tasks. A linear trajectory could be plotted for a proportion of the RTS inhibition composite data once a subset of participants who were at ceiling on the inhibition battery (higher MAs) was removed. However, this was not possible for the individual inhibition tasks. In addition, a large proportion of TD children were at ceiling on the inhibition tasks, which meant that it was not possible to isolate a satisfactory linear proportion of the inhibition composite data for the TD group. Despite this, a linear trajectory analysis was conducted to compare these groups on the composite inhibition score as a function of MA. When interpreting this analysis, the influence of ceiling effects on the TD trajectory should be considered. It is likely that the TD inhibition trajectory would be stepper if ceiling effects had been avoided by the inclusion of inhibition tasks for older children.

To compare the two trajectories the Analysis of Covariance function within the General Linear Model (ANCOVA) was adapted as described by Thomas et al. (2009; 2010) by adding an interaction term into the model (group x MA). This was necessary because, without an interaction term, a typical ANCOVA works on the assumption that the two trajectories are the same, rather testing whether the two trajectories differ.

Despite influence of ceiling effects, figure 4.3 depicts that a straight line affords a reliable fit to the TD data (R^2 = .24, F(1, 66) = 20.66, p<.001). This line has an intercept (constant) of 45.62 and a gradient of 0.54; 95% CI: 40.53-50.71. A straight line also reliably fits the RTS data (R^2 = .64, F(1, 19) = 32.21, *p* <.001), with an intercept (constant) of 22.63 and a gradient of 0.83; 95% CI: 14.74-30.53.

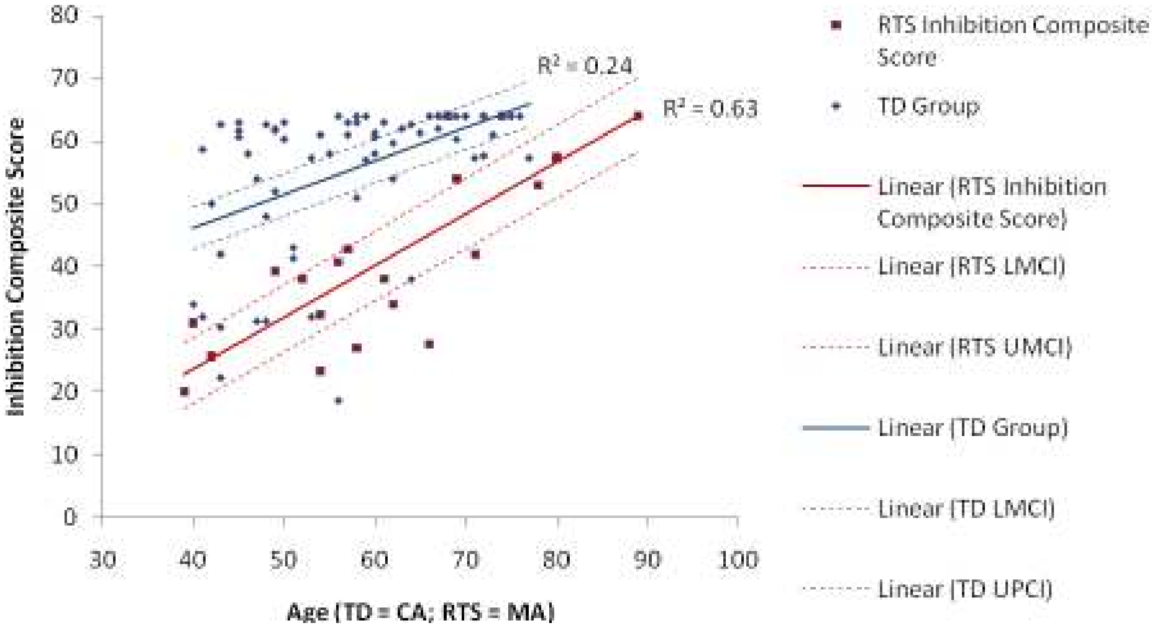

Figure 4.3
TD and RTS trajectories for the composite inhibition score.
Note. The four participants with higher MAs (MA > 100m) who were at ceiling on this battery were excluded so that a linear proportion of the trajectory could be isolated
Note. Age was rescaled from the youngest age of measurement in RTS.

Trajectory analysis was conducted. The R^2 explained by this model was .48. The model explained a significant proportion of this variance ($F(2,84) = 38.84$, $p < .001$, $\eta^2 = .48$). There was an overall effect of group ($F(1,84) = 42.56$, $p <.001$, $\eta^2 = .34$) illustrating a significant difference in scores at the youngest MA in RTS (39m). This indicated that the RTS group have a delayed onset of development for inhibition relative to the TD group. In fact, there is 22.99 point difference in the composite inhibition score at 39m. Age significantly predicted performance when the two groups were amalgamated ($F(1,84) = 45.42$, $p < .001$, $\eta^2 = .36$), but there was no significant interaction between group and age ($F(1,84) = 2.18$, $p = .144$, $\eta^2 = .03$). This would usually be interpreted as evidence that individuals with RTS are developing at the same rate as TD children; however it is possible that differences between the groups were masked by the ceiling effects in the TD group

4.5.3.3 Trajectory analysis for individual inhibition tasks using ANOVA

In this section, performance on the individual inhibition tasks is explored in RTS and TD groups using analyses of variance and t-tests. Figure 4.4 depicts the percentage of individuals in each group who passed the inhibition tasks in each age band. These graphs should be interpreted with reference to table 4.1 taking note of the small number of RTS participants in each age band. This is particularly important when interpreting the age at which individuals with RTS reach ceiling on these tasks as there are only six individuals with RTS with a mental age > 6 years. Therefore, each individual in the current sample exerts a fairly large influence on the developmental trajectories depicted within this chapter, and it is possible that any one of these individuals could be classified as outlier if it were possible to compare them to the wider RTS population.

Inspection of figure 4.4 suggests that TD children are reaching ceiling on the inhibition tasks included in the battery at an earlier age (at a MA of approximately 4 years) than the RTS group (at a MA of approximately 6 years). The RTS group's performance on the Bear-Dragon task is striking because there appears to be a sudden improvement on this task.

A 4 x 2 ANOVA with participant group (RTS, TD) as a between subject factor and task (Shape Stroop, Reverse Categorisation, Bear-Dragon, Black-White Stroop) as the within subject factor was conducted. Overall effects of task and group were observed ($F(3,282) = 19.67$, $p < .001$, $\eta^2 = .17$ & $F(3,282) = 8.18$, $p = .005$, $\eta^2 = 0.08$ respectively). There was a significant interaction between task and group ($F(3, 282) = 3.59$, $p = .014$, $\eta^2 = 0.03$).

Repeated measures ANOVAs indicated that there were significant differences between the tasks in the TD group ($F = 17.18$, $DF = 3,213$; $p < .001$; $\eta^2 = .195$) and the RTS group ($F = 7.91$, $DF = 3,69$; $p < .001$, $\eta^2 = .26$).

Paired sample t-tests were carried out for each group using a Bonferroni correction with an associated probability level of .008 to correct for multiple comparisons. The results are displayed in table 4.6.

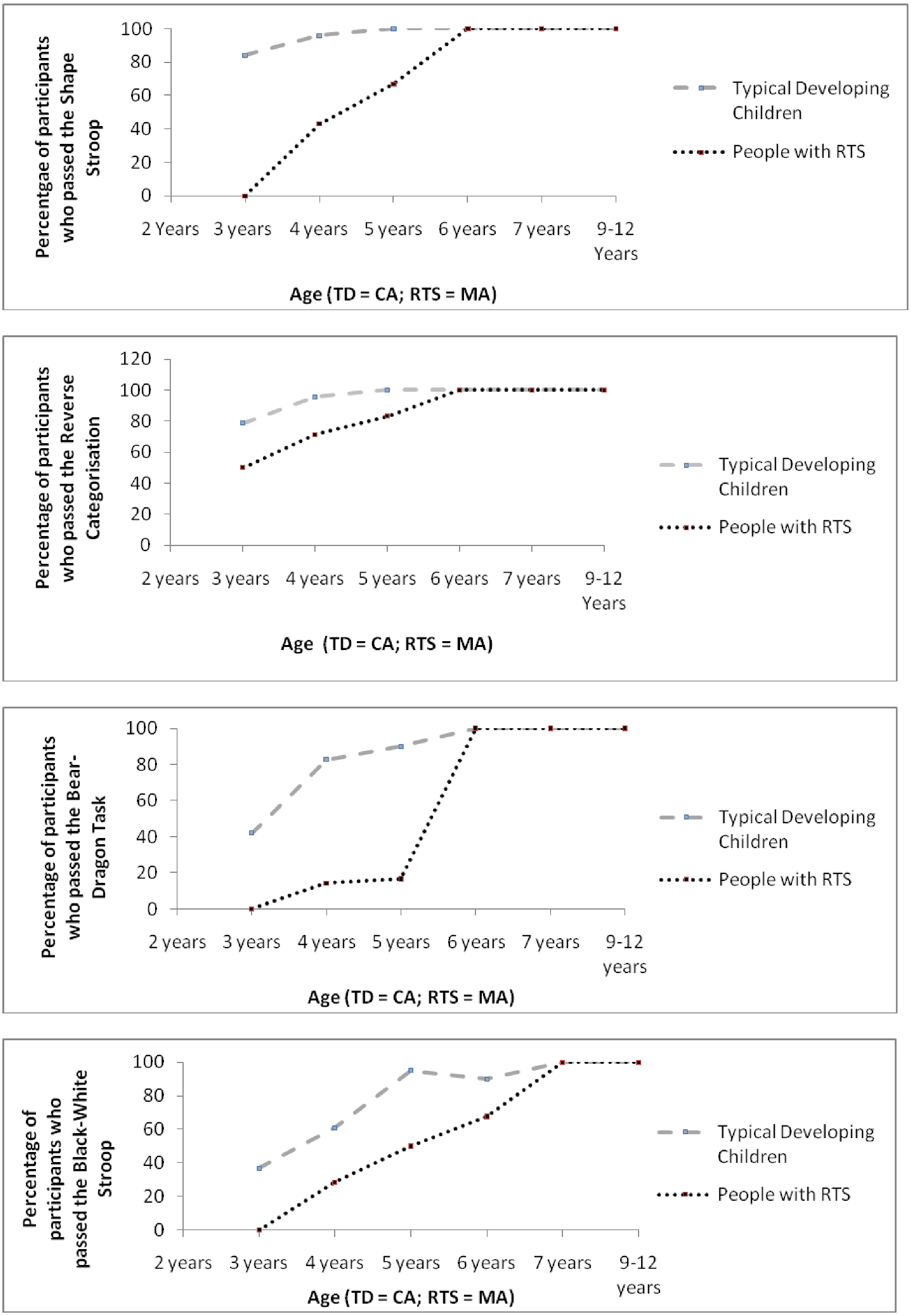

Figure 4.4 The percentage of participants in each age band who passed the four inhibition tasks. Participants were considered to have passed an inhibition task if they scored 75% correct on the measure in line with Carlson (2005).

4.5.3.3.1 Inhibition within groups analyses

For the TD group the Shape Stroop was significantly easier than Bear-Dragon, $t(71) = 3.94$, $p < .001$, $d = 0.66$, and the Black-White Stroop, $t(71) = 3.85$, $p < .001$, $d = 0.89$. The Reverse Categorisation was significantly easier than the Bear-Dragon, $t(71) = 2.19$, $p < .001$, $d = 0.45$ and the Black-White Stroop, $t(71) = 3.07$, $p < .001$, $d = 0.71$. There were no other significant differences.

In the RTS group the Shape Stroop and Reverse Categorisation were significantly easier than the Bear-Dragon task ($t(23) = 3.98$, $p = .001$, $d = 0.93$ & $t(24) = 3.75$, $p = .001$, $d = 0.91$ respectively). No other significant differences were found. The analyses were repeated with only participants below 78 months because after this age the majority of participants with RTS were at ceiling on the tasks. A significant difference emerged indicating that the Black-White Stroop was easier than the Bear-Dragon task, t(16) = 4.60, $p <.001$, $d = 1.22$.

The absence of task differences may have been a product of the small sample size for the RTS group. A power analysis was conducted based on these TD data indicated that a sample size of 44 would be needed for the difference between the Reverse Categorisation and Black-White Stroop to meet statistical significance ($p < .008$).

Table 4.6
The paired samples t-tests comparing the performance on inhibition tasks in each group.

	TD					RTS				
Pair	Mean Difference (SD)	T Score	DF	*p*	Cohen's *d*	Mean Difference (SD)	T Score	DF	*p*	Cohen's *d*
Shape Stroop - Reverse Categorisation	.78 (3.50)	1.89	71	.064[b]	0.30	.16 (6.41)	.10	16	.841	0.04
Shape Stroop – Bear Dragon	2.97 (6.41)	3.93	71	.000	0.66	7.80 (6.92)	4.65	16	.001[a]	0.93
Shape Stroop – Black-White Stroop	3.85 (5.22)	6.26	71	.000	0.89	1.86 (6.28)	1.22	16	.061	0.52
Reverse Categorisation – Bear – Dragon	2.19 (5.68)	3.28	71	.002	0.45	7.96 (7.65)	4.42	17	.001[a]	0.91
Reverse Categorisation – Black-White Stroop	3.07 (5.01)	5.20	71	.000	0.71	1.70 (5.99)	1.17	16	.077	0.49
Black-White Stroop – Bear Dragon	.88 (5.15)	1.44	71	.154	0.15	5.94 (5.32)	4.60	16	.026[a]	0.57

TD N = 72; RTS N = 24 – 25

[a] When this analysis was repeated with participants below 78 months (6.5 years) (N = 17) *p*s were significant at <.001.

[b] The analyses were repeated using Wilcoxon tests and a significant difference emerged between the Shape Stroop and the Reverse Categorisation for the TD group (z = -2.93, *p* = .003).

Note. Descriptive statistics for this subset of participants are in table 4.8.

Table 4.7

The independent samples t-tests comparing TD children to individuals with RTS on tasks from the inhibition battery.

	TD	RTS	F	Mean Difference	t	df	*p* value[a]	Cohen's *d*
Task	Mean (SD)	Mean (SD)						
Composite Inhibition Score	53.74 (13.46)	37.86 (12.92)	.39	15.87	4.41	87	<.001	1.20
Shape Stroop	15.33 (2.53)	11.92 (5.17)	15.69	3.41	2.65[a]	17.83	.017[b]	0.84
Reverse Categorisation	14.56 (2.64)	11.85 (4.92)	17.82	2.25	2.70[a]	19.50	.036[b]	0.68
Bear Dragon	12.36 (6.44)	3.89 (5.96)	.75	8.47	5.06	88	<.001	1.37
Black-White Stroop	11.49 (5.62)	10.06 (3.98)	4.71	1.43	1.22[a]	33.00	.231	0.29

TD N = 72; RTS N = 17-18

[a] Equal variances not assumed.

[b] The differences between groups on the Shape Stroop and Reverse Categorisation were <.05, which suggests an emerging trend.

Note. When the above analysis was repeated using non-parametric Mann-Whitney U tests the significant group differences were confirmed for the Bear-Dragon task (U = 286.50, $p < .001$) and the total inhibition score (U = 283.00, $p = .001$). A significant difference emerged between groups for the Shape Stroop task (U = 343.00, $p < .001$), and although not reaching the conservative alpha level adopted in this analysis the difference between the groups on the Reverse Categorisation task was approaching significance (U = 416.50, $p = .011$). There was no difference between performance on the Black-White Stroop task (U = 590.50, $p = .064$).

4.5.3.3.2 Inhibition between groups analyses

Individuals with RTS who were older than 78 months were excluded from the analysis because TD data was not collected beyond this age. The mean age for the RTS (MA) and TD (CA) groups was 56.47 (range 39-74; SD: 10.68) and 56.44 (range: 36-78; SD: 11.58) respectively. An independent samples t-test revealed that there was no difference in age between the groups ($t(88) = -.009$, $p = .993$).

Independent t-tests that were conducted to explore the differences between the two groups on the individual tests from the inhibition battery and the composite inhibition score. The results are displayed in table 4.7. The groups were significantly different on the composite inhibition ($t(87) = 4.41$, $p < .001$, $d = 1.20$) score and the Bear-Dragon task ($t(88)$, $= 5.06$, $p < .001$, $d = 1.37$). Examination of trends within the data suggest the groups may differ on all tasks apart from the Black-White Stroop, however, these trends did not reach statistical significance.

4.5.4 Working memory span task analyses

4.5.4.1 Working memory span tasks[6] descriptive statistics and correlations

The descriptive statistics for each span task and the results of the non-parametric correlations for the span tasks with MA and CA are displayed in tables 4.8 and 4.9. Given that there were no significant relationships between CA and the span tasks only the relationship between MA and task performance is explored for the remainder of the working memory span task analyses.

[6] The analysis for the span tasks (Verbal Animal Span and Corsi Blocks) is described separately from the analysis for the Scrambled Boxes task because different methods of analysis were applied.

Table 4.8
Descriptive statistics for the working memory span tasks

	TD		RTS	
	Mean (SD)	Range	Mean (SD)	Range
Verbal Animal Span	20.36 (8.56)	6-51	8.75 (3.67)	0-17
Corsi Blocks Span	12.98 (9.09)	0-37	4.05 (2.78)	0-10

TD N = 89; RTS N = 20-21
Note. RTS N lower than in previous analyses as four participants were excluded from this analysis.

Table 4.9
Correlations between the working memory span tasks, CA and MA

	MA	Verbal Animal Span	Corsi Blocks Span
CA	.38	.18	.09
MA		.61**	.16
Verbal Animal Span			.05
Corsi Blocks Span			

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).
***. Correlation is significant at the .005 level (2-tailed).
N RTS = 20 & 21
Note. RTS N lower than in previous analyses as four participants were excluded from this analysis.

4.5.4.2 Data analysis for working memory span tasks

The data obtained from the Verbal Animal Span task was suitable for linear trajectory analysis as described by Thomas et al. (2009, 2010). All assumptions of linear regression were met and a curve fit analysis revealed that the data for both groups was sufficiently linear in relation to age (TD = CA, RTS = MA). However, whilst a linear fit provided a good fit for the TD data, a curve fit analysis indicated that a power curve provided a better fit. Although applying a log10 transformation to the TD data improved linearity this transformation reduced linearity for the RTS group. As the RTS group were the clinical sample of interest, data were analysed without applying the transformation. Furthermore, visual inspection of the graphs generated by the curve fit analysis indicated that for the TD group a linear fit did not deviate far from the fit predicted by the power curve and hence the linear fit provided a good approximation of the rate of development in the TD group. Age (RTS: MA; TD: CA) was rescaled from the youngest age of the disorder group to aid interpretation of regression coefficients.

Similarly, for the Corsi Blocks task, the relationship between performance and age was suitable for linear trajectory analysis in the TD group; however, the data were better fit by a power curve. Transforming the TD data using a natural logarithum improved linearity. However, whilst a linear fit provided a good fit for the TD data pre and post transformation, there was no relationship between the RTS scores and MA (see figure 4.5). A curve fit analysis revealed that the RTS data did not fit any model.

Linear methods were applied to compare the groups despite the absence of a significant trajectory for the RTS group because the RTS data appeared to cluster along a flat trajectory below the TD group (see figure 4.5). The results are reported without the transformation to aid interpretation and to allow for the Corsi Blocks span trajectory to be compared to the Verbal Animal Span trajectory. Furthermore, applying the natural logarithum to the RTS data created a gradient for the RTS regression line that did not capture the original distribution of the data.

4.5.4.2.1 Results: Verbal Animal Span trajectory analysis using linear methods

Figure 4.5 depicts the straight line that produces a reliable fit to the TD data (R^2 = .24, F(1, 87) = 27.85, p<.001). The line has an intercept (constant) of 13.61 and a gradient of 0.28. A straight line also produces a reliable fit to the RTS data (R^2 = .31, F(1, 18) = 8.04, *p* = .01) with an intercept (constant) of 5.30 and a gradient of 0.16.

In the same way as for the composite inhibition score, the trajectories for the RTS and TD groups were compared using an adapted Analysis of Covariance function within the General Linear Model (ANCOVA), which included an interaction term (group x MA). The R^2 explained by this model is .43. A significant proportion of the variance is explained by this model (F(3,105) = 26.59, *P* < .001, η^2 = .43). An overall effect of group indicates that the intercepts of the groups differ reliably at the youngest age of measurement in the RTS group (F(1,105) = 5.95, *p* = .016, η^2 = .05). Thus, RTS have a delayed onset of development on this task, which is quantified by an 8.31 point score difference between the RTS and TD groups at the youngest age of measurement. When the groups are combined MA significantly predicts score on the Verbal Animal Span (F(1,105)=11.17, *p* = .001, η^2 = .10); however, an absence of a significant age x group interaction suggests that RTS is not developing more slowly than the TD group on the Verbal Animal Span (F(1,105) = .94, *p* = .334, η^2 = .01).

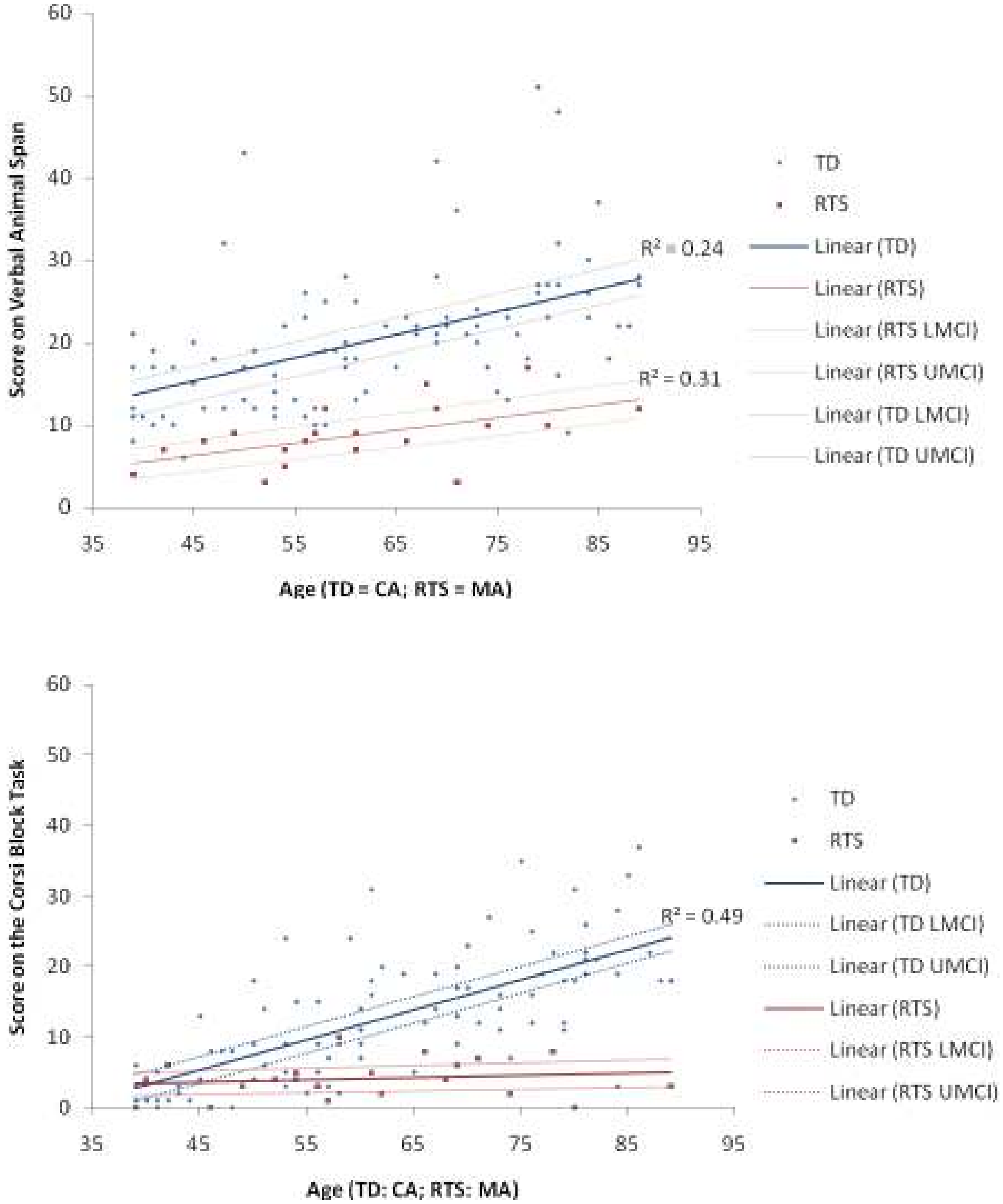

Figure 4.5
RTS and TD trajectories for scores on the span tasks as a function of mental age.

4.5.4.2.2 Results: Corsi Blocks Span trajectory analysis using linear methods

A straight line produced a reliable fit to the TD Corsi Blocks data ($R^2 = .49$, $F(1, 87) = 82.78$, $p<.001$), with an intercept (constant) of 2.81 and a gradient of .425. A straight line did not fit the RTS data ($R^2 = .02$, $F(1, 19) = 0.46$, $p = .505$). Examination of the (unstandardized) regression coefficients indicated an intercept (constant) of 3.38 and a gradient of .046.

A significant proportion of the variance is explained by the model ($F(3,106) = 44.69$, $P < .001$, $\eta^2 = 0.56$). The absence of an overall effect of group indicates that the RTS and TD group do not differ at the youngest age of measurement in the RTS group ($F(1,106) = .05$, $p = .837$, $\eta^2 < .01$). Thus, both groups are at floor at the youngest age of measurement.

MA significantly predicted Corsi Blocks score when the RTS and TD groups were pooled ($F(1,106)= 17.79$, $p < .001$, $\eta^2 = 0.14$). A significant group x age interaction, indicated that RTS and TD trajectories differ on the Corsi Blocks Span ($F(1,106) = 13.23$, $p < .001$, $\eta^2 = 0.11$), and it is clear from figure 4.5 that RTS may not be developing on this task during this developmental window.

At this point the four participants who were excluded from the analyses (MA > 90) should be mentioned. This subset of participants obtained higher scores on the Verbal Animal Span task (mean score = 19.50, SD = 6.95) and the Corsi Blocks Span (mean = 23.25, SD = 9.18). Their performance on the Verbal Animal Span did not deviate from what would be expected given the gradient of the Verbal Animal Span trajectory, however their performance on the Corsi Blocks span suggests a different trajectory to that displayed in figure 4.5. This may indicate that there is a late development on Corsi Blocks task in RTS; however, these individuals may also represent a small subset of the RTS population who are substantially less impaired. Alternatively, it may be that these four excluded individuals more accurately represent the performance of older individuals with RTS on the Corsi Blocks task, while those individuals (depicted in figure 4.5) who have higher mental ages and perform poorly on this task may be less representative of individuals with RTS. The visual depictions of the trajectories with these participants included are displayed in Appendix K to aid interpretation.

4.5.5 The Scrambled Boxes, DCCS and Spatial Reversal analyses

The data for the Scrambled Boxes tasks (Three, Six and Nine Scrambled Boxes) and the composite score for both groups violated the assumption of normality. This was most striking for the TD children because many of the children were at ceiling on the six box scrambled task. Data from the dimensional change card sort task and Spatial Reversal task also violated assumptions of normality. It was not possible to isolate a linear proportion of the developmental trajectories for these tasks or for the composite scores and transformation of the data was not possible. Non-parametric correlations, between group ANOVAs and independent samples t-tests were used, as opposed to trajectory analysis, to examine how these tasks related to MA/CA, and to compare group differences.

Scrambled Boxes analysis

4.5.5.1 Descriptive statistics and correlations between Scrambled Boxes, MA and CA

The descriptive statistics and non-parametric correlations for the relationships between the Scrambled Boxes tasks and MA/CA are displayed in table 4.10 and 4.11.

There was no relationship between performance on these tasks with either CA or MA in the RTS group.

Table 4.10.
Results of the independent samples t-tests comparing TD children to individuals with RTS on working memory tasks.

Task	TD Mean (SD)	TD Range	RTS Mean (SD)	RTS Range	F	Mean Difference	t	df	*p* value[a]	Cohen's *d*
Three Scrambled Boxes	3.58 (3.05)	1-4	3.05 (1.53)	0-4	22.08	.53	1.54[b]	22.65	.137	0.22
Six Scrambled Boxes	5.09 (1.90)	0-7	3.95 (2.60)	0-7	7.66	1.09	1.78[b]	25.02	.087	0.50
Nine Scrambled Boxes	2.21 (3.78)	0-10	1.10 (2.86)	0-10	8.31	1.12	1.51[b]	38.20	.140	0.33
Scrambled Boxes Composite Score	10.95 (5.50)	2-21	8.14 (5.72)	4-21	.15	2.31	2.09	107	.039	0.50

TD N = 88; RTS N = 21 (MA < 91 m)
[a] Independent samples t-tests were conducted with an Alpha level of .01.
[b] Equal variances not assumed
Note. Non parametric Mann-Whitney U tests confirmed that there was no difference between the groups. The analysis was repeated without assigning those who had not directly completed the task a score and still no differences were found between the groups

Table 4.11.
Spearman correlations between chronological age, mental age and Scrambled Boxes tasks

	Menta l Age	Three Scrambled Boxes	Six Scrambled Boxes	Nine Scrambled Boxes	Scrambled Boxes Composite
Chronological Age	.50*	-.21	-.10	.04	-.10
Mental Age		.26	.30	-.03	.27

RTS N = 25
*. Correlation is significant at the 0.05 level (2-tailed).
Note. Correlations between the versions of the Scrambled Boxes tasks were omitted because correlations were likely to be exaggerated due to post hoc coding.
Note. N is higher than analyses for the working memory span tasks as correlations conducted with the total RTS sample.

4.5.5.2 Scrambled Boxes between group analysis using t-tests

The groups were well matched for the between group analysis. The TD group (N = 90) had a mean age of 62.63 months (range: 38-89; SD: 15.10) and the RTS group (N = 21) had a mean MA of 60.16 months (range: 39-89; SD: 13.61). An independent samples t-test confirmed that there was no difference in age between the groups (t(109) = 0.69, *p* = .493).

The results from the independent samples t-tests examining group differences on the Scrambled Boxes tasks are displayed in table 4.10. The independent samples t-tests were conducted with an associated probability level of .01 to correct for multiple comparisons for this subsection of the analysis. There were no significant differences between the RTS and TD groups on the Three Scrambled Boxes (t(22.65) = 1.54, *p* =.137, *d* = 0.22), Six Scrambled Boxes, (t(25.02) = 1.78, *p* = .087, *d* = 0.50), Nine Scrambled Boxes, (t(38.20) = 1.78, *p* =.140, *d* = 0.33), or the total score, (t(107) = 2.31, *p* = .039, *d* = 0.50).

DCCS analyses

4.5.5.3 DCCS descriptive statistics and correlations

The descriptive statistics for each DCCS task and the results of the non-parametric correlations for the DCCS tasks with MA and CA are displayed in tables 4.12 and 4.13.

Table 4.12.

Descriptive Statistics for the three versions of the DCCS and the DCCS composite score

Task	TD		RTS	
	Mean (SD)	Range	Mean (SD)	Range
Separated Dimensions DCCS	11.01 (2.91)	0-12	7.68 (5.39)	0-12
Standard DCCS	10.11 (3.89)	0-12	5.79 (5.57)	0-12
Border DCCS	5.36 (3.73)	0-12	2.58 (3.53)	0-9
DCCS Composite Score	26.55 (9.19)	0-12	16.05 (13.33)	0-21

TD N = 91; RTS N = 19 (MA < .91m)
[a] Independent samples t-tests were conducted with an associated probability level of .01.
[b] Equal variances not assumed.
Note. Descriptive statistics are for participants with MAs < 90 that were included in the between groups analysis

Table 4.13.

The relationship between the versions of the DCCS, DCCS composite score, mental age and chronological age in RTS.

	Mental Age	Separated Dimensions DCCS	Standard DCCS	Border DCCS	Composite DCCS Score
Chronological Age	.50*	.58***	.34	.28	.42*
Mental Age		.66**	.44*	.39	.46*

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).
*** Correlation is significant at the .005 level (2-tailed).
RTS N = 23
Note. N is higher than in descriptive statistics table because all participants were included

A higher MA was associated with better performance on the separated dimensions DCCS (R = .66, p = .001). CA was also positively correlated with performance on the separated dimensions DCCS (R = .58, p = .004). There was a weak positive correlation between MA and composite score (R = .46, p = .029), and between CA and composite score (R = .42, p = .046), which did not reach significance at $p < .01$. No other significant relationships were found for CA or MA. In keeping with the analyses presented in this chapter, only comparisons based on MA will be presented in this section. However, the relationship between CA and performance on the separated dimensions task is presented in Appendix L.

4.5.5.3.1 Visual depiction of developmental trajectories for the three versions of the DCCS based on mental age

The percentage of individuals in each age band who scored over 75% correct on each version of the DCCS are displayed in figure 4.6. It appears that from a MA of approximately 5 years the TD group are at ceiling on the separated dimensions and standard DCCS and that the RTS group lag behind, reaching a similar level of performance between six and seven years (MA). However, the difference between groups appears most pronounced in the younger age groups (3 and 4 years). Performance on the border version of this task is particularly striking for the RTS group because only one individual with RTS passed this task and no improvement was seen even in the oldest individuals who are aged 9-12 years of age.

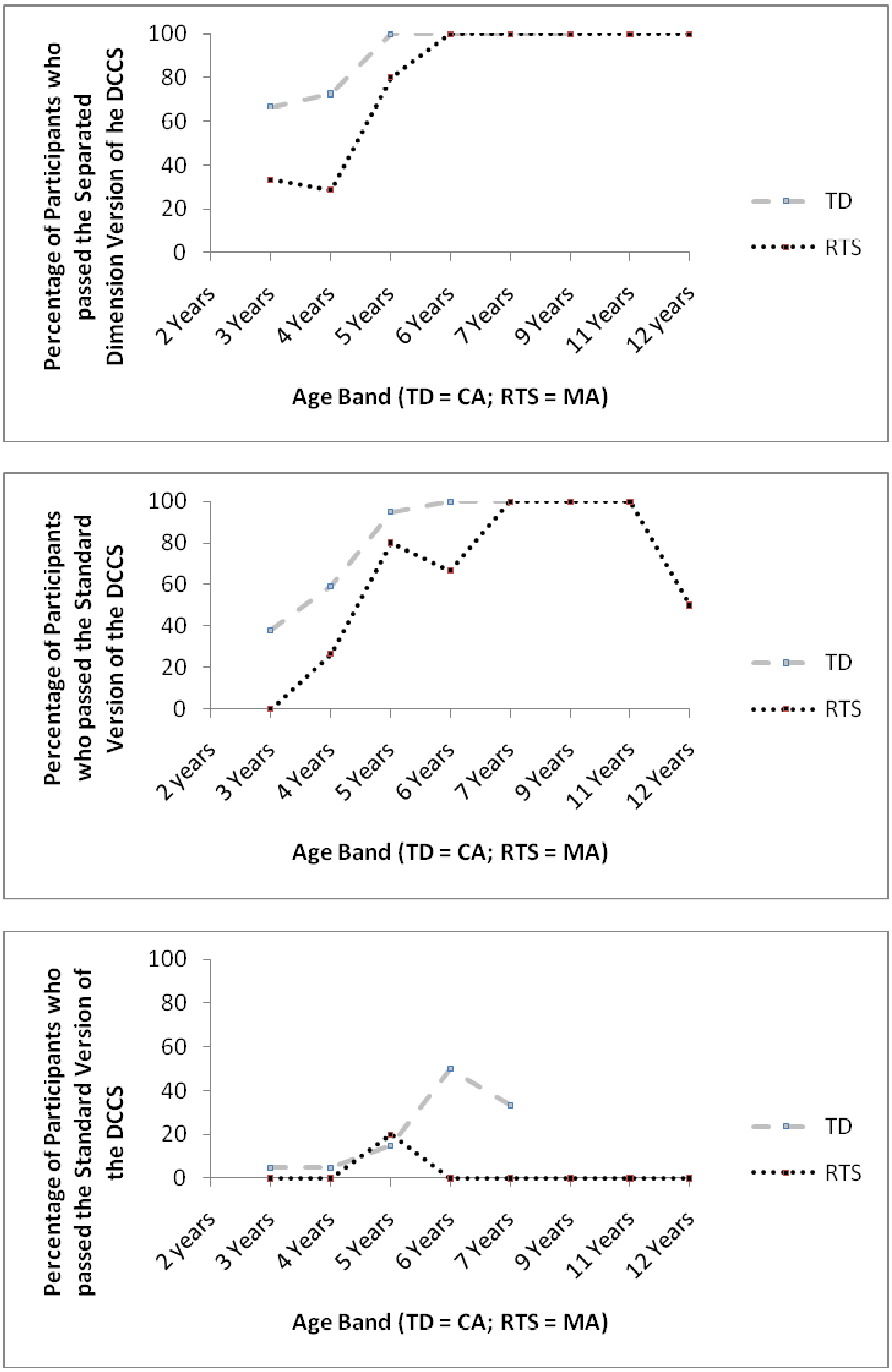

Figure 4.6. The percentage of participants in each age group that passed each of the versions of the DCCS.

Note. For this diagram an individual was thought to have passed the task if they scored more than 75% correct on the measure in line with Carlson (2005).

This graph should be interpreted with reference to table 4.1 due to the low N in the RTS group

4.5.5.3.2 DCCS between groups analyses

Table 4.14

Independent samples t-tests comparing TD children to individuals with RTS on shifting tasks.

Task	Mean Difference	F	t	df	*p* value[a]	Cohen's *d*
Separated Dimensions DCCS	3.33	28.40	2.61[b]	20.25	.017	0.80
Standard DCCS	4.32	14.86	3.22[b]	21.81	.004	0.91
Border DCCS	2.78	.335	2.98	108	.004	0.77
DCCS Composite Score	10.50	10.89	3.27[b]	21.71	.004	0.93

RTS N = 19, TD N = 91

[a] Independent samples t-tests were conducted with an Alpha level of .01.

[b] Equal variances not assumed

Note. Non parametric Mann-Whitney U tests confirmed that there was no difference between the groups.

There were 91 individuals in the TD group with a mean age of 62.02 (range: 38-89, SD: 15.37) and 19 individuals in the RTS group with a mean age of 61.14 (range: 39-89, SD: 13.50). An independent samples t-test revealed that age did not differ between the groups (t(108) = .23, *p* = 816). For each group, the mean score and standard deviation on each version of the DCCS are displayed in table 4.12 and the results from the t-tests are displayed in table 4.14.

The independent samples t-tests revealed that the RTS group performed significantly poorer than the TD group on the standard DCCS, t(20.25)=3.33, *p* =.004, *d* = 0.91, the border version, t(108) = 2.98, *p* = .004, *d* = 0.77, and the composite score, t(21.71) = 3.27, *p* = .004, *d* = 0.93. The difference between groups of the separated dimensions DCCS approached significance, t(20.25) = 2.61, *p* =.017, *d* = 0.80.

When the analysis was repeated using non-parametric Mann-Whitney U tests a significant difference emerged between groups on the separated dimensions DCCS (U = 556.50, $p < .001$). All other significant relationships were confirmed except for the difference between groups on the border DCCS, which now approached significance (U = 554.00, $p = .012$).

Spatial Reversal analysis

4.5.5.4 Spatial reversal descriptive statistics and correlations

The descriptive statistics for the Spatial Reversal and the results of the non-parametric correlations for this task with MA and CA are displayed in tables 4.15 and 4.16. None of the correlations were significant (*p*s >.05). A visual inspection of the RTS and TD data revealed that it was non-linear.

Table 4.15.

Relationships between performance on the Spatial Reversal task, MA and CA for RTS.

	CA	Spatial Reversal (Attainment Stage)	Spatial Reversal (Reversal Stage)
Mental Age	.50*	-.34	.16
Chronological Age		.01	.41
Spatial Reversal (Attainment Stage)			-.29

* Correlation is significant at the 0.05 level (2-tailed).
Attainment Stage RTS N = 22
Reversal Stage RTS N = 16

Table 4.16.
Descriptive Statistics and results of independent samples t-tests comparing performance of the RTS and TD groups on the attainment and reversal stages of the Spatial Reversal task.

	TD		RTS		F	Mean Difference	t	df	*p* value[a]	Cohen's *d*
Task	Mean (SD)	Range	Mean (SD)	Range						
Attainment Stage	7.21 (1.68)	0-9	6.00 (2.37)	0-9	4.19	1.21	1.99[b]	20	.060	0.59
Reversal Stage	7.10 (1.65)	0-9	6.75 (1.36)	4-8	.004	.35	.67	62	.505	0.02

[a] Independent samples t-tests were conducted with an associated probability level of .01.
[b] Equal variances not assumed
Attainment Stage TD N = 72; RTS N = 17 Reversal Stage TD N = 52; RTS N = 12

4.5.5.5 Spatial reversal between group analyses

A group comparison using a repeated measures ANOVA and independent measures t-tests was conducted. Once participants with RTS whose MAs were outside the scope of the TD data (> 78 months) were excluded there were 17 RTS participants in the attainment data set and 12 in the reversal data set. There was no difference between the MAs of the RTS and TD groups after these participants were excluded (t(87) = -.06, *p* =.551).

The independent sample t-tests were carried out between the measures using an associated probability level of .01 to correct for multiple comparisons. There were no significant differences between the RTS and TD groups on either the attainment or reversal stages (t(20.02) =1.99, *p* = .060, *d* = 0.59 & t(62) = 0.67, *p* = .505, *d* = 0.23 respectively).

4.6 The influence of working memory on the results of the inhibition analyses

In addition to the trajectory analyses an analysis was conducted to explore whether the performance of individuals with RTS on the inhibition tasks was influenced by working memory difficulties. This was conducted because the inhibition tasks contained complex working memory demands (retaining the rules of the tasks) and it was found that individuals with RTS have difficulties with working memory span tasks.

Firstly, correlations between the inhibition and working memory tasks were calculated. It can be observed in Table 4.17 that the Verbal Animal Span correlates strongly with performance on the Reverse Categorisation (R = .58, p = .003), the Bear-Dragon (R = .66, p < .001), and the Black-White Stroop (R = .53, p = .009) in the RTS group. This was not unexpected because working memory develops as children get older alongside inhibitory control in TD children (Davidson et al., 2006), however, the presence of correlations suggests working memory may have contributed to performance on the inhibition tasks.

Table 4.17.
Correlations between inhibition and working memory tasks in the RTS group

	Verbal Animal Span	Corsi Blocks Span	Three Scrambled Boxes	Six Scrambled Boxes	Nine Scrambled Boxes	Composite Scrambled Boxes Score
Shape Stroop	.39	.11	.20	.50*	.12	.44*
Reverse Categorisation	.58**	.46*	.06	.20	-.02	.18
Bear Dragon	.66***	.14	.21	.29	-.06	.26
Black-White Stroop	.53**	.01	.54**	.38	.02	.39
Inhibition Composite	.71***	.16	.45*	.54**	.01	.51*

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).
***. Correlation is significant at the 0.005 level (2-tailed).
RTS N = 23- 25

To further explore this possibility, the memory check questions that were incorporated into the inhibition tasks were examined. The check question asked at the end of the Bear-Dragon task was, "who don't we listen to?" 88% of participants responded correctly to this question after they finished the task indicating that they still understood the rules of the game. This suggests that the participants comprehended the instructions and that an inability to hold the rules in mind over a delay was not the primary cause of poor performance on this task.

The performance of participants on the memory check questions from the Black-White Stroop and the Reverse Categorisation were examined. While most participants passed the practice trials, few participants with RTS answered the check questions correctly. This may have occurred because the questions made substantial demands on receptive language, or participants gave incorrect responses to the check questions because the format of the question was similar to the trials, hence making similar inhibitory demands.
McNemar tests were conducted to assess whether poor performance was the result of individuals failing to hold the rules of the tasks in mind. The first trial of each task was compared to the trial before the rules were repeated, and performance on the first trial after the rules were repeated was compared to the last trial. No difference were found between the trials for the Black-White Stroop (ps = .727 & .219 respectively) or Reverse Categorisation (ps = .625 & 1.00 respectively). This analysis was repeated excluding the participants who were at ceiling on the task but this did not change the results.

In conclusion, although working memory was correlated with performance on inhibition tasks, poor comprehension of the rules or an inability to hold the rules in mind are unlikely to be the main factors underpinning low scores on these tasks. If poor retention of the rules was impacting on performance on the Bear-Dragon task, participants should not have been able to answer the check question. If holding the rules in mind was impacting on performance on the Reverse Categorisation and Shape Stroop the scores on trials temporally separated from the repetition of the rules would have been expected to differ from trials immediately after the rules were given. Despite this, it is not possible to rule out the influence of working memory entirely because the phenomena of goal neglect could still account for these findings (Duncan, Emslie, Williams, Johnson, & Freer, 1996). Goal neglect is discussed further in the following section.

4.7 Discussion

The primary aim of this chapter was to apply a developmental trajectory approach to study the development of the executive functions in RTS in comparison to a TD sample. Secondary aims included examining the convergent validity and the developmental trajectories of the mental age estimates, and examining the influence of working memory on inhibition task performance in the RTS group. These aims were largely achieved, and while it was not possible to apply sophisticated developmental trajectory analyses for all components of the executive function battery (as described by Thomas, 2009, 2010), all of the analyses were approached from a developmental perspective.

Firstly, the convergent validity of the mental ages generated from the psychometric and adaptive assessments were explored (MSEL-WASI-II combination and the VABS). Developmental trajectories were also plotted for mental ages derived from these assessments. Convergent validity was good and an inspection of the developmental trajectories for the mental age assessments suggested that mental age is higher in individuals with RTS who are older (CA). The cross-sectional nature of this analysis means that it cannot be concluded that mental age *increases* as individuals with RTS develop; however, it is difficult to see how this pattern of results could occur as the result of a cohort effect. While convergent validity was good, mental ages should only be taken as estimates due to limitations with mental age calculations. Limitations include the theory driven nature of assessments used to calculate mental age and the use of an adaptive behaviour assessment to calculate convergent validity. Limitations of mental age calculations are discussed further in the general discussion of this thesis (section 6.5.1) but for the executive function analyses presented in this chapter it was judged that the mental ages provided *good enough* estimates to allow for meaningful interpretation of the results.

The next aim to be addressed was the primary aim of this chapter: describing the developmental trajectories for three executive functions (inhibition, working memory and shifting) in people with RTS. It was predicted that individuals with RTS would demonstrate a specific profile of strengths and weaknesses on the executive function battery relative to the TD comparison group. Predictions about the direction of these relationships were not made due to the exploratory nature of these analyses.

Better performance on EF tasks was linked to higher mental age in RTS generally; however, when task performance was compared across groups, the performance of individuals with RTS lagged behind TD children relative to mental age for all tasks apart from the Spatial Reversal and Scrambled Boxes tasks. There is also some evidence to suggest performance on certain tasks such as the visuo-spatial span task and DCCS border version may be deviant in RTS for the period of development examined. These results fit with findings from the TD literature that indicate executive function development is related to age (Davidson et al. 2006; Carlson, 2005; Garon et al., 2008), but also suggest a profile of strengths and weaknesses in RTS not present in TD children. In contrast to mental age, the correlational analyses revealed that chronological age was only related to performance on two versions of the DCCS shifting task. One reason for the lack of correlations between chronological age and task performance may have been the wide variation of ability levels in the sample.

There were a number of specific findings that are of interest in this chapter. The inhibition composite score (described in section 4.3.2.3.1) may be a useful way of calculating overall performance on inhibition tasks in RTS, and when the inhibition composite score was plotted as a function of mental age it clearly had a linear trajectory. This trajectory illustrates that the onset of the development of preschooler-like inhibition might be later in RTS, but that it appears to develop steadily in individuals throughout childhood (between 39-89 months). Individuals with RTS appear to reach ceiling on these tasks at approximately 89 months (MA: 7 ½ years). Again, the cross sectional design does not allow for a conclusion that inhibition improves in individuals with RTS as they get older, but the relationship between mental age and chronological age points towards this interpretation.

These results, based on the inhibition composite score, should be interpreted with caution because the composite score was not calculated using standardised scores (Hendrick & Vercruyssen, 2011). The composite score was calculated using an alternative method: weighing all inhibition tasks out of 16 and then summing these scores (described in section 4.3.2.3.1). This method was adopted so that tasks with more trials (for example, the Black-White Stroop) would not contribute more to the composite score. The resulting composite consisted of the proportion of correct and incorrect responses for each task. However, if standardised z-scores had been used it would have also ensured that those tasks with larger standard deviations did not contribute more to the composite. This is because when z-scores are used SDs are equal to 1 and mean scores are equal to 0 (Hendrick & Vercruyssen, 2011). In this chapter, differences in standard deviations for the individual inhibition tasks are not likely to have unduly influenced the composite score for the RTS group. This is because the standard deviations for each task were fairly equal for the RTS group; however, standard deviations did vary substantially in the TD group. Another potential confound relating to the calculation of the composite score is that a single error from a task with fewer trials had more influence on the composite score than a single error from a task with more trials. Thus, although the comparison of the TD and RTS trajectories indicates that the onset of the development of inhibition is delayed in RTS, this may have been driven by performance on the Bear-Dragon task because this task had fewer trials than the Reverse Categorisation and the Black-White Stroop, and individuals with RTS performed more poorly on this task.

It will be important to conduct further work to understand the factors underpinning the group differences in the developmental trajectories for the inhibition composite. This is because a potential delay in the development of inhibition has a number of implications. For example, it is of interest that the youngest RTS participant with a mental age of 7½ years was 13 years old (CA); this participant was one of the most able participants in the sample. This suggests that throughout childhood individuals with RTS may have executive function skills that are comparable to those in TD children prior to the preschool period. This is likely to impact on academic achievement, the acquisition of adaptive skills and the development of other cognitive processes. These may include attention, behaviour regulation, theory of mind and counterfactual thinking, all of which have been associated with the development of inhibition in the TD literature (Hughes, 1998; Hughes, & Ensor, 2007; Carlson, Moses and Breton, 2002, Diamond & Taylor, 1996; Lyon & Krashegor, 1996; Beck, Riggs, & Gorniak, 2009; Carlson, Mandell & Williams, 2004). A more in depth exploration of performance on each of the inhibition tasks revealed that within the RTS group there were no differences in performance across three of the inhibition tasks (Shape Stroop, Reverse Categorisation and

Black-White Stroop). This pattern of results does not fit with findings from TD literature; however, these results probably emerged because of a lack of statistical power.

Performance on Bear-Dragon and Shape Stroop was poorer in RTS than the TD group relative to mental age. In line with the composite inhibition score, inspection of the percentage of individuals passing these tasks suggested that the RTS group were reaching ceiling on the inhibition tasks at a later mental age (approximately six years) whilst the TD group were reaching this level of performance between a mental age of 3 and 4 years.

Visual inspection of scores on the Bear-Dragon task illustrated a dramatic difference in performance at 6 years in comparison to 5 years (MA) in RTS. The Bear-Dragon task is a well known conflict inhibition task, which is similar in format to the other conflict inhibition tasks (Carlson, 2005). However, this task is the only conflict inhibition task whereby a participant must withhold a response to succeed. Individuals with RTS may have difficultly not responding on every trial, which could lead to an increased likelihood of very low scores until this task is mastered. Thus, the Bear-Dragon task could be acting as a sensitive measure, capturing a general shift in inhibition between the 5-6 years (MA).

It is possible that Bear-Dragon is making further demands on participants apart from asking them to simply withhold a response. In comparison to the other inhibition tasks in the EF battery this task is more socially engaging and may have an affective (hot) component, which may be particularly salient for individuals with RTS who are thought to be highly sociable (Stevens et al., 1990). In addition, participants produce exaggerated gross motor responses while completing this task, which are in contrast to finer motor responses on other inhibition tasks. It is possible that one or all of these components made this task harder for people with RTS.

Inspection of the working memory span task trajectories suggests that the RTS group have poor verbal and visuo-spatial working memory span. However, the verbal working memory span differed from visuo-spatial span because a higher mental age was associated with better performance on the verbal working memory span in RTS. This suggests that in terms of intervention, there may be greater potential for supporting individuals with RTS to develop their verbal memory span using computerised training programs and their ability to rehearse information verbally.

Despite this, there is some uncertainty as to whether visual-spatial working memory span may be related to mental age in RTS. While the trajectory analyses presented in this chapter indicated performance was not related to mental age in individuals with mental ages up to 90 months, four individuals who were excluded from the analysis had higher visuo-spatial spans on the Corsi Blocks task. This suggests that there is either a very late onset of development for the visuo-spatial span, that these individuals are outliers who are significantly less impaired than individuals with RTS generally, or that these individuals represent a more accurate developmental trajectory of task performance in RTS. Hence, the older individuals who were included in the analysis with poorer performance may be outliers. There is uncertainty about which of these explanations accounts for the findings; however, because over 80% of the individuals in the RTS sample had poor-visuo spatial working memory span it can still be concluded that a large percentage of individuals in the wider RTS population are likely to share these difficulties.

It is also important to note that the RTS group did not differ from the TD group on the Scrambled Boxes tasks, another visuo-spatial working memory task, although the differences between groups were approaching significance for the composite score. This may have occurred because the three and nine box versions of this task were less sensitive measures -

most participants were at ceiling on the three box task and at floor on the nine box task. Alternatively, the absence of significant differences in comparison to the span tasks may have been underpinned by differing task demands. For example, during the Scrambled Boxes task participants are required to actively open boxes and update the information between trials, whereas Corsi Blocks Span does not have an updating component. As with all these tasks, further investigation would be necessary to extrapolate the underlying mechanism of these differences.

As noted previously, intellectual disability associated with RTS has been linked to mutations in the CREB binding protein and the effects on long term memory associated with hippocampal functioning. A number of studies have been conducted with genetically altered knock-out mice to explore the link between these mutations on phenotypic characteristics. It appears that while these mice develop LTM difficulties, short-term memory is not affected (see Josselyn (2005) for a review). The mice models of RTS do not fit neatly with the working memory difficulties found in this chapter. However, because the human brain is complex, it is possible hippocampal dysregulation may have upstream effects on the frontal lobes that impact on working memory in humans (this argument is expanded on section 6.3.3 of the General Discussion).

The results from the shifting tasks indicate that when compared to the TD group, the RTS group's performance was significantly lower on the separated dimensions and standard versions of the DCCS. Similarly to the inhibition tasks, individuals with RTS approach ceiling on these tasks at approximately 5-6 years. Inspection of the percentage of individuals passing the border DCCS indicated that only one participant with RTS passed this task. Participants with RTS who had the oldest mental ages (7-12 years) did not pass the border version and it would be interesting to collect data from older TD children to allow for a direct comparison with these individuals. It is likely that the TD children would continue to improve on the border DCCS after 7.5 years, in line with previous literature indicating that shifting develops into adolescence (Huizinga, Dolan & der Molen, 2006). If confirmed this would indicate an large disparity between the TD and RTS groups on more complex shifting tasks. The absence of significant differences on the Spatial Reversal task suggests that response shifting may be presevered in this group relative to attention shifting. Attention shifting has been linked to higher level repetitive behaviours in the literature including adherence to routine, insistence on sameness and repetitive questioning (Woodcock, Oliver & Humphreys, 2009a, 2009b, 2009c), hence attentional set-shifting may underpin these behaviours in RTS.

The final aim in this chapter was to explore the influence of working memory inhibition task performance in RTS. This was particularly important because of the difficulties with working memory found in this syndrome. The check questions were examined and scores on trials that followed an explanation of the rules were compared to scores on trials immediately before the rules were given. There was no apparent reason to suspect that an inability to hold the rules in mind contributed to poor performance on the inhibition measures. Despite this it is still possible that while the task instructions were held in working memory, participants with RTS did not turn these instructions into active goals. Duncan et al. (1996) have written extensively on goal-neglect in typical adults and adults with frontal lobe lesions. Goal neglect is associated with damage to the frontal lobes and occurs when adults fail to act in accordance with task instructions even though they are able to retain the instructions and demonstrate that they have understood them verbally. The primary problem is using verbal instructions to set up an active goal. Poor inhibition may also contribute to goal neglect because once a goal is neglected an individual may continue to perseverate on an incorrect response, rarely adjusting their performance unless they receive an external cue. However, inhibition does not appear to be the primary issue because Duncan et al. (1996) found that even participants with lesions to their frontal lobes are able to complete these tasks if they are given enough prompts to act in accordance with their goals.

Goal neglect tends to occur in novel situations and is usually restricted to trials before a correct response. Duncan et al. (1996) note that once a correct response has been executed in its entirety goal neglect usually subsides. It has been argued that in order for task instructions to be acted upon it is first necessary for a hierarchy of related subgoals to be unpacked and initiated. This is likely to occur when the individual first initiates a correct response. Goal neglect is particular relevant in the current study because it has been found to occur more often in individuals with lower IQs and when a task is complex, containing several pieces of information that may be competing for control. In these situations the last instructions to be given are likely to be those neglected. Hence, it is possible that goal neglect was contributing to the performance of individuals with RTS on the inhibition tasks. This is more likely for the bear-dragon task because more individuals failed the practice trials on this task. In line with Duncan et al.'s (1996) observations, successful completion of even one trial (for example, practice trials on the Black-White Stroop and Reverse Categorisation) should have reduced the likelihood of goal neglect. Further work could study goal neglect in RTS by varying the numbers of prompts given to individuals with RTS during these tasks to observe how this impacts on performance.

There are several alternative explanations,, which may account for the discrepancy between the TD and RTS groups' performance on the tasks relative to mental age. It may be that physical difficulties associated with RTS lead to fewer opportunities for interaction with the external environment in early infancy. Interaction with the social and physical world has been shown to impact on cognitive development (Bernier, Carlson & Whipple, 2010; see Rakison & Woodward, 2008 for a review). Another explanation is that the psychometric assessments (MSEL-WASI-II combination) overestimated the ability of the RTS group; however, this is unlikely given the agreement between the psychometric assessments and the VABS. Furthermore, although not significantly different, the combination of the psychometric assessments (MSEL-WASI-II combination) produced slightly lower mental ages than the VABS so the most conservative mental ages have been used in the analysis (see section 6.5.1 of the General Discussion).

Additional caveats of the study are that only one disorder group was included and therefore it cannot be concluded that this EF profile is unique to RTS, and as previously mentioned results need to be interpreted with caution due to the small sample of individuals with RTS and the influence of ceiling effects on TD trajectories. Thus, it is only possible to consider how the RTS group differs from the TD group in terms of the rate of development to ceiling on the tasks included in the test battery. Further research could extend the test battery to include tasks that are administered to older children e.g. as the Simon Says game (similar to the Bear-Dragon task).

Five key things are been achieved: EF tasks from the TD literature have been applied to compare the performance of people with RTS to a TD sample, the general cognitive profile of RTS has been described relative to CA, links between MA and the development of EF have been observed in RTS, the areas of potential strengths and weaknesses have been outlined in RTS that warrant further study, and it has been demonstrated that battery is adequate for highlighting dissociations in executive function profiles. This battery could be administered to other syndrome groups in the future to map comparison trajectories.

CHAPTER 5

Relationships Between the Executive Functions and Repetitive Behaviour in Rubinstein Taybi Syndrome

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5.1 Preface

In chapter 1 the three research areas of this thesis were introduced. The first is concerned with the varying profiles of repetitive behaviour across rare genetic syndromes and neurodevelopmental disorders, the second is concerned with how the executive functions (EFs) develop in atypical populations, and the last is concerned with the links between EF development and repetitive behaviour in atypical populations.

In chapter 2 the repetitive behaviour profiles of four disorders were described. This lent further support for heterogeneous profiles of repetitive behaviour across syndrome groups. The chapter also highlighted the interesting repetitive behaviour profile of Rubinstein-Taybi syndrome (RTS), which shares some features with the repetitive behaviour profile of ASD but diverges from the ASD profile in other aspects.

Chapter 3 focused on the development of an EF battery suitable for use in a developmental trajectory framework. This battery was developed to help describe the development of EFs in RTS and to allow for the links between EFs and repetitive behaviour to be explored.

In chapter 4 of this thesis the development of the EFs in RTS was described applying the newly developed EF battery. Using a cross sectional analysis it was found that better performance on EF tasks was linked to higher mental age (MA) in RTS; however, the development of EFs (inhibition, working memory and set-shifting) may lag behind that of TD children relative to MA. More specifically, the development of inhibition appears to have a delayed but linear developmental progression in RTS, and visuo-spatial working memory appears to be particularly compromised in this syndrome. Building on this, the current chapter explored whether a relationship exists between EF development and repetitive behaviour in RTS by comparing performance on the newly developed EF battery to parental reports of EF and repetitive behaviour.

5.2 Introduction

Repetitive behaviour and the executive functions (EFs) were introduced and defined extensively in chapter 1, as well as the links between them. A number of arguments have been made throughout this thesis that come together to form the rationale for this chapter. Rather than repeating these arguments in full, a bulleted summary of the key arguments is provided below that signposts the reader back to the relevant parts of this thesis. The aims and predictions for this chapter are then discussed. The key arguments are as follows:

- Lack of interest in repetitive behaviour partly stemmed from the belief that repetitive behaviour was related to intellectual disability serving either stimulatory or regulatory functions (Turner, 1997; Rapp & Vollmer, 2005; Lovaas, Newson & Hickman, 1987; see section 1.3.6).
- Specific repetitive behaviour profiles have been found for specific syndrome groups. These cross syndrome differences do not appear to be a function of intellectual disability and some repetitive behaviours are not accounted for by the presence of

Autism Spectrum Disorder (ASD) (Moss, Arron, Burbidge & Berg, 2009, see sections 1.3.2 and 2.4.1.4).

- The repetitive behaviour profile of RTS is characterised by high levels of body stereotypy, repetitive questioning and adherence to routine (see section 2.4.1).
- Exploring repetitive behaviour at a gross level of description (e.g. a repetitive behaviour composite score) may mask subtle relationships between individual repetitive behaviours and underlying cognitive mechanisms (Turner, 1997; see section 1.3.1).
- It is advantageous to explore potential underlying mechanisms of repetitive behaviours in syndrome groups so that more effective interventions can be developed to help manage these behaviours, for example, memory aids and cognitive training (see section 4.2).
- Previous research has indicated that repetitive behaviour may be underpinned by executive dysfunction in a number of disorder groups and atypical populations (Turner, 1997; Woodcock, Oliver & Humphreys, 2009a, 2009b & 2009c; Cullen et al. 2005; Morrens, Hulstijin, Lewi, de Hert & Sabbe, 2006; Lawrence, Wooderson, Mataix-Cols, David, Specken & Phillips, 2006) (see sections 1.5.1 to 1.5.5).

The overarching aim of this chapter was to explore the relationships between specific repetitive behaviours and EFs using correlational analyses. The Repetitive Behaviour Questionnaire (RBQ; Moss et al., 2009) was employed, as in chapter 2, so that repetitive behaviours could be studied at a fine-grained level of description. Prior to conducting the correlational analyses the repetitive behaviour profile of the RTS sample included in this chapter was compared to the profile of the larger RTS sample from chapter 2. This was to check that the pattern of repetitive behaviour in the current RTS sample did not deviate unexpectedly from the pattern of behaviours described in the larger sample. This ensured there was no reason for suspecting the current sample was not representative of RTS as a whole.

The EFs that were explored were those discussed in the previous chapter (inhibition, working memory and shifting). Links between emotional regulation and repetitive behaviour were also explored. The EF battery that was designed in chapter 3 (BEF-ID) was utilised to achieve this aim and a parental report measure of EF was included as an alternative measure. It was predicted that the subdomains of these two EF measures would be related to the same repetitive behaviours. Two measures of EF were included because a large number of correlations were conducted in this chapter; if the results were consistent across these measures this would increase the validity of the findings.

It was hypothesised that as EF ability increases repetitive behaviour would decline. In chapter 4, EF was more developed in older individuals with RTS; however, it was hypothesised that while repetitive behaviour may also be linked to MA, any links found between the EFs and repetitive behaviour in RTS would be maintained if MA was controlled for. Predictions were not made about how certain repetitive behaviours that occur frequently in RTS (e.g. repetitive questioning and body stereotypy) would relate to specific EFs in RTS as previous links between these constructs in the literature have been mixed. However, it was anticipated that adherence to routine in RTS may be related to set-shifting as this link has been clearly defined in Prader-Willi syndrome (Woodcock, Oliver and Humphreys, 2009a, 2009b & 2009c).

5.3 Methods

5.3.1 Design

Informant questionnaire methodology was combined with direct tests of EFs and cognitive ability.

5.3.2 Participants

32 participants with RTS completed the study[1] (16 males; mean chronological age: 222 months; age range: 45 – 533m; SD; 121.03). Eight participants were non-verbal. Where possible all participants were included in the analysis.

Seven participants were not able to understand the instructions for a number of the EF tasks due to their degree of intellectual disability or distractibility (mean MA: 25 months; range: 15 – 31m; SD: 6.60), so they only completed the simplest EF tasks (Object Retrieval, Spatial Reversal, A not B, Reverse Categorisation and the Scrambled Boxes tasks). Of the remaining 24 participants who completed the entire EF battery the numbers of participants completing each task mirrors that of chapter 4; however, one additional participant was excluded from the analysis because their questionnaire pack was not returned. The Gift Delay task and Secret Gift task were included in this chapter. Of the 24 participants who completed these tasks, three participants did not complete the Gift Delay task, and six did not complete the Secret Gift task. The number of participants was lower for the Gift Delay task because this task did not appear developmentally appropriate for three of the most able individuals. Fewer participants completed the Secret Gift task because it was not always possible to identify a

[1] These are the same participants who completed the executive function battery in chapter 4. This information is repeated here because the exclusion criteria differed between chapter 4 and chapter 5.

suitable adult to participate in this task because some participants were living in residential settings. Other parents did not comply with the test protocol and prompted participants too explicitly during the Secret Gift task. One participant did not complete the Secret Gift task because he was non-verbal.

5.3.3 Questionnaire Measures

5.3.3.1 Behaviour Rating Inventory of Executive Function - Preschooler Version

(BRIEF-P; Gioia, Espy & Isquith, 2003; Appendix M)

The BRIEF-P is a 63 item informant questionnaire of EF impairment for typically developing children aged 2-5. The measure utilises a three point likert scale format (never, sometimes and often). A higher score on this assessment indicates greater executive dysfunction. The BRIEF-P measures the behavioural manifestations of EF impairment across five domains: inhibition, working memory, set-shifting, plan/organise and emotional regulation. The measure has good internal consistency for parents (.80-.95) and for teachers (.90-97). Test-retest reliability is .78-.90 for parents and (.64-.94) for teachers. Convergent and discriminant validity have been demonstrated with other rating scales e.g. Child Behavior Checklist and the Assessment System for Children - Parent Rating Scale (Gioia, Espy & Isquith, 2003).

5.3.3.2 Repetitive Behaviour Questionnaire (RBQ; Moss et al., 2009)

The RBQ is an informant questionnaire that measures 19 operationally defined repetitive behaviours. The measure has good inter-rater reliability at subscale and item level (see section 2.2.3.3 for an extended description of this measure).

5.3.4 Experimental measures

5.3.4.1 Mullen Scales of Early Learning and Wechsler Abbreviated Scales of Intelligence (MSEL, Mullen, 1995; WASI-II, Wechsler, 1999)

Mental ages (MAs) were derived for each participant from the raw score tables of either the Mullen Scales of Early Learning (MSEL) or the Wechsler Abbreviated Scales of Intelligence – II (WASI-II). For a detailed description of how MAs were calculated and validated against the Vineland Adaptive Behaviour Scales see section 4.4.1.

5.3.4.2 Battery of Executive Function for People with Intellectual Disabilities (BEF-ID; Chapter 3)

The BEF-ID includes tests of inhibition (Shape Stroop, Reverse Categorisation, Bear-Dragon, Black-White Stroop and Gift Delay), working memory (Verbal Animal Span, Corsi Blocks, and Three, Six and Nine Scrambled Boxes), set-shifting (standard, separated and border versions of the DCCS, Spatial Reversal and the A not B task), and emotional regulation (Secret Gift task). Full task descriptions and task protocols can be found in chapter 3 and Appendix F respectively.

5.4 Data analysis

5.4.1 Data analysis - Analytical approach and Alpha levels

Prior to the analysis the distributions of the data were inspected to confirm that there were no non-linear relationships that required a different analytical approach. Visual inspection of the data revealed that there were no relationships that followed a non linear trajectory (e.g. a Sigmoid curve). Kolmogorov-Smirnov tests revealed that the data from the RBQ (item and subscale level) and EF battery were not normally distributed and transforming the data was not possible. Therefore, non-parametric Spearman Rho correlations were conducted to explore the relationship between performance on the EF measures (BRIEF-P and BEF-ID) and repetitive behaviour in RTS.

Correlations were conducted at item level of the RBQ. Each individual item represents an individual operationalised repetitive behaviour and previous analyses in this thesis (see section 2.4.1.2) have indicated that in a given syndrome group it is possible for an individual behaviour within a subscale to occur at a greater intensity or frequency than other behaviours in that subscale. Therefore, item level analysis was warranted to avoid masking relationships. Furthermore, by excluding subscale analysis fewer correlations were conducted, helping to reduce the Alpha level problem that is unavoidable in a large scale correlational design.

An Alpha level of $p < .005$ was used throughout in line with chapter 1 (see section 3.7 for further discussion on Alpha levels). To aid interpretation relationships are reported at Alpha levels $p <.01$, $p <.005$ and $p <.001$.

Given that the Secret Gift task had pass/fail criteria, using correlational analysis to analyse this task is questionable. Only nine participants failed this task so latency to reveal the secret could only be coded for a small number of participants and hence correlations between latency and items of the RBQ were likely to lack the necessary power to demonstrate relationships. Therefore, a secondary Chi Square analysis was conducted to explore the relationship between performance on the Secret Gift task and items of the RBQ. For the Chi square analysis, participants who scored 4 (more than once a day) or 3 (once a day) on an item from the RBQ were categorised as engaging in this repetitive behaviour and those with a score below 3 were categorised as not engaging in repetitive behaviour. This criterion reflects the clinical cut-off levels devised by Moss (2009) for items of the RBQ.

5.4.2 Data analysis – Assessment issues.

Only the subscales relating to the constructs of interest on the BRIEF-P were included in the analysis (inhibition, working memory, shifting and emotional regulation subscales). The BRIEF-P has been demonstrated to be a reliable and valid measure of EF; however, some of the items on the shifting subscale ask directly about adherence to routine (a higher level repetitive behaviour). Therefore, it was likely that a relationship would be found between the adherence to routines item on the RBQ and the shift subscale of the BRIEF-P due to the overlap of these items rather than because of a true relationship between routine and a shifting. To address this problem correlations between the routines item on the RBQ and the shift subscale of the BRIEF-P were repeated using a conservative shift subscale that was recalculated using only those items that did not include routine (items 40, 50 and 25). Two of the remaining items asked about aversion to loud noises or crowded areas and the other asked about difficulty joining in at family events.

One participant was excluded from the correlational analysis between the BRIEF-P and RBQ because they were deemed to have an inflated score on the inhibition subscale of the BRIEF-P. The items on the BRIEF-P are fairly subjective and for older, more able participants it is possible that these items could be interpreted differently than for younger or less able participants. The IQ assessment indicated that the participant in question was more able and independent than other participants in the sample. While the participant's mother rated the participant as having very poor inhibitory control on the inhibition subscale of the BRIEF-P an interview with the participant's mother strongly suggested that the basis for this judgement was not comparable to that of the other participants.

Finally, in accordance with chapter 4 the Object Retrieval and A not B task were excluded from this analysis because all participants with RTS and TD children were at ceiling on these tasks. Tasks from the EF battery were coded as described previously in chapters 3 and 4 of this thesis (sections 3.4.2 and 4.3.2.3.1).

5.5 Results

The results section is divided into subsections to address the aims laid out at the start of this chapter. The pattern of repetitive behaviour in the current sample is compared to the larger sample from chapter 2. The correlations between repetitive behaviours, age and ability level, and correlations between the two EF measures are presented early in this chapter to aid interpretation of later results. The relationships between the parental report measures are then examined, followed by the individual analyses between the subdomains of the EF battery (BEF-ID) and repetitive behaviour items (RBQ).

5.5.1 The repetitive behaviour profile of the current RTS sample

The purpose of this analysis was to examine the repetitive behaviour profile of the current RTS sample to determine whether it was similar to that described for the larger RTS sample in chapter 2. It was important to check that the pattern of repetitive behaviour in the current sample did not diverge far from what was expected given the previous analysis as deviation would suggest that the current sample was not representative of the wider RTS population. The overall occurrence of behaviours in the current sample, and the relationship between these behaviours and age (CA and MA) were examined. Visual inspection of figure 5.1 suggests that the pattern of repetitive behaviour is consistent across the samples and that overall the current sample is representative of RTS as a whole.

Mean scores on each item of the RBQ for the current sample and the sample of participants from chapter 2 are displayed in table 5.1. Inspection of the mean scores suggests differences between the groups are minimal. The greatest differences appear to be for body stereotypy, organising objects, attachment to people, repetitive phrases and echolalia. The current sample scored higher on these items than the sample from chapter 2. This suggests that overall the current sample may engage in a slightly higher frequency of repetitive behaviour. However, this may be advantageous when studying the underlying mechanisms of these behaviours because relationships will not be established if the behaviour is virtually absent in a sample. Mann-Whitney U tests were conducted and none of the differences reached significance (all *ps* > .05).

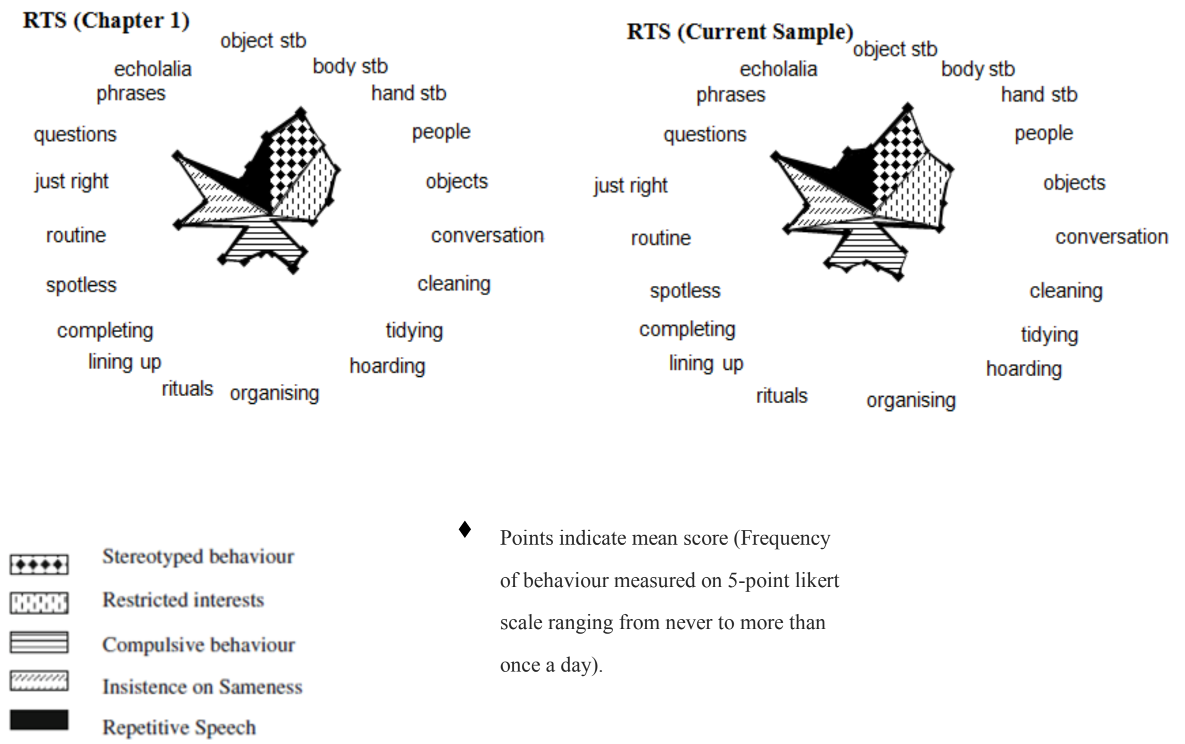

Figure 5.1. The pattern of repetitive behaviour in the RTS sample from chapter 1 (n = 87) and current RTS sample (N = 31).
Note. 5 point likert scale: 0 = never, 1 = once a month, 2 = once a week, 3 = once a day, 4 = more than once a day.

Table 5.1

The mean score on each item of the RBQ for the RTS sample from chapter 2 and the RTS sample reported on in the current chapter.

RBQ Repetitive Behaviour Item	Total RTS Sample (Chapter 2) – Mean Score on Item	Current RTS Sample – Mean Score on Item	Difference between means
Stereotyped behaviour			
Q1 Object stereotypy	1.77	1.60	0.17
Q2 Body Stereotypy	2.44	2.65	-0.21
Q3 Hand stereotypy	2.01	1.97	0.04
Compulsive behaviour			
Q4 Cleaning	.11	0.19	-0.08
Q5 Tidying	1.13	1.00	0.13
Q6 Hoarding	1.30	1.35	-0.05
Q7 Organising objects	0.78	1.00	-0.22
Q12 Rituals	0.79	0.86	-0.07
Q16 Lining up objects	1.10	1.16	-0.06
Q18 Completing behaviour	1.38	1.32	0.06
Q19 Spotless behaviour	0.51	0.61	-0.01
Restricted preferences			
Q8 Attachment to people [a]	1.90	2.12	-0.22
Q10 Attachment to objects	1.48	1.68	-0.02
Q13 Restricted conversation[a]	1.06	1.56	-0.05
Insistence on sameness			
Q15 Preference for routine	2.05	1.90	0.15
Q17 Just right behaviour	1.41	1.48	-0.07
Repetitive Speech			
Q9 Repetitive questions [a]	2.48	2.60	-0.12
Q11 Repetitive phrases/signing	0.96	1.39	-0.46
Q14 Echolalia[a]	1.17	1.60	-0.43

[a] Analysis only includes participants who are verbal

5.5.2 Relationships between repetitive behaviour, chronological age and ability level

The relationships between repetitive behaviour items, chronological age (CA) and MA for the current RTS sample are displayed in table 5.2. There was a strong negative relationship between score on the repetitive questions item and MA and between the echolalia item and MA. This indicates that higher MAs were related to fewer occurrences of repetitive questions and echolalia. Although the correlations did not reach significance there was a trend between MA and body stereotypy. There was also a trend between CA and hand stereotypy, CA and body stereotypy, and CA and just right behaviour.

Partial correlations were conducted and indicated that the relationship between MA and repetitive questions (R = -.52, p = .009) approached significance when chronological age was controlled for. The relationship between echolalia and MA did not reach significance at the stringent Alpha level after controlling for CA (R = -.45, p = .027). No other significant relationships emerged when partial correlations were conducted for the other repetitive behaviour items.

Table 5.2.

Spearman Rho correlations between the items of the RBQ, chronological age and mental age

	Chronological Age	Mental Age (MSEL & WASI-II)
Stereotyped behaviour		
Q1 Object stereotypy	-.13	-.12
Q2 Body Stereotypy	-.46[b]	-.36[b]
Q3 Hand stereotypy	-.36[b]	-.26
Compulsive behaviour		
Q4 Cleaning	-.04	-.04
Q5 Tidying	-.12	-.29
Q6 Hoarding	.16	.27
Q7 Organising objects	.18	.17
Q12 Rituals	-.27	-.35
Q16 Lining up objects	-.02	-.01
Q18 Completing behaviour	-.27	-.22
Q19 Spotless behaviour	-.04	.01
Restricted preferences		
Q8 Attachment to people[a]	-.09	-.40
Q10 Attachment to objects	-.16	-.18
Q13 Restricted conversation[a]	-.05	-.02
Insistence on sameness		
Q15 Preference for routine	-.01	.16
Q17 Just right behaviour	.36[b]	.11
Repetitive Speech		
Q9 Repetitive questions[a]	-.40[b]	-.72***
Q11 Repetitive phrases/signing	-.31	-.33
Q14 Echolalia[a]	-.42[b]	-.65***

* significant at < .01 ** significant at <.005 *** significant at < .001

[a] Analysis only includes participants who are verbal

[b] Results show a trend (*ps* < .05)

N = 30 for verbal items and 24 for non-verbal items

Note. Red shaded areas represent correlations of most importance for the interpretation

5.5.3 Relationships between the BEF-ID and BRIEF-P

The relationships between the BRIEF-P, MA and CA are displayed in table 5.3 along with relationships between the BRIEF-P and the corresponding subdomain tasks from the BEF-ID. MA and chronological age did not correlate with the subscales of the BRIEF-P; however there were trends between inhibition and MA, and working memory and MA in the anticipated direction (higher MA was related to better EF ratings). No significant relationships were found between the subscales of the BRIEF-P and the experimental tasks from the BEF-ID. However, there were trends between the Verbal Animal Span (phonological working memory) and the BRIEF-P working memory and inhibition subscales (R = -.49, p = .017 & R = -.42, p = .044 respectively).

5.5.3.1 Interim discussion – The relationships between the BEF-ID and BRIEF-P

It is surprising that no relationships were found between the BEF-ID and BRIEF-P given that both measures were designed to tap EF. The BRIEF-P has been well validated with typical developing children and it has been suggested as an appropriate tool for measuring EF in individuals with developmental disorders (Gioia et al., 2003). Similarly, the BEF-ID contains a number of tasks that are well-established within the typically developing literature. The BRIEF-P was also unrelated to MA, an unusual finding given EF development and MA are correlated in typical development. One possibility is that the BRIEF-P is not a useful measure for individuals with RTS who have varying degrees of intellectual disability and a wide range of ages. The absence of relationships between the BRIEF-P and MA, and the BRIEF-P and the BEF-ID could have been a product of the subjective nature of the BRIEF-P items. This

Table 5.3. *The Relationships between the subscales of the BRIEF-P and the tasks from the BEF-ID.*

	BRIEF-P Inhibition Subscale	BRIEF-P Working Memory Subscale	BRIEF-P Shift Subscale	BRIEF-P Emotional Regulation Subscale
Mental Age	-.27	-.33	.13	.11
Chronological Age	-.34	-.20	.12	.03
BRIEF-P Inhibition Subscale	-	.87***	.44	.71***
BRIEF-P Working Memory Subscale		-	.40	.57**
BRIEF-P Shift Subscale			-	.74***
Shape Stroop	-.13	.00	.00	-.04
Reverse Categorisation	-.12	-.08	.09	.10
Bear-Dragon	-.26	-.39	-.09	-.08
Black-White Stroop	.01	-.22	.16	.21
Inhibition Composite Score	-.17	-.24	.13	.06
Gift Delay (Peak Score)	-.06	.09	.32	.23
Gift Delay (Touch Score)	-.38	-.26	.22	-.05
Gift Delay (Seat Score)	-.22	-.12	.14	.02
Animal Span	-.42	-.49	.23	-.14
Corsi Blocks Span	-.25	-.12	.03	-.11
Scrambled Boxes Composite Score	-.02	-.11	.08	.05
DCCS Separated Dimensions	-.37	-.16	.02	-.03
DCCS Standard Version	-.17	.14	-.08	-.09
DCCS Border Version	-.25	.06	-.15	-.22
Spatial Reversal (Attainment Stage)	-.09	.03	-.34	.35
Spatial Reversal (Reversal Stage)	-.41	-.42	.21	-.12
Secret Gift	-.03	-.30	-.14	-.02

** <significant at .01 ** significant at <.005 *** significant at < .001*
Note. The shaded red areas indicate the correlations between the BEF-ID and the BRIEF-P for the same EF construct (e.g. inhibition).
Note. Scrambled Boxes total score presented. Individual tasks = ns.
Note. Chi Square analysis for the secret keeping task = ns
Note. Controlling for MA and CA did not lead to significant findings.

may have led to additional variability in ratings, which could have diminished the likelihood of finding significant correlations. It is of interest that the trends between the inhibition and working memory measures were mostly negative in direction, which is agreement with the hypothesis that these measures should be related. Furthermore, there appears to be a trend between the Verbal Animal span and the working memory subscale of the BRIEF-P.

5.5.4 Relationships between the Behavior Rating Inventory of Executive Function – Preschool Version and the Repetitive Behaviour Questionnaire

The following analyses were exploratory and were concerned with the relationships between scores on the subscales of the BRIEF-P and scores on the items of the RBQ. The purpose of this analysis was to examine whether EFs are related to repetitive behaviour in RTS using parental report measures. The results of the non-parametric Spearman-Rho correlations are displayed in table 5.4.

There was a strong positive correlation between scores on the working memory subscale of the BRIEP-P and the repetitive question item of the RBQ ($R = .66$, $p < .001$) indicating that poorer working memory, as measured by the BRIEF-P, was related to more occurrences of repetitive questions. There was also a strong positive correlation between the shift subscale of the BRIEF-P and the preference for routine item of the RBQ ($R = .61$, $p < .001$).

Table 5.4
Spearman Rho correlations between the subscales from the BRIEF-P and items from the RBQ

Items from the RBQ	BRIEF-P Inhibition Subscale	BRIEF-P Working Memory Subscale	BRIEF-P Shift Subscale	BRIEF-P Emotional Regulation Subscale
Chronological Age	-.34	-.20	.12	.03
Mental Age (MSEL/WASI-II)	-.27	-.33	.13	.11
Stereotyped behaviour				
Q1 Object stereotypy	.47*	.37	.23	.43
Q2 Body Stereotypy	.32	.25	.21	.19
Q3 Hand stereotypy	.19	.11	.20	.25
Compulsive behaviour				
Q4 Cleaning	.38	.43	.42	.42
Q5 Tidying	.34	.42	.03	.16
Q6 Hoarding	.33	.29	.32	.46
Q7 Organising objects	.11	.08	.30	.24
Q12 Rituals	.34	.27	.29	.33
Q16 Lining up objects	.21	.13	.35	.33
Q18 Completing behaviour	.49*	.36	.55**	.52**
Q19 Spotless behaviour	.27	.22	.10	.11
Restricted preferences				
Q8 Attachment to people [a]	.29	.31	.16	.30
Q10 Attachment to objects	.31	.29	.05	.17
Q13 Restricted conversation[a]	.40	.28	.29	.22
Insistence on sameness				
Q15 Preference for routine	.27	.20	.61***	.51**
Q17 Just right behaviour	.25	.30	.43	.38
Repetitive Speech				
Q9 Repetitive questions [a]	.57**	66***	.21	.34
Q11 Repetitive phrases/signing	.59**	.45	.18	.52**
Q14 Echolalia[a]	.62**	.62**	.08	.40

[a] Analysis only includes participants who are verbal
* significant < .01 ** significant <.005 *** significant <.001
Note. Shaded pink areas represent correlations interest for subsequent interpretation.
Note. N = 30 for verbal items and 24 for non-verbal items
Note. A higher score on the BRIEF-P indicates a greater degree of EF impairment.

Additional relationships were present at the less conservative Alpha level of p <.005 between the working memory subscale of the BRIEF-P and the echolalia item on the RBQ (R = .62, p = .001); the inhibition subscale of the BRIEF-P and all repetitive speech items on the RBQ (repetitive questions: R = .57, p = .004; repetitive phrase/signing: R = .59, p = .001, and echolalia: R = .62, p = .001); the emotional regulation subscale of the BRIEF-P and preference for routine (R = .51, p = .004), repetitive phrase/signing (R = .52, p = .003) and completing behaviour (R = .52, p = .004) from the RBQ; and between the shift subscale of the BRIEF-P and the completing behaviour item of the RBQ (R = .55, p = .002).

As previously noted in the data analysis section for this chapter, a relationship between the adherence to routines item from the RBQ and the shift subscale of the BRIEF-P was anticipated given that items on the shift subscale mirror the adherence to routines item. Correlations were conducted between the conservative shift subscale and the adherence to routines item. The correlation between adherence to routines and the shift subscale remained robust (R = .50, p = .003).

5.5.5 Relationships between the Battery of Executive Function for People with Intellectual Disabilities (BEF-ID) and the Repetitive Behaviour Questionnaire (RBQ)

The following analysis further explored the hypothesis that delays to the development or deficits in EFs are related to heightened rates of repetitive behaviour in RTS.

5.5.5.1 Relationships between inhibition tasks from the BEF-ID and items of the RBQ

Table 5.5 displays the results of Spearman Rho correlations between the inhibition tasks and the items of the RBQ.

A significant negative relationship was found between the Bear-Dragon task and the repetitive questioning item of the RBQ (R = -.85, $p < .001$). This indicates that better performance on the Bear-Dragon task was related to fewer occurrences of repetitive questions. At the less stringent Alpha level of $p < .005$, more spotless behaviour (as measured by the RBQ) was related to a higher likelihood that the individual would get out of their seat during the Gift Delay task (R = - .55, $p = .003$).

Given that MA was also strongly correlated with repetitive speech and performance on the Bear-Dragon task (chapter 4, section 4.5) it is possible that the relationships between the Bear-Dragon task and repetitive questions were mediated by MA. Partial correlations were conducted to explore this. Partial correlations indicated that the relationship between the Bear-Dragon task and repetitive questions remained significant after controlling for MA (R = -.78, $p < .001$), and although not quite reaching the stringent Alpha level of .005 the relationship approached significance when MA was calculated purely from the language subscales of the MSEL/WASI-II combination (R = -.55, $p = .008$), and when MA was calculated using only the expressive language subscales of the MSEL/WASI-II combination (R = -.57, $p = .006$).

The relationship between the Bear-Dragon task and the repetitive questions item is displayed in figure 5.2.

Table 5.5.
Spearman Rho correlations between the inhibition tasks from the BEF-ID and repetitive behaviours measured by the RBQ.

Age and Repetitive Behaviours	Shape Stroop	Reverse Categoris-sation	Bear-Dragon	Black-White Stroop	Inhibition Composite Score	Gift Peek Score	Gift Touch Score	Gift Seat Score
Age								
Chronological Age	.31	.57	.22	-.00	.26	.48	.61	.33
Mental Age	.73	.80	.73	.48	.82	.29	.65	.23
Stereotyped behaviour								
Q1 Object stereotypy	-.25	-.25	-.30	-.11	-.31	-.32	-.32	-.20
Q2 Body Stereotypy	-.16	-.35	-.21	.15	-.13	-.17	-.29	-.21
Q3 Hand stereotypy	-.27	-.40	-.11	.14	-.13	-.05	-.17	-.15
Compulsive behaviour								
Q4 Cleaning	.15	-.06	-.05	.15	.10	-.06	-.00	-.23
Q5 Tidying	.14	-.32	-.26	-.38	-.35	-.26	-.33	-.51*
Q6 Hoarding	.12	.24	-.16	-.22	-.07	.08	.14	-.30
Q7 Organising objects	-.09	.26	-.17	.19	-.12	-.09	.35	-.26
Q12 Rituals	-.34	-.34	-.40	-.36	-.22	-.02	-.06	-.14
Q16 Lining up objects	-.09	.01	-.08	.12	-.11	-.14	.19	-.28
Q18 Completing behaviour	-.47	-.26	-.40	.01	-.41	-.04	-.04	-.19
Q19 Spotless behaviour	.18	-.06	-.13	.01	-.11	-.28	-.09	-.55**
Restricted preferences								
Q8 Attachment to people [a]	.07	-.26	-.49	-.12	-.23	-.03	-.26	-.16
Q10 Attachment to objects	-.27	-.13	-.38	-.35	-.40	-.19	-.11	-.28
Q13 Restricted conversation [a]	.05	-04	-.12	-.14	-.05	-.27	-.18	-.23
Insistence on sameness								
Q15 Preference for routine	-.24	.13	-.09	-.16	-.23	.07	-.08	-.05
Q17 Just right behaviour	-.01	.14	-.31	-.46	-.34	.01	.14	-.32
Repetitive Speech								
Q9 Repetitive questions [a]	-.48	-.27	-.85***	-.31	-.67***	-.16	-.40	-.03
Q11 Repetitive phrases/signing	-.45	-.21	-.42	-.24	-.51	-.27	-.46	-.21
Q14 Echolalia[a]	-.19	-.20	-.46	-.14	-.34	-.12	-.47	-.13

[a] Analysis only includes participants who are verbal
* significant < .01 ** significant <.005 *** significant <.001
Note. Shaded red areas represent correlations interest for subsequent interpretation.
Note. Correlations with MA and CA may vary for Reverse Categorisation and Shape Stroop in comparison to chapter 4 due to larger sample size.
N = 30 for verbal items and 24 for non-verbal items

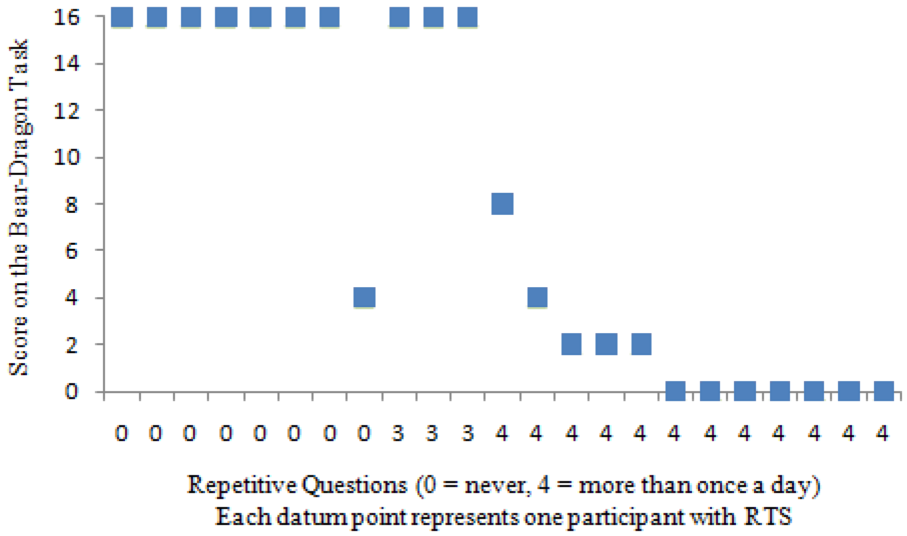

Figure 5.2. The relationship between Bear-Dragon score and the occurrences of repetitive questioning.

5.5.5.2 Relationships between working memory tasks and items of the RBQ

Table 5.6 displays the results of Spearman Rho correlations between the working memory tasks from the BEF-ID and the items of the RBQ. Better performance on the Verbal Animal Span was related to fewer repetitive questions (R = -.67, p <.001) and repetitive phrases/signing (R = -.61, p = .002) as measured by the RBQ. No other significant relationships emerged. The relationship between repetitive questions and verbal working memory was not maintained once MA was controlled for (R = -.30, p = .17). While the repetitive phrases/signing item of the RBQ was related to verbal working memory it was not related to mental or chronological age so partial correlations were not conducted.

5.5.4.3 Relationships between emotional regulation and shifting tasks from the BEF-ID and items of the RBQ

Table 5.6 displays the results of Spearman Rho correlations between the shifting and emotional regulation tasks and the items of the RBQ. No correlations were significant at the Alpha level of p < .005. However, there was a moderate negative relationship between performance on the DCCS Separated Dimensions and the completing behaviour item of the RBQ (R = -.54, p = .008) indicating that better performance on the shift task was related to fewer occurrences of completing behaviour. This relationship was also present between completing behaviour and the DCCS Standard Version (R = -.56, p = .006). There were no other significant relationships.

The relationship between the Secret Gift task and the items of the RBQ were explored using Chi Square analysis as outlined in the data analysis section. No significant relationships emerged.

Table 5.6. *Spearman Rho correlations between the working memory tasks from the BEF-ID and repetitive behaviour measured by the RBQ*

	Three Scrambled Boxes	Six Scrambled Boxes	Nine Scrambled Boxes	Scrambled Boxes Composite Score	Verbal Animal Span	Corsi Blocks Span
Chronological Age	-.18	-.00	.13	-.02	.38	.21
Mental Age	.20	.41	.13	.39	.75**	.50
Stereotyped behaviour						
Q1 Object stereotypy	-.18	-.16	.17	-.16	-.36	-.05
Q2 Body Stereotypy	.18	.08	.05	.08	-.15	-.19
Q3 Hand stereotypy	.28	-.06	.03	-.01	-.17	-.14
Compulsive behaviour						
Q4 Cleaning	.17	-.02	-.10	.01	.17	.15
Q5 Tidying	-.35	-.24	-.09	-.31	-.27	-.1
Q6 Hoarding	-.01	.09	.00	.05	-.20	.28
Q7 Organising objects	-.02	-.05	-.01	-.05	.04	.32
Q12 Rituals	.06	-.00	.03	-.01	-.19	-.06
Q16 Lining up objects	-.20	-.21	-.17	-.24	.05	.23
Q18 Completing behaviour	.04	-.03	.10	-.03	-.27	-.10
Q19 Spotless behaviour	.01	.17	.04	.12	-.01	.15
Restricted preferences						
Q8 Attachment to people	.01	.02	.25	.03	-.36	-.28
Q10 Attachment to objects	-.09	-.09	.03	-.09	-.29	.01
Q13 Restricted conversation [a]	-.04	.25	.20	.19	-.00	.16
Insistence on sameness						
Q15 Preference for routine	.23	-.06	-.06	-.06	.08	.20
Q17 Just right behaviour	-.21	-.06	.08	-.10	-.14	.09
Repetitive Speech						
Q9 Repetitive questions [a]	-.19	-.34	-.06	-.31	-.67***	-.22
Q11 Repetitive phrases/signing	-.18	-.22	-.10	-.24	-.61**	-.29
Q14 Echolalia[a]	-.18	-.17	-.01	-.16	-.52*	-.34

[a] Analysis only includes participants who are verbal
* significant < .01 ** significant <.005 *** significant <.001
Note. Shaded red areas represent correlations interest for subsequent interpretation.
Note. Correlations with MA and CA may differ from those reported in chapter 4 due to increased sample size.
N = 30 for verbal items and 24 for non-verbal items

Table 5.7

Spearman Rho correlations between the emotional regulation and shifting tasks from the BEF-ID and repetitive behaviour measured by the RBQ.

	DCCS Separated Dimensions	DCCS Standard	DCCS Border	Spatial Reversal (Attainment)	Spatial Reversal (Reversal)	Secret Gift Task
Age						
Chronological Age	.58**	.34	.28	-.18	.25	.37
Mental Age	66**	.44	.39	-.43	.02	.15
Stereotyped behaviour						
Q1 Object stereotypy	-.17	-.15	.06	-.49	-.26	.07
Q2 Body Stereotypy	-.37	-.45	-.45	-.19	-.23	-.03
Q3 Hand stereotypy	-.10	-.21	-.08	-.36	-.13	-.01
Compulsive behaviour						
Q4 Cleaning	.17	.22	.28	-.03	-.23	-42[b]
Q5 Tidying	-.22	-.01	.03	.02	-.34	-27
Q6 Hoarding	-.02	.20	.21	-.01	-.16	-.22
Q7 Organising objects	-.16	-.22	-.23	-.11	.41	-.05
Q12 Rituals	-.26	-.18	-.22	.19	-.02	.11
Q16 Lining up objects	-.15	-.17	-.15	-.09	.26	-.08
Q18 Completing behaviour	-.54*	-56*	-.47	-.17	-.01	-.04
Q19 Spotless behaviour	-.19	-.16	-.17	.18	-.16	.12
Restricted preferences						
Q8 Attachment to people[a]	-.02	-.12	-.06	-.19	-.13	-.02
Q10 Attachment to objects	-.10	.10	.19	.26	-.38	-.16
Q13 Restricted conversation[a]	-.03	.22	.15	-.27	-.27	.12
Insistence on sameness						
Q15 Preference for routine	-.19	-.11	-.03	-.29	-.05	-.11
Q17 Just right behaviour	.01	.07	.10	-.06	-.11	-.06
Repetitive Speech						
Q9 Repetitive questions[a]	-.48	-.17	-.15	-.18	-.07	.26
Q11 Repetitive phrases/signing	-.50	-.36	-.37	-.05	-.15	-.08
Q14 Echolalia[a]	-.32	-.14	-.19	.17	-.16	.07

[a] Analysis only includes participants who are verbal

[b] Approaching significance at .018

* significant at < .01 ** significant at <.005 *** at significant <.001

N = 30 for verbal items and 24 for non-verbal items

Note. Shaded red areas represent correlations interest for subsequent interpretation.
Note. Correlations may differ from chapter 4 for spatial reversal due to increased sample size.

5.6 Discussion

The overarching aim in this chapter was to explore the relationship between repetitive behaviour (as measured by the Repetitive Behaviour Questionnaire; Moss, 2009) and EFs, measured by the BRIEF-P (Gioia, Espy & Isquith, 2003) and a newly developed experimental EF battery (BEF-ID). Given the previous literature, it was anticipated that scores on the BRIEF-P and BEF-ID would be related, and that better performance on specific EF measures would be linked to fewer occurrences of specific repetitive behaviour. Finally, it was predicted that EF and repetitive behaviour would correlate with age and ability level because in chapter 4 a higher mental age was related to better performance on EF measures in RTS and typically developing children.

The first aim to be addressed in this chapter was how repetitive behaviour related to age and ability level, as this would aid interpretation of the results. It was found that repetitive speech items are related to mental age in RTS, with a younger mental age being related to increased frequency of repetitive questions and echolalia. Echolalia was also related to ability level in chapter 2; however, this was not true for repetitive questions. This finding may have emerged in the current chapter because a more sensitive measure of ability was used (MSEL-WASI-II Combination). Ability was only measured using parental report of adaptive behaviour in chapter 2 (self help score on the Wessex Questionnaire). There were no other significant relationships between repetitive behaviour and age or ability; however, for the majority of repetitive behaviours there were trends in the anticipated direction. These trends may not have met statistical significance because of the small sample size in the current study.

Significant correlations and trends between repetitive behaviour and mental age could be interpreted as evidence that repetitive behaviour is simply an index of intellectual disability.

As noted in the introduction to chapter 4, this belief was one of the reasons repetitive behaviour has been studied less frequently than other behaviours in disorder groups (Turner, 1997). However, relationships between repetitive behaviour and age are to be expected given that the cognitive constructs that may underpin repetitive behaviour are known to be related to ability level (i.e. EFs). It is not satisfactory to simply argue that behaviour occurs because of an individual's disability without further explanation of the mechanism by which this occurs (e.g. executive dysfunction or delay). Furthermore, as noted previously these repetitive behaviours are not universal in syndrome groups characterised by a similar degree of intellectual disability (i.e. high repetitive behaviour in Fragile-X syndrome, but low repetitive behaviour in Down syndrome).

The next aims to be addressed were those concerned with the relationships between the EF measures and repetitive behaviour. Analyses of relationships between the BRIEF-P (parental report measure of EF) and the RBQ (parental report measure of repetitive behaviour) revealed an association between better inhibition and lower scores on all repetitive speech items. An association was also found between better working memory and less frequent repetitive questions and echolalia. Other relationships supporting the prediction that better EF would be linked to fewer occurrences of repetitive behaviour emerged between two subscales (shift and emotional regulation) and adherence to routines, and these subscales were also related to completing behaviour. One consideration was that the relationship between adherence to routines and the shift subscale may have been a product of the similarity of the items across the two questionnaire measures. Therefore, a secondary analysis using a more conservative shift subscale (overlapping items removed) was conducted and the results remained consistent.

The relationships between the BRIEF-P and repetitive behaviour emerged even though the BRIEF-P subscales did not correlate significantly with mental age. The absence of significant correlations between the BRIEF-P and MA suggests that mental age does not account for the relationships between EF and repetitive behaviour in RTS. Conversely, this absence of significant relationships was unexpected because mental age was related to EF when the BEF-ID was administered to individuals with RTS in chapter 4. However, examination of the correlation coefficients suggests that there may be an emerging trend between mental age and the inhibition and working memory subscales of the BRIEF-P in the anticipated direction. It was noted in the interim discussion that the BRIEF-P has fairly broad items that could be interpreted in a number of ways depending on the age and ability level of the individual in question. Therefore, it is possible that relationships between mental age and the BRIEF-P were weaker because of variation in parental ratings due to the subjective nature of this measure. The relationships between EF and repetitive behaviour may have reached significance because these relationships were less vulnerable to variability in parental ratings than the relationship between EF and mental age in RTS. Variation in parental ratings could also have accounted for the absence of significant relationships between the BRIEF-P and the BEF-ID.

The correlational analyses between the BEF-ID and the RBQ suggested fewer occurrences of repetitive questions are related to better performance on the Bear-Dragon (an inhibition task) and the Verbal Animal Span (phonological working memory). This was in agreement with the relationships described above between the BRIEF-P and repetitive speech items. The relationship between repetitive questions and the Bear-Dragon task is striking. In chapter 4 a sharp improvement on the Bear-Dragon task was noted at a mental age of approximately 5 ½ - 6 years of age in RTS. In the current chapter, examination of the relationship between the

Bear-Dragon task and repetitive questions indicates that repetitive questions appears to rapidly decline in RTS at the same time that these individuals start passing the Bear-Dragon task.

When mental age and language abilities were controlled the relationship between the Bear-Dragon task and repetitive questions remained, while the relationship between the Verbal Animal Span task and repetitive questions did not. This indicates that the decline in repetitive questions may be underpinned by the development of inhibitory control; however, it is difficult to conclude this with certainty given that working memory is correlated more strongly with repetitive questions than inhibition on the BRIEF-P.

A further relationship was found between performance on the DCCS (an extra-dimensional set-shifting task) and the completing behaviour item of the RBQ. This relationship was also found between the BRIEF-P and the RBQ. Unlike the BRIEF-P/RBQ analysis no relationships were found between the set-shifting tasks of the BEF-ID and adherence to routine, nor was a relationship found between the Secret Gift task (emotional regulation) and adherence to routine or completing behaviour.

It is clear that the majority of the relationships that are present between the BRIEF-P and the RBQ are also present when the relationships between the BEF-ID and the RBQ were examined. Although the current results should be interpreted with caution given the large number of correlations conducted, the agreement across measures makes the findings more convincing and worthy of further study. Despite the agreement between measures, relationships between repetitive behaviours and tasks from the BEF-ID were only found for one task from each sub-domain of the battery. For example, the relationship between repetitive questions and inhibition was not found for the Black-White Stroop and Reverse

Categorisation, nor was the relationship between the DCCS separated dimensions task and completing behaviour found for the DCCS border task.

There could be a number of methodological factors contributing to the absence of these relationships. As noted in chapter 4, the Bear-Dragon task might be different from the other conflict inhibition tasks in the battery. The task does not require a response on every trial and it is a social task that requires gross motor responses. Thus, the relationship between this task and repetitive questions may be underpinned by an additional underlying task demand. It may be that repetitive questions occur because of a failure in motor inhibition as opposed to cognitive inhibition, or that repetitive questions occur because of a failure in inhibition in relation to social stimuli. Furthermore, there is a clear point in development where individuals with RTS begin to pass this task; hence performance does not gradually improve. While there is some variability in the scores obtained on this task, scores are more likely to be distributed in a more dichotomous fashion. This is also the case for the repetitive questions scores, and therefore, the relationship between improved performance on this task and reduction in repetitive questions may be more apparent because of the distribution of scores on these tasks.

The relationship between the set-shifting (measured by the DCCS) and completing behaviour may have only occurred with the separated dimensions and standard versions of the DCCS because too few individuals completed the border version of the DCCS because the task was too difficult. This warrants further exploration and demonstrates the necessity of using more than one measure of a construct and for the measures to be of varying difficulty.

The relationships between EF and repetitive behaviour that are reported in this chapter are supported by previous studies in the literature. Firstly, the relationships between working memory, inhibition and repetitive speech correspond to some degree with the results of Cullen et al. (2005) who found that repetitive questions were related to short term memory deficits on word list learning in people with Alzheimer's disease. If working memory plays a role in repetitive questions in RTS it may be that the inability to hold information in mind leads to questioning because an individual tries to elicit the forgotten information, or alleviate anxiety associated with uncertainty. A relationship between inhibition and repetitive questions has not been reported in the literature; however, inhibition has been linked to repetitive behaviour more generally (e.g. Lopez, Lincoln, Ozonoff, & Lai, 2005). If an individual has difficulty inhibiting a previously adaptive behaviour once it has been initiated they may continue to perseverate with this behaviour. Alternatively, an individual may be unable to stop the activation of prepotent responses in response to environmental cues. In this circumstance asking a question could serve as a reaction to an external cue (i.e. seeing a parent) in order to elicit social interaction.

As noted in section 1.5.2 a relationship between the shifting and adherence to routine has been described in Prader-Willi syndrome. Woodcock, Oliver and Humphreys (2009a, 2009b & 2009c) found that some individuals with this syndrome have a set shifting deficit that stops them from moving their attention flexibly to allow them to cope with sudden changes. They argued that when these individuals are forced to shift their attention it can lead to temper outbursts. There are no published studies linking shifting and emotional regulation to completing behaviour but, similarly to adherence to routines, completing behaviour is concerned with actions being done in a complete and predictable manner. Therefore, although relationships between the BRIEF-P and RBQ are sparse, those that have emerged fit with the previous literature.

There a number of caveats of this study that should be noted. Firstly, it could be argued that the distribution of scores on the repetitive speech item may be artificially creating relationships with the working memory and inhibition measures. It could also be argued that the large number of correlations in this chapter maximise the potential of making a type I error. However, the results are strengthened by the consistency across measures. If the repetitive speech item was artificially producing relationships we might expect to see inconsistent relationships emerging when the BRIEF-P was compared to BEF-ID.

Despite finding significant associations between executive function and specific repetitive behaviours in this chapter, these results do not provide sufficient evidence to support a causal link between these constructs nor can these correlations be used to specify the direction of causation if a link did exist. These associations could have occurred because repetitive behaviour impacts on executive function development or on performance on executive function tasks, or alternatively, another unmeasured variable could be driving the association. Thus, the correlations found in this chapter point towards a possible link between these constructs because where causation exists there will usually be correlation; however, as it is possible to have correlation without causation further research will be necessary to examine these relationships in more detail (see section 6.5.2 for an expanded discussion).

The results are also limited by sample size because whilst they support the possibility that certain repetitive behaviours may be linked to EF development in RTS, the executive underpinnings of other repetitive behaviours (e.g. lining up objects) are less certain. The trends in the data suggest possible links with EF development and mental age and it may be that further significant relationships would emerge if a larger sample was used in the analyses. However, one of the difficulties of conducting a study with individuals with a rare genetic syndrome is that it is difficult to recruit large numbers of people, and it takes a long time to collect data from each participant.

To conclude, in this chapter a number of aims were addressed. These aims included describing how age and ability level relate to repetitive behaviour and drawing links between specific EFs and specific repetitive behaviour. Echolalia and repetitive questioning were found to be related to mental age. A relationship was found between working memory, inhibition and repetitive speech items, in particular, repetitive questions. Further relationships were found across measures between the EF constructs shifting and emotional regulation, adherence to routine and completing behaviour. While these analyses cannot infer causality they are an important preliminary step towards understanding repetitive behaviour in RTS by highlighting a number of avenues for further research. Furthermore, they demonstrate how links between specific EF constructs and observable behaviour can be established. These latter points will be discussed more in the following general discussion.

CHAPTER 6

General Discussion

6.1 Introduction

In the introduction to this thesis repetitive behaviour profiles were introduced and it was argued that cross syndrome comparisons are warranted to understand similarities and differences in these profiles. The concept of an endophenotype was introduced and it was argued that executive dysfunction may underpin phenotypic repetitive behaviours. Finally, developmental processes were discussed and it was proposed that adopting a developmental trajectory approach to understanding cognition and behaviour in syndrome groups is likely to supplement traditional matching approaches. The aims of the thesis were to explore repetitive behaviour and executive function (EF) development in an understudied syndrome group, Rubinstein Taybi syndrome (RTS), and to evaluate each of these arguments.

In this thesis the repetitive behaviour profile of Rubinstein-Taybi syndrome has been explored relative to three other groups, an executive function battery was developed and the development of executive functioning in RTS was explored relative to typically developing (TD) children using developmental trajectory methodology. Finally, the relationships between repetitive behaviour and executive functioning were explored in RTS using correlational analyses. In this general discussion the findings presented in the previous chapters will be integrated focusing on the main hypothesises that underpinned each chapter. This will be followed by a discussion of the wider implications of these findings in relation to the literature, the strengths and weaknesses of this thesis and a discussion of further research that would supplement the current findings.

6.2 Main findings

In chapter 2 it was predicted that repetitive behaviour profiles would vary in RTS, Autism Spectrum Disorder (ASD), Down (DS) and Fragile-X (FXS) syndromes at a fine-grained level of description. In particular it was hypothesised that repetitive behaviour would be heightened in ASD and FXS relative to DS, but that the RTS group would have an uneven profile of repetitive behaviour. These predictions were confirmed. Individuals with FXS were found to have comparable levels of repetitive behaviour to ASD, while individuals with RTS had heightened repetitive questions, adherence to routine and body stereotypy in comparison to other forms of repetitive behaviour. Repetitive behaviour in RTS did not correlate with the social and communication deficits that form part of the triad of impairments in ASD. The dissociations within the repetitive behaviour profile of RTS fitted with previous reports of repetitive behaviour in RTS (Stevens, Carey & Blackburn, 1990), lent support for studying this profile at a fine-grained level and lent support for studying the potential cognitive underpinnings of the this profile.

In chapter 3 the development of an executive function battery was described. In this chapter the limitations of published executive function batteries were discussed and a series of pilot studies were presented that documented the development of a new battery. This chapter did not set out any firm hypothesises; however, it demonstrated that modifications could be made to executive function tasks to make them appropriate for non-verbal participants without significantly altering the difficulty of the tasks, and that it was possible to scale the inhibition battery by including tasks with a hierarchy of difficulty.

In chapter 4 the battery was applied and the development of EFs was described in RTS relative to a TD sample. It was anticipated that the EF profile of RTS would deviate from the TD profile because RTS engage in a range of repetitive behaviours and hence were hypothesised to have some form of EF delay or impairment. No predictions were made as to whether the EF development would be delayed, deviant or static in RTS as these cognitive constructs have not been previously explored; however, it was predicted that certain EFs may be more impaired than others. A cross sectional design was employed and it was demonstrated that individuals with RTS who had a higher mental ages performed better on most executive function tasks; however, their scores on these tasks lagged behind TD children relative to mental age in the developmental window studied. The performance on the individual inhibition tasks appeared to be delayed by around two years (MA). It was found that some EFs such as visuo-spatial working memory may be particularly impaired in RTS.

In chapter 5 scores on EF tasks were linked to repetitive behaviour using correlational analyses. It was hypothesized that repetitive behaviour would decrease as EF task performance increased and more specifically that adherence to routines may be related to shifting and emotional regulation as these links have been established in other disorder groups (Turner, 1997; Woodcock, Oliver & Humphreys, 2009a, 2009a, 2009c). The findings presented in chapter 5 are tentative but they support this hypothesis because just right behaviour was linked to shifting and/or emotional regulation, and adherence to routine was linked to shifting and/or emotional regulation. It was also found that repetitive speech, particularly repetitive questioning may be underpinned by difficulties with inhibitory control and/or working memory even when mental age was controlled. These findings are displayed in the model in figure 6.1. While these links are tentative they are the first steps in demonstrating a pathway between the cognitive endophenotype and behavioural phenotype of RTS.

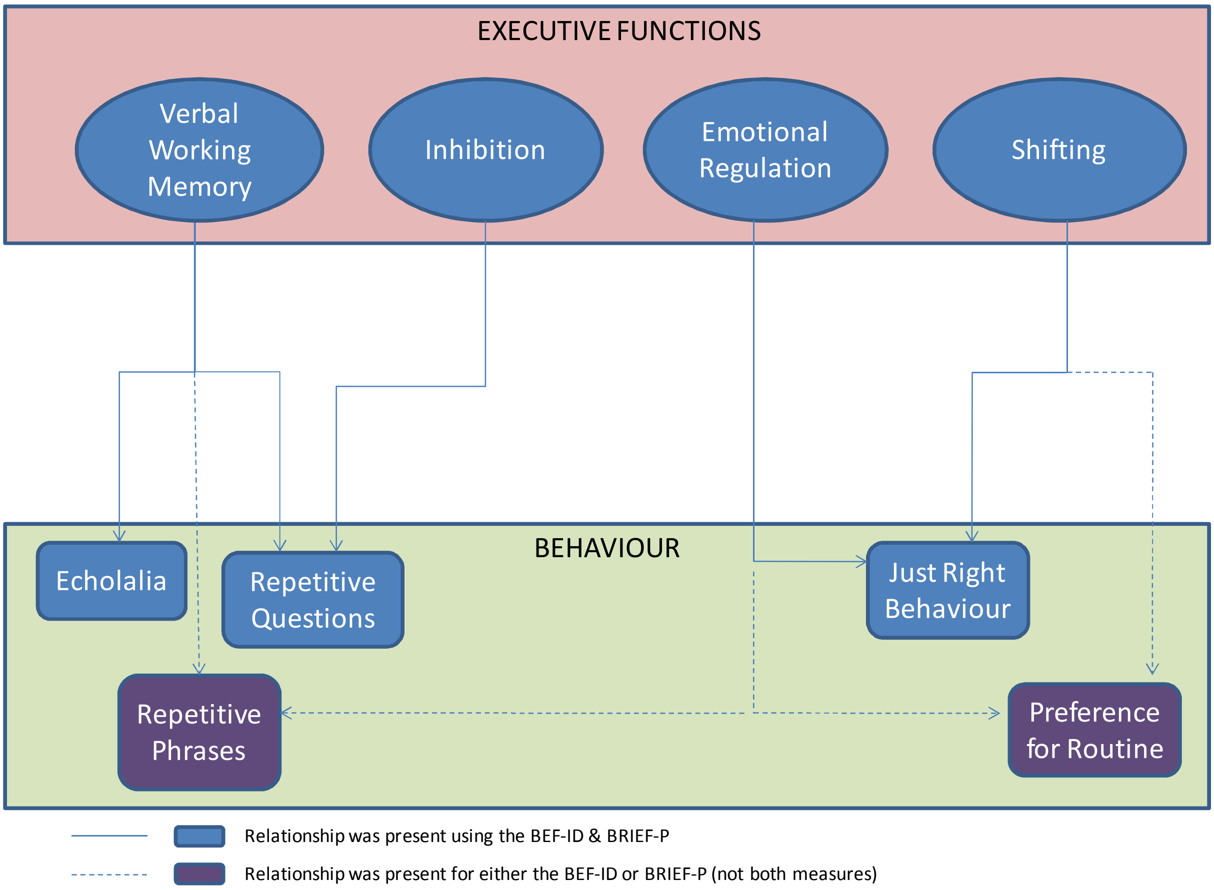

Figure 6.1. A model of potential pathways between executive functions and repetitive behaviours in RTS.

6.3 <u>Wider implications of these findings</u>

The findings presented in this thesis have a number of implications that can be split into a number of broad subsections, although there is a lot of overlap between these subsections. These implications will be addressed below and include implications relating to a) the construct of repetitive behaviour b) studying cognition and behaviour from a developmental perspective c) genetic underpinnings of repetitive behaviour d) the link between cognition and phenotypic behaviour.

6.3.1 Implications arising from repetitive behaviour profiles

As discussed in the introduction to this thesis the construct of repetitive behaviour is an umbrella term that encompasses a broad range of diverse behaviours. Turner (1997) argued that these behaviours need to be studied individually and provided sufficient evidence in individuals with Autism Spectrum Disorder to lend support to this argument. Over ten years later Woodcock, Oliver & Humphreys (2009a, 2009b, 2009c) made a similar argument in their series of studies conducted in Prader-Willi syndrome. While practical constraints mean that repetitive behaviour cannot always be studied in such detail, research is still conducted that attempts to study the underlying etiology of repetitive behaviour without an acknowledgement that this construct is diverse and that it may be inappropriate to study it in this manner. The findings presented in this thesis lend further support to the merit of studying repetitive behaviour at a fine-grained level of description by demonstrating the dissociations within and across profiles. Continuing to group repetitive behaviours into one construct may hinder our understanding of these behaviours (Turner, 1997; Moss et al. 2009).

The repetitive behaviour profiles presented for RTS, ASD and DS represent the first fine-grained systematic study of repetitive behaviour in these groups in comparison to a range of disorder groups. For example, in RTS reports of repetitive behaviour have largely been anecdotal and in ASD repetitive behaviour has largely been described at a gross level of description. If a fine-grained level of description has been employed in ASD, the repetitive behaviour profile has either been compared to a heterogeneous intellectual disability group or individuals with Down syndrome. In these previous studies a greater number of topographies of repetitive behaviour have been found in ASD, and individuals with ASD were found to engage in these behaviours more often that control groups (Hermelin & O'Conner, 1963; Lord, 1995; Lord & Pickles, 1996).

The findings presented in this thesis demonstrate that while individuals with ASD may engage in a broad range of repetitive behaviours at a high frequency, other syndrome groups may engage in a similar number of topographies at a similar frequency (e.g. FXS), or that a syndrome group may engage in highly specific behaviours at a similar frequency to those in ASD (e.g. RTS). These observations challenge the view that repetitive behaviour is uniformly heightened in ASD relative to other disorders and suggest that this depends on which comparison group is chosen and which repetitive behaviour is under study. This highlights the importance of choosing comparison groups carefully for further repetitive behaviour studies. Indeed, a range of disorder groups should be chosen where possible. It is should also be noted using ASD as the only comparison group in a repetitive behaviour study would not suffice. ASD is behaviourally defined by high levels of repetitive behaviour so would be expected to differ from other groups. Including a syndrome like FXS, that is known to have high levels of repetitive behaviour but is defined by genetic status rather than behavioural characteristics, provides a useful reference group and helps to reduce these difficulties.

The repetitive behaviour profiles provided in this thesis supplement those provided in the literature for Lowe, Prader-Willi, Angelman, Cornelia de Lange, Smith-Magenis and Cri du Chat syndromes (Moss et al., 2009). These profiles can be used to target further research towards behaviours of most significance within a syndrome (e.g. repetitive questioning in RTS). These profiles may also be useful for identifying individuals who have a co-diagnosis of another disorder. For example, as repetitive phrase and repetitive conversation are less common in RTS a heightened presence of these behaviours may allude to a co-morbid condition such as ASD that should be investigated further. Repetitive behaviour profiles could also be compared and contrasted to help generate further hypothesises about the underpinnings of these behaviours using models like the one presented in figure 6.1.

In chapters 2 and 5 the relationships between repetitive behaviour and age were also explored in RTS. Certain behaviours appear to occur less frequently in individuals with higher mental ages, in particular repetitive questions and echolalia. In chapter 5 there appeared to be an emerging trend between these behaviours and chronological age, which would most likely be confirmed if more participants could be included in the analyses. Thus, a further implication of these results is that they can be used to advise families who are concerned about particular behaviours, particularly because in many individuals it appears these behaviours decrease over time. However, it is also important to note that repetitive behaviour does not appear to be simply an index of ability level because phenotypic repetitive behaviour profiles were robust in the matched group analyses in chapter 2.

A further implication of the repetitive behaviour profile of RTS is that it supports a dissociation of the triad of impairments typically associated with ASD. Thus, the findings in RTS suggest that high levels of specific repetitive behaviours may not always be associated with reduced social interaction in disorder groups. This finding fits with a wider body of accumulating evidence that suggests that each part of the triad of impairments may have different underlying aetiology (see Happe, 2008 for review). This has implications for the way ASD is conceptualised and lends support to viewing ASD as a product of impairments in three key domains rather than a distinct disorder caused by one underlying problem. Ultimately, this potential dissociation of the triad should influence how ASD phenomenology is studied and in the future and more may be learnt about the underpinnings the triad of impairments from cross syndrome comparisons like these presented in this thesis. This conclusion would be strengthened by further studies investigating the social motivation of individuals with RTS syndrome relative to other syndrome groups. To date, extensive research is being conducted into the cognitive underpinnings of the social phenotype of RTS (Powis, Waite, Oliver, Beck & Apperly, 2009; Nelson, 2010) and it is hoped that this research will lend further support to these conclusions.

6.3.2 Implications of studying cognition and behaviour from a developmental perspective

It was noted in the introduction to this thesis that developmental disorders are intrinsically tied to development. Karmiloff-Smith (1997, 1998) has argued that chromosomal rearrangement may set in motion a deviant or delayed developmental trajectory for a syndrome group. Karmiloff-Smith argued that comparing a syndrome group to another syndrome group without an acknowledgement of the developmental processes leads to a description of the end point of development without an acknowledgement of how this was arrived at, and that this may mask subtle developmental changes. The findings presented in this thesis lend support for adopting a developmental perspective because the cross sectional analyses of executive function performance suggest that executive function is not static in RTS but is linked to mental age. Given that mental age is closely linked to chronological age in RTS these results suggest that executive functioning potentially continues to develop in people with RTS but at a much slower rate than in TD children.

If executive function does continue to develop in RTS it has a number of important implications for this group. From the current sample it appears that the development in EFs seen in preschoolers does not occur in individuals with RTS until adolescence; therefore, this suggests that for a large proportion of childhood individuals with RTS will have impaired executive function. This may impact on their ability to learn, pay attention and respond flexibility across a wide range of situations. An awareness of these potential difficulties will allow parents, teachers and professionals to support children to draw on their strengths (e.g. verbal working memory) and develop strategies to overcome their weaknesses. The fact that executive function continues to develop suggests that training programmes for executive function may be successful. A further implication is that other developments that are related to executive functioning such as theory of mind, counterfactual thinking and the experience of regret may be effected by the delays to the development of executive functioning, but they may still develop (Beck, Riggs, & Gorniak, 2009; Carlson, Mandell & Williams, 2004; Carlson, Moses and Breton, 2002; Diamond & Taylor, 1996; Hughes, 1998; Hughes & Ensor, 2007; Lyon & Krashegor, 1996).

Examination of the developmental trajectories indicated that particular skills may not develop in the majority of people with RTS i.e. visuo-spatial working memory and complex attentional shifting. Further research could focus specifically on why these tasks are difficult for individuals with RTS. For example, it could be argued that poor performance on the Corsi Span indicates a visuo-spatial working memory deficit; however, poor performance on this task could be caused by a difficulty tracking the experimenter's hand movements or a difficulty holding the positions of individual blocks in mind because of interference from the surrounding stimuli that look alike. Motor movements have also been found to interfere with performance on span tasks and the execution of the tapping sequence may have posed additional demands for individuals with RTS, leading to difficulties on this task. (Symth & Pelky, 1992; Symth & Scholey, 1994).

There are a number of methodological implications arising from this research. Firstly, in chapter 4 it was demonstrated how a battery of tests could be employed to explore the development of executive function in a rare genetic syndrome. This demonstrates the utility of borrowing and adapting tasks from the developmental literature. In particular, the inhibition tasks worked particularly well when brought together to form a composite score and the resulting inhibition trajectory for RTS had relatively narrow confidence intervals. It would be interesting to compare this trajectory to other syndrome groups in the future.

It could be argued that the lack of a syndrome comparison group in this thesis limits the results. Indeed, it is impossible to say which developmental trajectories are specific to RTS, however, this does not mean that these results do not have direct implications for people with RTS, and the demonstration that trajectories can be constructed in this manner to profile cognitive constructs provides proof of principle for applying this methodology in other groups in the future.

6.3.3 Implications for the Genetic Underpinnings of Repetitive Behaviour

A discussion is warranted regarding the developmental trajectories of the executive functions and their possible correlates. As noted throughout this thesis RTS is caused by chromosomal rearrangements of the CREB binding protein and these rearrangements are thought to impact on long term memory in RTS (Petrij et al., 1995). It has been suggested that the associated intellectual disability in RTS may be underpinned by long term memory (LTM) impairments and reductions in synaptic plasticity, due to the role of the CREB binding protein in hippocampal functioning. This suggestion is supported by a series of studies that have explored the role of the CREB protein in genetically altered knock-out mice (Oike et al., 1999; Alarcon et al., 2004; Tanaka et al., 1997; Bartsch et al., 1995; Korzus, Rosenfeld & Mayford, 2004; Wood et al., 2005).

These knock-out mice have a number of phenotypic similarities to humans with RTS and it has been demonstrated that the mice have LTM impairments as opposed to short term memory impairments (STM). This specific deficit to LTM would be expected given that hippocampal circuitry is usually associated with consolidation of LTM. Spatial LTM appears to be particularly impaired in mice when tested using the water maze (Wood et al., 2005). It has been suggested that the intellectual disability associated with RTS may eventually be remedied because histone deacetylases have been found to rescue the LTM difficulties in the knockout mice (Alarcón et al., 2004).

This thesis was not concerned with LTM and hippocampal functioning in RTS and instead was concerned with cognitive processes associated with the frontal lobes. Despite this, the current findings raise a number of important considerations. The hippocampal circuitry is known to project to many cortical regions including the frontal lobes and it is implicated in information processing, learning, attention, imagination, perception, short-term memory and goal orientated behaviour (Chun, Turk & Brown, 2007; Dégenètais, Thierry, Glowinski and Gioanni, 2003; Hartley et al., 2007; Hassabis, Kumaran, Vann & Maguire, 2007; Kumaran & Maguire, 2008; Lee et al, 2005; Whitlock, Heynen, Shuler & Bear, 2006). While STM difficulties have not been found in the knock-out mice, Lipska, Aultman, Verma, Winberher and Moghaddam (2002) found that rats with developmental lesions to the hippocampus, but not those acquired in adulthood, performed more poorly than controls on tasks that measured working memory. Dégenètais et al. (2003) used intracellular recordings in rats to provide evidence of a 'co-operative' relationship between the prefrontal cortex and hippocampus. In addition, there is evidence that when rats employ STM in search tasks information is exchanged between these regions (Floresco et al., 1997). Thus, it is possible that problems with the hippocampal circuitry may have cascading effects on the development of working memory in individuals with.RTS.

6.3.4 Implications for the link between cognition and phenotypic behaviour

Links between cognition and phenotypic repetitive behaviour have been demonstrated in this thesis. More specifically decreases in particular repetitive behaviours have been linked to better performance on specific executive functions tasks. The developmental trajectory approach allows for speculation about specific ages (MA) at which individuals with RTS may begin to improve on EF tasks and hence engage in a lower frequency of repetitive behaviour. This was most striking for the bear-dragon task (inhibition) and repetitive questioning at a mental age of approximately six years.

As noted above, the findings in this thesis appear robust because of the agreement across assessments and because similar findings have been found before in the literature (Woodcock, Oliver & Humphreys, 2009a, 2009b, 2009c). However, to date the links between specific executive functions and specific repetitive behaviours have only been explored in a small number of disorder groups. Of those groups with associated intellectual disability this is limited to a handful, including Prader-Willi syndrome and Autism Spectrum Disorder (Woodcock, Oliver & Humphreys, 2009abc; Turner, 1997). Turner (1997) argued that the executive underpinnings of repetitive behaviour in ASD were likely to be ASD specific and not related to disorder groups *per se*. However, the current findings suggest that the relationship between executive functions and repetitive behaviours may not simply be limited to a small number of disorder groups, but may occur in a wide range.

6.4 Summary of the strengths of the thesis

A number of strengths of this thesis have been discussed above. To summarise these include:

- The application on a range of methodological approaches including a developmental trajectory approach to explore repetitive behaviour, executive functions and the links between them in RTS.
- The demonstration of proof of principle for applying the developmental trajectory approach in rare genetic syndromes.
- An illustration of how tasks can be adapted and applied from the typically developing literature.
- A focus on fine-grained descriptions of behaviour.
- A demonstration of how the cognitive endophenotype may be linked to the behavioural phenotype.
- A demonstration of key areas of interest in the repetitive behaviour profile and the executive function profile of RTS that warrant further investigation.

6.5 Limitations of the thesis

A number of limitations have also been raised and addressed above. These include that further work needs to be conducted to address the specific reasons for poor performance on certain tasks, that there are no syndrome comparison groups in chapter 4, and that the specific biological mechanisms underpinning performance on these tasks are uncertain. It has been argued that these limitations should be viewed as opportunities for further research. There are several other limitations that need to be addressed.

6.5.1 Limitations relating to mental age assessments

In chapter 4 developmental trajectories for executive function tasks were plotted against mental age. Thomas et al. (2009) note that plotting performance as a function of mental age is theory driven. The conversion of scores derived from psychometric measures into mental age equivalents depends on the normative data that were originally collected for this assessment. The scores obtained on these assessments also rely heavily on adherence to the test protocols and many psychometric assessments have overlapping demands with the dependent variable under scrutiny (i.e. executive function). Thus, there are a number of ways that aspects of psychometric measures can confound the findings of a study.

Thomas et al. (2009) recommended that, where possible, chronological age trajectories should be constructed and used alongside the theory driven mental age trajectories. Despite this, in the thesis mental age trajectories were used over chronological age trajectories, mainly because chronological age did not correlate with test performance for the majority of the battery. Furthermore, sampling a CA matched comparison group would have required the administration of tests to older TD children and adults. This would have been fairly uninformative because the older CA children and adults would have been at ceiling on the majority of the battery and to continue to administer tests would have been developmentally inappropriate. This was largely due to the nature of the tests used in the battery. The span tasks and the border DCCS are exceptions to this general rule because these tasks would have been appropriate for older individuals, and could be utilised for this purpose in the future.

If computerised tests had been used in this battery it may have been easier to map CA trajectories as subtle reaction time measures could have been used; however, when computerised tasks were piloted with individuals with RTS participants were not motivated to complete these tasks. Therefore, it may not have been possible to use tasks within this thesis without limiting the sample to more able individuals, which would have reduced the developmental scope of the thesis and the sample size.

Two further issues that relate to the mental age calculations in chapter 4 are that mental age was not measured in the typically developing sample and instead was assumed to align with chronological age in this group, and mental age scores were derived from the raw score tables for the RTS group, which may have reduced the accuracy of these estimates. To address each in turn, while the TD group did not receive the psychometrics their performance is as expected from the TD literature and the pilot studies conducted in chapter 3 (Carlson, 2005). In terms of the RTS sample, it should be noted that individuals with RTS typically received higher mental ages from the psychometric assessments than would be expected given their performance on executive function tasks. For example, the RTS participants who were passing the inhibition tasks were approximately two years older (MA) than the TD children who passed these tasks. Relying on mental ages derived from the psychometric assessments would be more concerning if no differences had been found between mental age and EF performance; however, mental ages of approximately two years older is a considerable difference in the typically developing literature and TD children pass a number of developmental milestones between the ages of four and six years. It is very unlikely the RTS group could have performed to such a high degree on the MSEL-WASI-II combination that it would have inflated their mental ages artificially. So, while one limitation of this thesis is that the mental ages can only be assumed to be estimates, there is no reason to doubt that the mental ages represent a good estimate of the general level of ability for the two groups. Therefore, these estimates should be sufficient to highlight the general patterns within the data, for example, that RTS have delayed develop on measures of inhibition.

6.5.2 Limitations relating to samples and measures

The results may not have reached statistical significance for some analyses because there were too few participants to show an effect. This may be particularly true in chapter 5 where there appears to be a number of emerging trends in the RTS group that suggest a number of repetitive behaviours may be linked to executive constructs and mental age. Unfortunately, this is a limitation of many research studies focusing on individuals with rare genetic syndromes. The rarity of these syndromes makes recruitment difficult and often participants are not able enough to complete the tests. This difficulty is heightened when a construct like executive function is measured because the very nature of executive function (a higher order cognitive construct) means that the tests are usually complex in nature. Indeed, most tests that measure executive functioning require an individual to hold a rule in mind and to comprehend test instructions. While tests have been developed that are suitable for measuring inhibition in infants (i.e. the Object Retrieval), these tests are usually carried out in highly controlled laboratory environments so that subtle behavioural differences can be detected (for example Diamond, 1990). Due to the rarity of RTS conducting a laboratory study might lead a smaller sample size due to difficulties with recruitment; however, it is demonstrated in the current thesis that even with small sample sizes significant and meaningful results can be obtained.

It is important to note that the correlational analyses conducted in this thesis cannot be used to discern a direct causal link between executive function and repetitive behaviour, nor the direction of the associations. An alternative explanation is that repetitive behaviour impacts on executive function development or performance on executive function tasks, or that another unmeasured variable is driving the association. There was no reason to suspect that repetitive behaviour impacted on performance on the executive function tasks during testing. For example, participants did not say an item repetitively during the verbal animal span or perseverate on the Corsi box span. To rule out the possibility of repetitive behaviour impacting on executive function development further research could focus on monitoring subtle changes in repetitive behaviour and executive function in adolescents with RTS. Adolescence was highlighted in this thesis as the most likely developmental window during where EF could develop in RTS. It may be that improvements in EF would found to be a precursor to reductions in repetitive behaviour.

A final limitation is the reliance on one questionnaire measure to measure repetitive behaviour. The Repetitive Behaviour Questionnaire was chosen because it has a number of advantages over alternative measures: it is one of the only questionnaire that measures repetitive behaviour at a fine-grained level of description, it is short in duration as opposed to an interview method, it has item level reliability, and it has been used previously to explore the repetitive behaviour profiles of a number of syndrome groups. Direct observations of repetitive behaviour were unlikely to have given an accurate representation of the range of behaviours across a number of contexts, and other questionnaire measures have tended to pool repetitive behaviour into one construct, or include behaviours that are outside the scope of this thesis (e.g. self injury). Therefore, although only one measure was employed it was the best measure that was available.

6.6 Future Directions

To summarise a number of points touched on in this discussion further research should focus on mapping the developmental trajectories of performance on executive function tasks for other syndrome groups and disorders. This would allow for the identification of disorder groups with the deviant or delayed executive function trajectories and it may lead to the early identification of changes with age that may indicate serious cognitive decline, for example, the decline in executive function that has been linked to the onset of Alzheimer's disease in Down syndrome (Ball et al., 2006). It is anticipated that executive development in a syndrome like FXS (with a heightened specificity for generalised repetitive behaviour) may be very different to the developmental profile of RTS.

Further research may also involve continuing to sample individuals with RTS when possible to increase the numbers of participants included in the analyses presented in this thesis. Research could also be conducted that focuses on whether the executive function difficulties observed in RTS are underpinned by difficulties within the frontal lobe, or whether the main seat of the difficulties is the hippocampal regions that project to the frontal lobes. This may draw on the research methods described by Woodcock, Oliver and Humphreys (2009a, 2009b, 2009c) who applied brain imaging techniques to explore shifting deficits in a subset of more able people with Prader-Willi syndrome. A limitation of a brain imaging study is that it would not be possible to administer tasks face to face with the participant, and it would limit the sample to more able/older participants, which would make it less developmental in nature. However, it has been demonstrated in this thesis that applying a range of approaches can also be useful, and thus further research should continue to adopt an integrative approach that explores RTS from a number of methodological positions.

Further research could also be more targeted and less exploratory, hence, focusing on specific repetitive behaviours like repetitive questions or just right behaviours in RTS. The reasons for poor performance on a specific task could be explored. For example, building on this thesis, four versions of the bear-dragon task were piloted with seven children with RTS to compare performance on a social version of the task to a non-social version with gross motor movements, and a non-social version without motor movements. This was to explore whether individuals were failing this task because of engagement with the researcher, gross motor movements or a general inhibition problem. This task needs to be conducted with more individuals before conclusions can be drawn, but it highlights the potential for studying these constructs further.

If further research was more targeted it may be possible to use more sensitive measures such as computerised measures as participants would be required to complete fewer tasks overall. Having to complete fewer tasks will reduce fatigue and the likelihood of participants not complying with the test procedures. Furthermore, Burns, Riggs and Beck (2011) have recently developed a battery of computerised executive function tasks that have considerably fewer trials than computerised tests trialled with individuals with RTS during battery development. Burns et al. (2011) successfully tested five year olds using this battery. Given that Diamond (personal communication, 2008) recommended computerised tests with considerably more trials for children who were 3.5 years old this newly developed battery may have potential applications for younger children.

6.7 Closing Statement

The importance of clearly defining and operationalising constructs has been demonstrated in this thesis and a pathway has been mapped between cognition and behaviour in a rare genetic syndrome group. The research presented in this thesis forms the first systematic series of studies to explore cognitive profiles and development in Rubinstein-Taybi syndrome. Thus, this thesis has provided a basis for further research within this syndrome.

This thesis has also drawn upon a number of methodological approaches to demonstrate how pathways can be profiled between cognition and behaviour. Total group, matching approaches and developmental trajectory methodology have been employed at different stages of the thesis and each has been demonstrated to be a worthwhile and informative approach. It is hoped that in the future researchers will continue to integrate a range of methodological stances when studying developmental disorders.

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Appendix A

The RBQ removed due to copyright

BACKGROUND INFORMATION

Please tick or write your response to these questions concerning background details:
Please answer the following about the <u>person you care</u> for:

1. **Today's date:** ________________________

2. **Gender:** Male ☐ Female ☐

3. **Date of Birth**: ___/___/____ **Age:**______________

4. **Is the person you care for verbal?** (i.e. more than 30 signs/words in their vocabulary)

   Yes/No (delete as appropriate)

5. **Is the person you care for able to walk unaided?**

   Yes/No (delete as appropriate)

6. **Has the person you care for been diagnosed with a syndrome?** Yes/No (delete as appropriate)

If yes, please indicate which syndrome in 5a. and answer questions 6 to 8. If no, please move on to question 9

6.a

Cornelia de Lange syndrome	☐	Cri du Chat syndrome	☐
Prader-Willi syndrome	☐	Rubinstein Taybi syndrome	☐
Fragile X syndrome	☐	Down syndrome	☐
Lowe syndrome	☐	Soto Syndrome	☐
Rubinstein-Taybi syndrome	☐	9q34 deletion	☐
8p23deletion	☐	Tuberous Sclerosis	☐
Other ______________________________			

7. **What is the genetic mechanism causing the syndrome in the person you care for?**

Uni-parental disomy	☐	Sequence repetition	☐
Deletion	☐	Translocation	☐
Unknown	☐	Other _____________________________	

8. **When was the person you care for diagnosed?** ____

9. **Who diagnosed the person you care for?**

Paediatrician	☐	Clinical Geneticist	☐
GP	☐	Other ______________________	

10. **Has the person you care for had any medical/health difficulties in the last six months? If yes, please give details:**

____

____

In the information sheet and consent form we informed you that we may need to contact your child's/person you care for's GP in order to clarify any information regarding your child's health and diagnostic status (see consent form and information sheet for more information). If you have already indicated on the consent form that you are happy for us to do this, please complete the relevant details below:

11. Name of your child's/person you care for's

GP____

GP Address____

____

GP Telephone number__________________________

The following questions ask for background information about you and your family. Please tick the appropriate boxes or write in the spaces provided.

1. Are you male or female? Male ☐ Female ☐

2. What was your age in years on your last birthday? _____________years

3. Please tick the highest level of your educational qualifications.

No formal educational qualifications.. ☐
Fewer than 5 GCSE's or O Level's (grades A-C), NVQ 1, or BTEC First Diploma……. …. ☐
5 or more GCSE's or O Level's (grades A-C), NVQ 2, or equivalent…………………..…….. ☐
3 or more 'A' Levels, NVQ 3, BTEC National, or equivalent... ☐
Polytechnic/University degree, NVQ 4, or equivalent.. ☐
Masters/Doctoral degree, NVQ 5, or equivalent……….. ☐

4. What is your relationship to your child with a genetic syndrome (e.g. mother, father, stepmother, grandmother, adoptive parent)? ______________________________

5. In total how many people currently live in your home? ______Adults ______Children

6. Does your child with a genetic syndrome normally live with you?

Yes ☐ No ☐

If no, then where do they live?

____

7. What is your current marital status?

Married, and living with spouse.. ☐

Living with partner.. ☐

Divorced/Separated/Widowed/Single and NOT living with a partner......... ☐

If living with partner/spouse, please answer the following questions, if not, please go to question 12.

8. Is your partner male or female? Male ☐ Female ☐

9. What was their age in years on their last birthday? _____________ years

10. Please tick the highest level of your partner/spouse's educational qualifications.

No formal educational qualifications.. ☐

Fewer than 5 GCSE or O Level (grades A-C), NVQ 1, or BTEC First Diploma……...… ☐

5 or more GCSE or O Level (grades A-C), NVQ 2, or equivalent……………………..… ☐

3 or more 'A' Levels, NVQ 3, BTEC National, or equivalent.. ☐

Polytechnic/University degree, NVQ 4, or equivalent... ☐

Masters/Doctoral degree, NVQ 5, or equivalent………….. ☐

11. What is your partner/spouse's relationship to your child with a genetic syndrome (e.g. mother, father, stepmother, adoptive parent)? _______ ________________________

12. Recent data from research with families of children with special needs has shown that a family's financial resources are important in understanding family member's views and experiences. With this in mind, we would be very grateful if you could answer the additional question below. We are not interested in exactly what your family income is, but we would like to be able to look at whether those with high versus lower levels of financial resources have different experiences.

What is your current total annual family income? Please include a rough estimate of total salaries and other income (including benefits) before tax and national insurance/pensions.

Please tick one box only:

Less than £15,000………………………………………………………………..…………..… ☐

£15,001 to £25,000………………………………………………………………...…………. ☐

£25,001 to £35,000……………………………………………………………..…….………. ☐

£35,001 to £45,000……………………………………………………….…..………… ☐

£45,001 to
£55,000………………………………………………………..……………..…… ☐

£55,001 to
£65,000……………………………………………………….…………………..….. ☐

£65,001 or
more…………………………..…………………………………….…………………. ☐

Appendix C

Wessex Questionnaire removed due to copyright

Appendix D
Social Communication Questionnaire removed due to copyright

Date

Opt-out
In a few weeks' time [researcher's name] will be visiting your child's nursery to conduct a research study. The research is concerned with children's early 'Theory of Mind' and 'Executive Function' abilities. 'Executive function' is an umbrella term that encompasses a wide range of abilities, including: holding things in memory, monitoring ongoing behaviours, stopping unwanted behaviours that have been previously learned, and switching attention from a current task to a new task. 'Theory of Mind' involves understanding the mental states (beliefs, desires, feelings and intentions) of others.

The research will involve children playing very simple games and tasks with the researchers. For example, in one task - the bear-dragon game (a simplified version of Simon Says) children will be introduced to a 'nice' bear puppet and a 'naughty' dragon puppet and told that they should do what the 'nice' bear says but not what the 'naughty' dragon says.

If you would prefer your child **not** to participate in this study, please sign the permission slip below and return it to your child's school/nursery within one week of receiving this letter.

~~~~~~

I prefer that my child, {child's name}, does not participate in [researcher's name]'s study.

Parent's (or guardian's) signature

Date
~~~~~~

Object Retrieval

Look at this [produce box]!

Name – what's this?" Then comment on the toy [warm up]
Can you get it out for me? Can you get the toy?

Participants will be praised for correct retrieval of the object. If they fail to retrieve the object in 60 seconds the experimenter will demonstrate how to reach inside for the object and the trial shall be repeated.

Trials will be as follows:

Control trials
1. **Opaque box, opening at front**
2. **Opaque box, opening on left**
3. **Opaque box, opening on right**
4. **Opaque Box, opening at the top, object at back**
5. **Opaque box, opening at the top, object at front**

Experimental trials
6. **Transparent box, opening at front**
7. **Transparent box, opening on left**
8. **Transparent box, opening on right**
9. **Transparent Box, opening at the top, object at back**
10. **Transparent box, opening at the top, object at front**

The researcher will hold the box down firmly to stop the participant turning the box over or dragging it towards them.

<u>Reverse Categorisation</u>

Let's play another game. Look I have some buckets here, a red one and a blue one, and I have lots of coloured balls. We are going to play a fun game with these!

In this game the **red** balls go in here (demonstrate) and the **blue** balls go in here (demonstrate). Now you try!

<u>Practice:</u>

Blue ball	Score:

Well done, remember, the blue balls go in here.

Red ball	Score:

Well done, remember, the red balls go in here.

If the individual fails the first practice trial then repeat the practice once more. If the individual still fails after the second practice trial, proceed straight to the experiment.

<u>Experiment:</u>

"Ok, lets do some more! Ready?"

E Calls	B	R	B	R	R	B	B	R	B	R	R	B
Pp Response												
SCORE												

Instructions repeated Rule check

Repeat the instructions after 6 trials. Remember that these (blue) balls go into this bucket and these (red) balls go into this bucket"

Rule Check
"Well done! You tried really hard! See this bucket, what colour ball?"

Participant's response

Notes: At end of all the testing check that the individual can correctly sort by asking them to pack them away into the colour-matched buckets.

<u>END</u>

Shape Stroop

"Ok, let's play another game!"

Control Stage

"Here are some pictures of different kinds of fruit. Let's have a look at them together. Can you point to the":

	Big Banana	**Little Apple**	**Little Orange**	**Big Apple**	**Little Banana**	**Big Orange**
L. Apple						
L. Banana						
L. Orange						
B. Apple						
B. Banana						
B. Orange						

If the participant hesitates say:
"Which one is the XXX? I want you to point to the XXX for me."

Response:
"Not quite, that is the XXX. This is the XXX." (Show the participant the correct card).
OR
"Well done, that is the XXX."

(If the participant makes one error during this control stage, repeat the stage. If the participant still makes errors they will not progress to the next stage).

Practice

[Speaking with excitement], "Here's a different sort of picture. This time the little apple is inside the big orange!"

"Can you point to the *little* APPLE?!"		"Well done, that is the little apple, it is inside the big orange!" OR "Not quite, that's the big orange. This is the little apple it's inside the big orange (show participant the correct picture). Lets try another picture."
Can you point to the *big* ORANGE?!		Well done, that is the big orange! Not quite, that's the little apple. The big orange is (trace the orange with hand).

(If the participant makes one error during this practice stage, repeat the stage. If the participant still makes errors don't progress to the next stage).

Experiment

"Ok, you're doing great! Now I'm going to show you some pictures just like this one and I want you to point to the fruits when I say their names, just like you did before!

	Big Banana	Little Apple	Little Orange	Big Apple	Little Banana	Big Orange
L. Apple						
L. Banana						
L. Orange						
B. Apple						
B. Banana						
B. Orange						
SCORE						

END

<u>Bear/Dragon</u>

Let's play a game. I'm going to do some actions, see whether you can copy what I am doing:

Touch your nose	Touch your chin	Wave your hand
Touch your knee	Touch your tummy	Touch your mouth
Clap your hands	Touch your ears	Touch your feet

Well done. Now I'm going to introduce you to some animals who like doing those actions too.

This is Nice Bear, and **when Nice Bear tells us to do something, we will listen to him. If he tells us to do something, we do it.**

And this is Naughty Dragon, and **when Naughty Dragon tells us to do something, we don't listen to him. If he tells us to do something, we don't do it.**

[Slowly say] So-o-o-o, just do what the bear says, not the dragon [shake head], just the bear [nod], ok?

Practice:

Bear says……………. Touch your chin	Score:

-Well done- Remember, when Nice Bear tells us to do it, we do what he says.

Dragon says…………. Touch your tummy	Score:

-Well done- Remember, when Naughty Dragon tells us to do something, we don't do what he says.

(If the participant makes an error during this practice stage, repeat the instructions that are in bold text above and practice again.

If the participant still makes an error on the practice ask them, "Who don't we listen too". RECORD ANSWER ___________). If the participant answers incorrectly say, "no we listen to the bear, not the dragon". Proceed to the Experiment:

<u>Experiment</u>

Lets have a few more goes. Remember do what nice bear says.

Test:

Bear says Touch your nose	**Dragon says** Touch your tummy	**Bear says** Touch your ears	**Bear says** Clap your hands
0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move

Dragon says Touch your mouth	**Dragon says** Touch your knee	**Bear says** Wave your hand	**Dragon says** Touch your feet
0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move

Well done. Remember, when Nice Bear talks to use, we do what he tells us to do. But when Naughty Dragon tells us to do something, we won't do what he tells us to do. Let's do some more.

Bear says Touch your tummy	**Dragon says** Touch your ears	**Bear says** Touch your ears	**Dragon says** Wave your hand
0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move

Dragon says Clap your hands	**Bear says** Touch your knee	**Bear says** Touch your mouth	**Dragon says** Touch your nose
0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move	0 – no move 1 - move

Ask the participant, "Who don't we listen too". RECORD ANSWER ___________).

<u>END</u>

<u>Black-White Stroop</u>

Let's play another game!

Control:
Look, here's a black card and here's a white card.

Can you point to the white card for me?	Score:

Yes, that's great, that is the white card.
OR
No, that's the black card, this one is the white card (point to white card)"

Can you point to the black card for me?	Score:

Yes, that's great, that is the black card.
OR
No, that's the white card this one is the black card (point to black card)

(If the participant fails the control condition the control condition will be repeated once more. If the participant still fails the control condition they will not progress to the next stage).

Practice:
Well done! Now we are going to play a very special game. In the special game when I say BLACK, I want you to point to this card, like this (point to the white card). And when I say WHITE I want you to point to this card, like this (point to the black card). Do you think you can do that?

Lets try. What do you do when I say black?

Correct Answer:	**Participant Points to:**	**Response:**
White		(Well done), remember, when I say black, you don't point to this card (point to the black card and shake head) you point to this card (point to the white card and nod head).

And, what do you do when I say white?

Correct Answer:	Participant Points to:	Response:
Black		(Well done), remember, when I say white, you don't point to this card (point to the white card and shake head) you point to this card (point to the black card and nod head).

(If the participant makes one error during this practice stage, repeat the stage. If the participant still makes errors don't progress to the next stage).

"Ok, lets do some more! Ready?"

E Calls	B	W	B	W	W	B	B	W	B	W	W	B	W	B	B	W
Pp Response																
SCORE																

Instructions repeated

Rule check

<u>Repeat instructions (after 8 trials)</u>
(Well done), remember, when I say black, you don't point to this card (point to the white card and nod head). And (Well done) remember, when I say white, you point to this card (point to the black card and nod head).

Let's do some more

Rule Check
"Well done! You tried really hard! Now can you tell me, when do you point to this card?

Participant's response

<u>Gift Delay</u>
[Sit facing child with bag between you]
I have a present for you in this bag, but I want to wrap it up for you so it will be a surprise. Can you to help me. Can you sit in this chair and try not to look so that I can wrap up your surprise for you? Let's try it. Sit here and I'll wrap up your present for you. Try not to look!

[Take gift and walk behind the child to wrap it noisily for 60 seconds – try and hide the gift with your body]
[If participant looks, say, "remember not to peek!" - use a maximum of one reminders for peeking].
[Bring bag back to table but out of reach of child]

Ok I'm finished. Oh no, I've forgotten to put a bow on the gift, where is the bow?! I need to find the bow before I can give this to you. So stay in your seat [brief pause] Don't touch the gift until I come back!

– Move a to the corner of the room and search for the bow for 1 minute with back to the participant

Notes
Game finishes as soon as child takes present
If child opened present before end of game, say "that's ok"

Secret Gift Task

How old are you [participant's name]? Your mum told me that you are [X] years old? Is that right?

Do you like birthday parties [participant's name]? Do you like getting lots of presents? I love birthdays, it is so nice getting lots of presents isn't it….but then it is lovely to get presents any time of year. That reminds me, I have brought two presents today, they are in my car, one for you and one for your mum to say thank you for letting us come to visit you today. You and your mum can have the presents later! Oh…but don't tell your mum about the presents, I want it to be a big surprise! Lets keep it a secret!

The caregiver will enter the room and start talking to the participant. The experimenter will excuse herself announcing that she is going to the car to fetch something. After 30 seconds the caregiver will prompt the child by asking, "What did you and [experimenter's name] talk about, was it exciting?" "I wonder what [experimenter's name] has gone to get – do you know what it might be?

The experimenter will return after 2 minutes and resolve the situation. "Lets tell your mum about the big surprise, it's ok to tell her!"

Scrambled Boxes

General protocol

"Now let's play another game. Here are 3 boxes; each one has a different shape on top of it. Watch me"

[Open each box, one at a time, and put a foam star inside, then close the box]

Say, "I am putting a star in each box and I want you to find every star for me."

[Hide the boxes behind the cardboard screen, and mix up the positions of the boxes]

Say, "I'm going to hide the boxes for a little while [5 seconds]. I'm going to move the boxes around. Ok, let's have a go, choose a box."

If the participant chooses a box say, "Wow, that's exciting; you found a star, now put it in your treasure box." If the participant doesn't choose a box gently encourage them. If they still don't choose a box, choose one for them and get them to open it in order to start them off."

Repeat the mixing procedure.

"I'm going to hide the boxes again. I'm moving the boxes around. Now try to find another star. Remember to look in a new box"

If the participant searches in the same box twice say,

"Oh no, there is no star in this box, lets try again."

There are three versions of this task all which have a similar procedure. In the six box scrambled and nine box scrambled versions of the task the delay whilst scrambling is 10 seconds as opposed to five.

Record which box the individual chooses below.

Three Box Scrambled

Attempt	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
Box No.																		

Stage 2 = Repeat stage 1 with 6 boxes (delay is now 10 seconds)

Six Box Scrambled

Attempt	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
Box No.																		

Nine Box Scrambled

Attempt	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
Box No.																		

[If child perseverates on one box three times] Remember to look in a new box

[If child perseverates consecutively on one box four times, finish game]

Animal Span

"I am going to say the name of an animal. Listen carefully and when I have finished I want say exactly what I have said. For example, if I say bear, what would you say? Pause for the participant to respond.

If the participant responds correctly move onto the next example. If the participant responds incorrectly say, **"No you would say bear. I said bear so you would say it exactly the same, bear. Let's have a go at some more."**

"This time I will say two animals and when I have finished I want you to say them in the same order as me. If I say bear, cat, what would you say?".

If the participant responds correctly move onto item 1. If the participant responds incorrectly say, **"No you would say bear-cat, I said bear-cat so you would say them in exactly the same order as me, bear-cat. Let's have a go at some more".** Whether the participant succeeds or fails with the example, proceed to item 1. Ensure the participant understands the example given before moving on.

Read the animals at the rate of one per second, dropping voice inflection slightly on the last animal 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'.

Discontinuation rule: Discontinue after failure of all three trials on any item.

<u>**Practice 2**</u>
Duck, Cat

If the participant hesitates I will say, "what do you say now?". If the participant continues to hesitate I will say, "I said Duck, Cat – what do you say?"

<u>**Test**</u>
"That's great, well done. Lets do some more like this"

"Great, now I am going to add another animal each time. Remember to say what I say!"

ANIMAL SPAN

ITEM	RESPONSE	CORRECT / INCORRECT
1. **Cat Horse**		
Bear Sheep		
Mouse Bird		
2. **Dog Bird Horse**		
Cow Sheep Cat		
Bear Duck Mouse		
3. **Duck Cat Bird Sheep**		
Dog Cow Bear Mouse		
Cat Horse Sheep Bird		
4. **Cat Sheep Bear Mouse Bird**		
Horse Duck Dog Cow Mouse		
Cat Bear Dog Sheep Cow		
5. **Sheep Cow Duck Horse Mouse Bird**		
Dog Bear Mouse Bird Duck Cow		
Cat Duck Mouse Bird Cow Horse		
6. **Duck Bear Bird Mouse Sheep Horse Bear**		
Mouse Dog Bird Cow Duck Sheep Cat		
Bear Cat Mouse Duck Dog Horse Bird		
TOTAL		

Corsi Span Forward

Administration:
Place the board on the table with the cube numbers facing the examiner and with the board centred at the participant'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 block I touch. Let's practice. If I touch this block (cube 3)**, what would you do?"**

If the participant gets it correct, move onto the 2nd example. If the participant responds incorrectly say, **"No, I touched this one** (cube 3)**, so you would do the same** (examiner touches cube 3). **Let's do some more. This time I will touch 2 blocks. I want you to touch the blocks I touch, in the same order ".**

If I touch this block (cube 1) **then this block** (cube 9)**, what would you do?"**

If the participant gets it correct, move onto item 1. If the participant 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 do some more".** Whether the participant succeeds or fails with the example, proceed to item 1. Ensure the participant understands the example given before moving on.

Tap the blocks at the rate of one per second. After each sequence, pause to allow the participant to respond. Only fill in the columns labelled 'PARTICIPANT'S RESPONSE' and 'CORRECT/ INCORRECT'.

Discontinuation rule: Discontinue after failure of all three trials on any item.

CORSI FORWARD

ITEM	RESPONSE	CORRECT / INCORRECT
1. **2 9**		
4 6		
8 5		
2. **3 8 6**		
10 1 2		
9 5 7		
3. **3 4 1 7**		
6 1 5 8		
2 9 10 3		
4. **8 4 2 3 9**		
5 2 1 8 10		
4 8 3 5 7		
5. **3 8 10 1 7 4**		
7 9 6 4 8 10		
2 6 4 1 3 9		
6. **5 1 7 4 2 3 8**		
9 8 5 2 1 6 3		
7 1 3 9 4 2 6		
TOTAL		

Shifting Tasks

A not B Task

Equipment
- ❖ 2 identical cups

Procedure
- ❖ While the participant watches, the experimenter hides the object under the left cup
- ❖ "Can you find it; can you get it for me?"

Slide	L	L	L	L	L	L	L	L	L	L
Response										

- ❖ After four correct retrievals the hiding place is reversed

Slide	R	R	R	R	R	R	R	R	R	R
Response										

<u>Spatial Reversal Task</u>

Equipment

- 2 identical cups and a card board screen

Procedure

Interest participant in the toy **(use duck, sand fish, car, ball, ladybird, frog)**
While the participant watches the experimenter hides the cups behind a screen and pretends to hide an object under one of the cups, however, on the first trial to make sure that the participant doesn't fail to retrieve an item, an object is hidden under both cups.

"Name – watch me!"
"Can you find it, can you get it for me?"

When the participant retrieves the toy say

"Well done! Now there is a rule to where the object will be hidden. See if you can work out what the rule is".

Repeat the procedure and hide the item under the original cup only until the participant has retrieved it on four consecutive trials. The side of hiding is then reversed.

After each trial either congratulate or commiserate the participant and remember to say,

"Now there is a rule to where the object will be hidden. See if you can work out what the rule is".

Slide	L	L	L	L	L	L	L	L
Response								
L	L	L	L					

- After four correct retrievals the hiding place is reversed

Slide	R	R	R	R	R	R	R	R
Response								
R	R	R	R					

Dimensional Change Card Sort (DCCS) Tasks

Administration:
N.b. Put the trays on a table in front of the participants (tray with the blue rabbit card on the left and the tray with the red boat card on the right).

Dimensional Change Card Sort – Separated Dimensions

Administration:
N.b. Put the trays on a table in front of the participants (tray with the blue rabbit card on the left and the tray with the red boat card on the right).

<u>Pre-switch trials: colour game</u>
"This is a rabbit and this is a boat." Then the experimenter queried the child, "Can you point to the rabbit? To the boat?" Provide enthusiastic, supportive feedback.

"This is red and this is blue"
"Can you point to red? To blue?

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)".

Use 1 blue boat card and 1 red rabbit card for the example. 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 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 pre-switch test trials. Provide feedback if the participant gets the example incorrect.

Pre-switch test trials: present the cards in the same order as that specified on the pre-switch trial score sheet. **"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?"**

Pre-switch trials: colour		
Order in which cards presented	**Correct response**	**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?"**
Present the cards in the same order as on the score sheet for the post-switch trials on the score sheet. For each trial say, **"Here's a boat/rabbit. Where does it go?"**

Post-switch trials: shape		
Order in which cards presented	**Correct response**	**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	

Dimensional Change Card Sort – Standard Version

Pre-switch trials: colour game
"This is a rabbit and this is a boat." Then the experimenter queried the child, "Can you point to the rabbit? To the boat?" Provide enthusiastic, supportive feedback.

"This is red and this is blue"
"Can you point to the red one? To the blue one?

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)".

Use 1 blue boat card and 1 red rabbit card for the example. 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 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 pre-switch test trials. Provide feedback if the participant gets the example incorrect.

Pre-switch test trials: present the cards in the same order as that specified on the pre-switch trial score sheet. **"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?"**

Pre-switch trials: colour		
Order in which cards presented	**Correct response**	**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?"**

Present the cards in the same order as on the score sheet for the post-switch trials on the score sheet. For each trial say, **"Here's a boat/rabbit. Where does it go?"**

Post-switch trials: shape		
Order in which cards presented	**Correct response**	**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	

<u>Boarder version</u>

N.b. Only do administer this part of the assessment if the participant gets at least 5 of 6 post-switch trials correct.

For the Boarder version use the following cards: 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."**

Present the trials in the order specified on the score sheet below. On 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 / no border, where does it go? Let's do another"**

Border version trials		
Order in which cards presented	**Correct response**	**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	

UNIVERSITY OF BIRMINGHAM

Syndrome logo

UNIVERSITY OF BIRMINGHAM RESEARCH INTO CHARACTERISTICS OF INDIVIDUALS WITH RUBINSTEIN TAYBI SYNDROME

THE KEYSTONE PROJECT

This booklet should contain:

1. Letter of invitation
2. Professor Chris Oliver's contact details (See letter of invitation)
3. Information sheet
4. Background Questionnaire

Instructions for Completing Booklet:

1. Please read the booklet before deciding whether you want to take part in the study.

2. If you would like to take part in the study, please fill in the background questionnaire and return it to us in the *freepost* envelope provided.

Thank you for taking the time to read the information booklet.

Letter of Invitation

School of Psychology
Edgbaston
Birmingham
B15 2TT

Project Director: Professor Chris Oliver
Tel: [redacted]
E-mail: [redacted]

Dear [name of caregiver],

Re: Thought and Interaction Study

You may remember that you have previously taken part in research with the University of Birmingham. Thank you for your participation in that research. We are now writing to inform you of a new research project that is being carried out by the research team at the University of Birmingham that you and [name of participant] are being invited to take part in. Before you decide whether to participate, you may want to know why the research is being carried out and what it will involve. Enclosed is an information sheet which describes the aim of the project and what will happen during the study.

Please take the time to read the information sheet before agreeing to take part in the study. If you are unclear about any aspect of the study or have any questions, feel free to contact Professor Chris Oliver at the above address or by phone on [redacted] ***or by e-mail on*** [redacted]

In brief, the research project is an experimental study that aims to investigate how people with Rubinstein Taybi think about and interact with their environment. We feel that [name of person] would be appropriate for the study and we are writing to ask you whether you would like [name of participant] to participate in the study. If you feel that it is appropriate, you may wish to discuss the nature of the research with [name of participant]. You will receive a personalised feedback report for your interest which will contain information about [name of participant] and the results of the study.

If you would like [name of participant] to participate in the study then please complete the enclosed background questionnaire and return it to us in the freepost envelope provided.

Thank you for your time. We look forward to hearing from you soon.

Yours sincerely,

Jane Waite	Laurie Powis	Chris Oliver	Dr. Sarah Beck	Dr. Ian Apperly
PhD student	PhD Student	Prof. of Clinical Psychology	Lecturer & Reader	Lecturer & Reader

INFORMATION SHEET

Background:
A team at the University of Birmingham is carrying out an experimental study to look at how people with Rubinstein Taybi syndrome think about and interact with their environment. The study aims to improve our understanding of these processes and how they may differ between individuals. The study will aim to examine individuals' short term memory, the way in which they generate novel ideas, plan, initiate and inhibit actions and shift from one idea to another. The study will also assess the way in which people with Rubinstein Taybi syndrome understand other people's thoughts and beliefs

What does it involve?

The following section has been included to give you an idea of the types of tasks we may ask the person you care for to complete. However, whether or not the person you care for will be asked to complete these two tasks will depend on their level of ability. If you feel that the person you care for would find these tasks too easy or too difficult do not worry. We have tests to suit <u>all abilities</u> and we also have tests that are suitable for <u>adults</u>.

The person will be assessed at the University or at home. Testing will take place over two days. The person will then be asked to complete several tasks that are used to examine people's general ability, short-term memory, the way in which people with RTS generate novel ideas, plan, initiate and inhibit an action, maintain attention on a task and shift from one idea to another. For example, in the bear/dragon task the person will be introduced to a 'nice' bear puppet and a 'naughty' dragon puppet and told that they should do what the 'nice' bear says but not what the 'naughty' dragon says (e.g. touch your nose). The purpose of this game is to test the person's ability to suppress an unwanted response (to avoid responding on dragon trials).

The person will also be asked to complete several tasks that are used to examine people's ability to understand other people's thoughts and beliefs. For example, in the Tubes with Handles task the person with RTS and the researcher must work together to retrieve a toy that is inside a tube. The tube has a handle on each end and can only be opened by two persons simultaneously pulling at each end. The length of the tube will make it impossible for person with RTS to grasp both handles at the same time, therefore, in order to succeed on the task the person with RTS must understand the intentions of the researcher and incorporate them into their own intention.

Withdrawal:
Should you or your child / the person you care for decide that you no longer wish to be involved in the study, the information that you have provided can be withdrawn at any time without you giving a reason. Even after your child / the person you care for has taken part in the study, consent can be withdrawn and any data collected will be destroyed. This will not restrict access to other services and will not affect the right to treatment.

Confidentiality:
All details collected during this study will be kept on a confidential database that is only accessible to those working on the project. Anonymity is ensured by storing the questionnaire data separately from any material that identifies the participant. If published, information will be presented without reference to any identifying information.

At the end of the study:
Each parent/ carer will receive a personalised feedback report on their child or the person they care for. A summary of the project's findings will be circulated to anyone involved who wishes to see a copy and a report will be written for the RTS newsletter. Any requests for advice concerning your child/ the person you care for will be referred to Professor Chris Oliver, Clinical Psychologist. It is possible that you may be invited to participate in further research after the study however, consenting to participate in this study does not mean that you are obliged to do so.

Review:

This study has been reviewed by the University of Birmingham, School of Psychology Research Ethics Committee. If you have any concerns about the conduct of this study please contact Prof. Chris Oliver at the Centre for Neurodevelopmental Disorders, School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT.

Thank you very much for taking the time to read this information

If you would like the person you care for to take part in the project then please complete the background questionnaire and return it in the envelope provided.

BACKGROUND DETAILS

1. **Today's date: ________________________**

2. **Parent / carer's name: __________________________**

3. **Name of person you care for: __________________________________**

5. **Age of person you care for: __________________________**

6. **I would be interested in taking part in the current study** Yes ☐ No ☐

7. **The best times for me to be contacted about the current study are (dates / time etc.)**

____

LEVEL OF ABILITY

Please complete the following items to assist us in choosing the most appropriate tests for the person you care for.

The person you care for:

1. **Points to at least three major body parts when asked (for example, nose, mouth, hands, etc.).**
   Usually ☐ Sometimes or partially ☐ Never ☐

2. **Points to common objects in a book or magazine as they are named (for example, dog, car, cup, key etc.)**
   Usually ☐ Sometimes or partially ☐ Never ☐

3. **Follows instructions with one action and one object (for example, "bring me the book"; "Close the door"; "Touch your head"; etc.**
   Usually ☐ Sometimes or partially ☐ Never ☐

4. **Takes turns when asked when playing simple games**
   Usually ☐ Sometimes or partially ☐ Never ☐

Has the person you care for had a formal IQ test? If yes, what was the score?

IQ Test Score ______

Thank you for completing these items.

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UNIVERSITY OF BIRMINGHAM

UNIVERSITY OF BIRMINGHAM RESEARCH INTO CHARACTERISTICS OF INDIVIDUALS WITH RUBINSTEIN TAYBI SYNDROME

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Thank you for taking the time to read the information booklet.

School of Psychology
Edgbaston
Birmingham
B15 2TT

Project Director: Professor Chris Oliver
Tel: [redacted]
E-mail: [redacted]

Re: Thought and Interaction Study

Dear Parent or carer,

We are just writing to inform you of a new research project that is being carried out by the research team at the University of Birmingham that you and your child or the person you care for are being invited to take part in. Before you decide whether to participate, you may want to know why the research is being carried out and what it will involve. Enclosed is an information sheet which describes the aim of the project and what will happen during the study.

Please take the time to read the information sheet before agreeing to take part in the study. If you are unclear about any aspect of the study or have any questions, feel free to contact Professor Chris Oliver at the above address or by phone on [redacted] ***or by e-mail on*** [redacted]

In brief, the research project is an experimental study that aims to investigate how people with Rubinstein Taybi syndrome think about and interact with their environment. We feel that the person you care for would be appropriate for the study and we are writing to ask you whether you would like the person you care for to participate in the study. If you feel that it is appropriate, you may wish to discuss the nature of the research with the person you care for. You will receive a personalised feedback report for your interest which will contain information about the person you care for and the results of the study.

If you would like your child or the person you care for to participate in the study then please complete the enclosed background questionnaire and return them to us in the freepost envelope provided.

Thank you for your time. We look forward to hearing from you soon.

Yours sincerely,

Jane Waite	Laurie Powis	Chris Oliver	Dr. Sarah Beck	Dr. Ian Apperly
PhD student	PhD Student	Prof. of Clinical Psychology	Lecturer & Reader	Lecturer & Reader

INFORMATION SHEET

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A team at the University of Birmingham is carrying out an experimental study to look at how people with Rubinstein Taybi syndrome think about and interact with their environment. The study aims to improve our understanding of these processes and how they may differ between individuals. The study will aim to examine individuals' short term memory, the way in which they generate novel ideas, plan, initiate and inhibit actions and shift from one idea to another. The study will also assess the way in which people with Rubinstein Taybi syndrome understand other people's thoughts and beliefs

What does it involve?

The following section has been included to give you an idea of the types of tasks we may ask the person you care for to complete. However, whether or not the person you care for will be asked to complete these two tasks will depend on their level of ability. If you feel that the person you care for would find these tasks too easy or too difficult do not worry. We have tests to suit <u>all abilities</u> and we also have tests that are suitable for <u>adults</u> (i.e. no childish content).

The person will be assessed at the University or at home. Testing will take place over two days. The person will then be asked to complete several tasks that are used to examine people's general ability, short-term memory, the way in which people with RTS generate novel ideas, plan, initiate and inhibit an action, maintain attention on a task and shift from one idea to another. For example, in the bear/dragon task the person will be introduced to a 'nice' bear puppet and a 'naughty' dragon puppet and told that they should do what the 'nice' bear says but not what the 'naughty' dragon says (e.g. touch your nose). The purpose of this game is to test the person's ability to suppress an unwanted response (to avoid responding on dragon trials).

The person will also be asked to complete several tasks that are used to examine people's ability to understand other people's thoughts and beliefs. For example, in the Tubes with Handles task the person with RTS and the researcher must work together to retrieve a toy that is inside a tube. The tube has a handle on each end and can only be opened by two persons simultaneously pulling at each end. The length of the tube will make it impossible for person with RTS to grasp both handles at the same time, therefore, in order to succeed on the task the person with RTS must understand the intentions of the researcher and incorporate them into their own intention.

Withdrawal:
Should you or your child / the person you care for decide that you no longer wish to be involved in the study, the information that you have provided can be withdrawn at any time without you giving a reason. Even after your child / the person you care for has taken part in the study, consent can be withdrawn and any data collected will be destroyed. This will not restrict access to other services and will not affect the right to treatment.

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Thank you very much for taking the time to read this information

If you would like the person you care for to take part in the project then please complete the background questionnaire and return it in the envelope provided.

BACKGROUND DETAILS

1. Today's date: ________________________

2. Parent / carer's name: __________________________

3. Name of person you care for: __________________________________

5. Age of person you care for: __________________________

6. I would be interested in taking part in the current study Yes ☐ No ☐

7. The best times for me to be contacted about the current study are (dates / time etc.)

____

LEVEL OF ABILITY

Please complete the following items to assist us in choosing the most appropriate tests for the person you care for.

The person you care for:

1. Points to at least three major body parts when asked (for example, nose, mouth, hands, etc.).
Usually ☐ Sometimes or partially ☐ Never ☐

2. Points to common objects in a book or magazine as they are named (for example, dog, car, cup, key etc.)
Usually ☐ Sometimes or partially ☐ Never ☐

3. Follows instructions with one action and one object (for example, "bring me the book"; "Close the door"; "Touch your head"; etc.
Usually ☐ Sometimes or partially ☐ Never ☐

4. Takes turns when asked when playing simple games
Usually ☐ Sometimes or partially ☐ Never ☐

Has the person you care for had a formal IQ test? If yes, what was the score?

IQ Test Score ______

Thank you for completing these items.

Table I.
A comparison between the five RTS participants who received the working memory tasks and the remaining participants who received the inhibition tasks first.

Task	Mann-Whitney U	*p*
Animal Span	39.50	.568
Corsi blocks	45.00	.733
Six Scrambled Boxes	34.50	.281
Shape Stroop	32.50	.213
Reverse Categorisation	44.00	.664
Bear-Dragon	37.50	.368
Black-White Stroop	46.00	.914

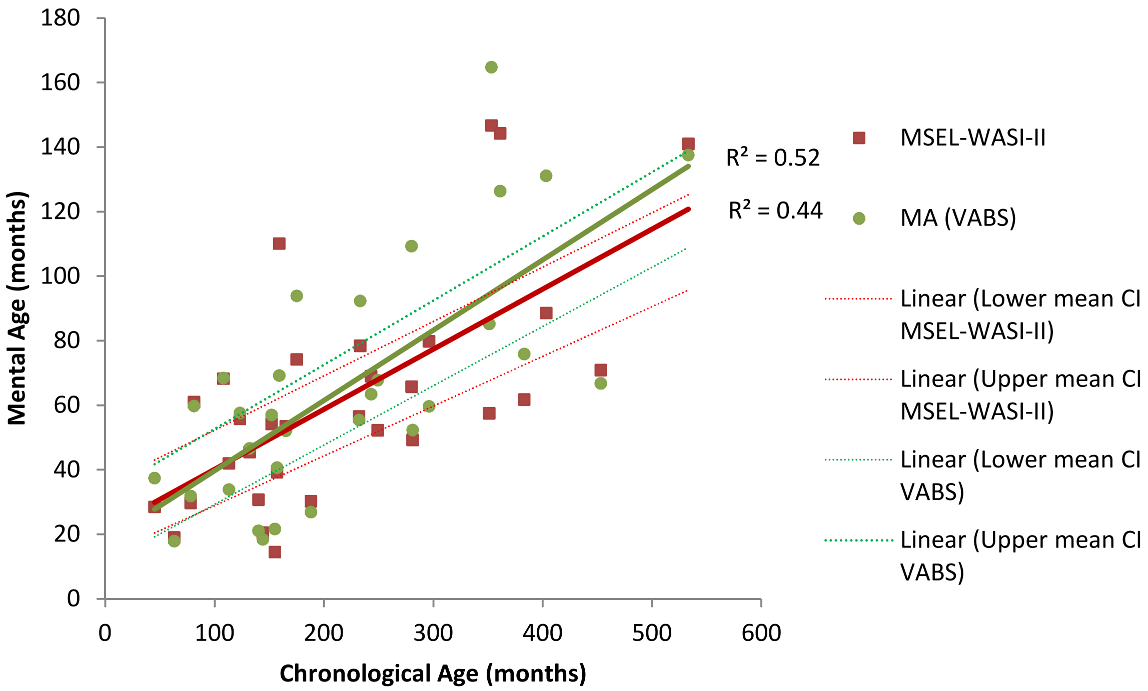
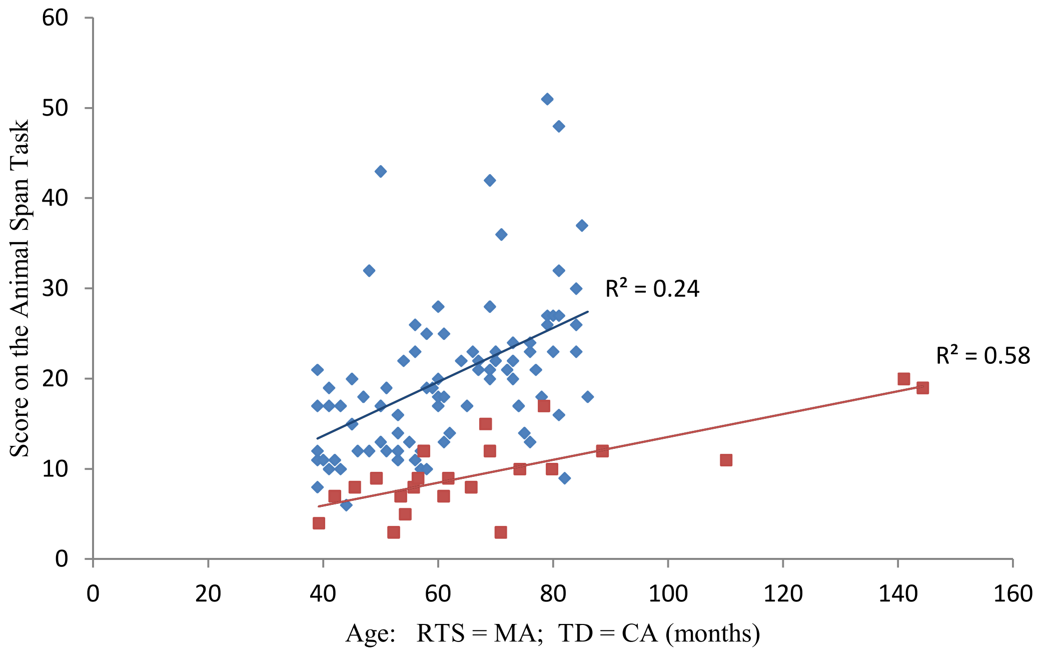


Figure J.
Mental age as a function of chronological age in RTS without the application of the Sq Root transformation.



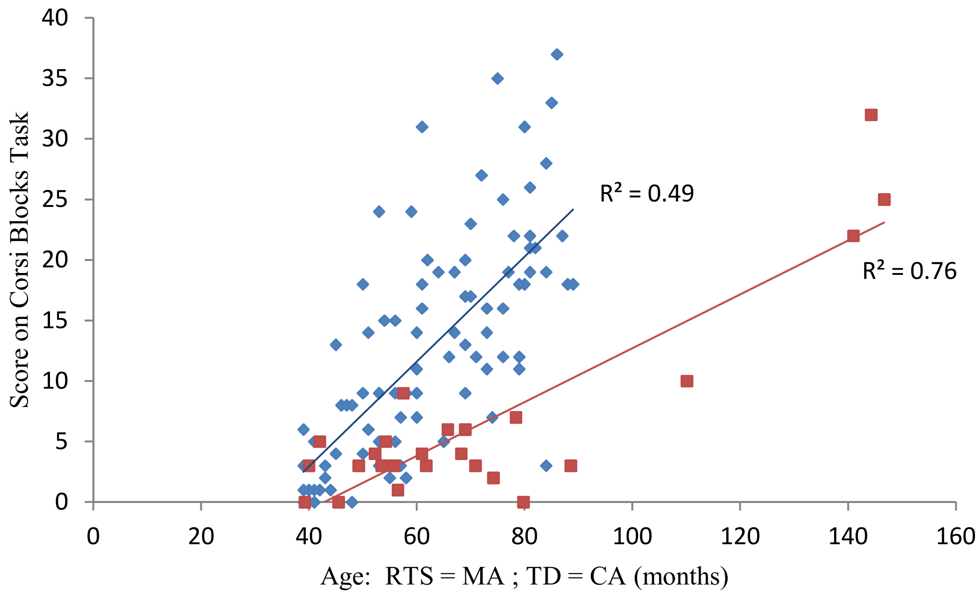


Figure K. The developmental trajectories for the Verbal Animal Span and Corsi Blocks task with more able participants included (participants with MA > 90).

Developmental trajectory: Chronological and Mental Age Comparison for the Separated Dimension DCCS

Chronological age was significantly related to performance on the separated dimensions version of the DCCS. This was one of the few tasks that was significantly related to chronological age. This relationship and performance relative to the TD group is displayed in figure L.

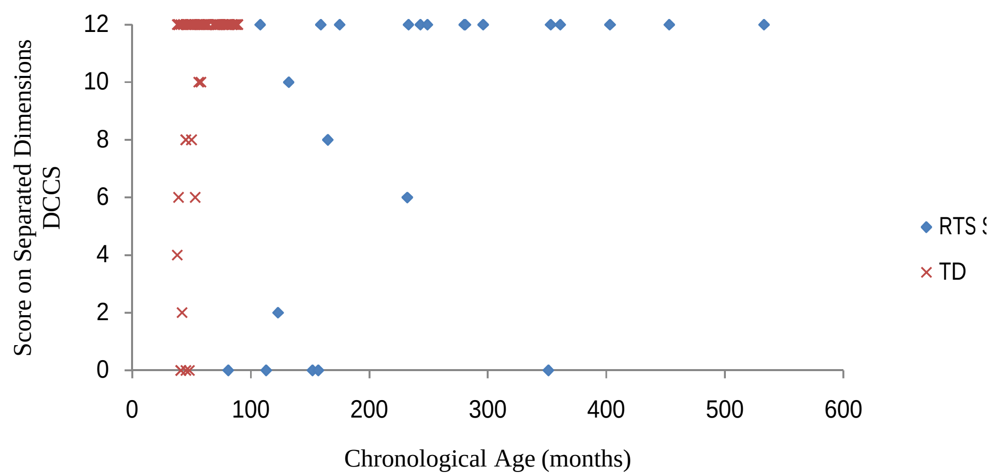


Figure L. The data distribution for performance on the separated dimensions version of the DCCS relative to chronological age.

Figure L clearly depicts how typically developing children improve on this task at between 40 and 50 months, and that this improvement is shifted to after 100 months for individuals with RTS syndrome.

Appendix M
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