

**THE BEHAVIOURAL AND
COGNITIVE PHENOTYPE OF
SMITH-MAGENIS SYNDROME**

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ABSTRACT

Background: Attention-seeking and impulsivity are reported to be problematic in Smith-Magenis syndrome (SMS) and have been linked to other challenging behaviours including self-injury and aggression. However, limited research has directly examined these aspects of the SMS behavioural phenotype.

Method: A survey study refined descriptions of atypical social behaviour. Two further studies directly observed social behaviour, in both naturalistic settings and structured social situations manipulating familiarity of interacting adults and level of attention. A final study evaluated whether response inhibition, measured using cognitive assessments, underpins impulsive behaviour in SMS.

Results: Caregivers reported elevated ‘attachment’ to particular people, but not generally elevated sociability. Natural observations revealed preferences for adult attention and manipulations of social variables indicated preference for familiar adults. Impulsivity was not associated with inhibition deficits, however emotional control was.

Conclusions: Reports of atypical social behaviour were supported, characterised by seeking attention from familiar adults. Associations between impulsivity and emotional control implicate specific deficits in delay of gratification (whereby delay causes aversive emotional responses). Considering these findings in an integrated model of the SMS behavioural phenotype, including pathways from genetic difference to behaviour and environmental influences, may facilitate targeted interventions for challenging behaviours.

DEDICATION

For Dad, Mum and Matt.

In turn, you started me off on this path, kept me going and had unfailing confidence that I would reach the end.

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
ADHD	Attention Deficit Hyperactivity Disorder
APA	American Psychological Association
AS	Angelman Syndrome
ASD	Autism Spectrum Disorder
ASQ	Autism Screening Questionnaire
BRIEF	Behavior Rating Inventory of Executive Function
BRIEF – P	Behavior Rating Inventory of Executive Function: Preschool
CARS	Childhood Autism Rating Scales
CSRS	Child Sociability Rating Scale
DS	Down syndrome
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders
fMRI	Functional Magnetic Resonance Imaging
FXS	Fragile X syndrome
ICD	International Classification of Diseases
ID	Intellectual Disability
PFC	Pre frontal cortex
PRISMS	Parents and Researchers Interested in Smith-Magenis Syndrome
PWS	Prader Willi syndrome
RAI1	Retinoic Acid-Induced 1
RBQ	Repetitive Behaviour Questionnaire
SCQ	Social Communication Questionnaire
SD	Standard Deviation
SMS	Smith-Magenis syndrome
SQID	Sociability Questionnaire for people with Intellectual Disabilities
SRS	Social Responsiveness Scale
TAQ	The Activity Questionnaire
VABS	Vineland Adaptive Behavior Scales
VS	Ventral Striatum
WASI	Wechsler Abbreviated Scale of Intelligence
WHO	World Health Organization
WORD	Wechsler Reading Dimensions
WS	Williams syndrome

CHAPTER 1

Behavioural phenotypes of genetic syndromes associated with Intellectual Disability

1.1 Prevalence and causes of intellectual disability

Intellectual Disability (ID) is defined within the World Health Organisation's International Statistical Classification of Diseases and Related Health Problems (ICD 10, 1992) as an IQ of less than 70 with concurrent impairments in adaptive functioning and onset before 18 years. A recent meta-analysis examining rates of ID found a prevalence rate of 10.37 per 1000 people in the population (Maulik, Mascarenhas, Mather, Dua & Saxena, 2011). It is evident therefore that ID affects a large number of individuals, and also those who care for them. Having an ID is associated with disadvantage across a range of indices of quality of life (Hensel, Rose, Stenfert Kroese & Banks-Smith, 2002), increased probability of showing challenging behaviour (Emerson *et al.*, 2001) and a high economic cost of care services (Knapp, Comas-Herrera, Astin, Beecham & Pendaries, 2005). ID can have a number of causes including postnatal causes (e.g. head injury, meningitis, psycho-social deprivation), perinatal causes (e.g. asphyxia during birth) and prenatal causes (e.g. chromosomal abnormalities). Chromosomal abnormalities resulting in ID include numerical abnormalities (e.g. trisomy of chromosome 21 in Down syndrome), structural abnormalities (e.g. loss of genetic material on chromosome 17p11.2 in Smith-Magenis syndrome, SMS) and single gene disorders (e.g. FMR1 gene mutations in fragile X syndrome, FXS) (Winnepenninckx, Rooms & Kooy, 2003). Such chromosomal causes account for nearly 30% of the incidence rate of ID (Curry *et al.*, 1997), thus genetic causes represent a large number of causes of ID in individuals

worldwide. Understanding behavioural outcomes in genetic disorders associated with ID is therefore important and may enable some of the negative impacts of ID to be reduced. Increased likelihood of specific behavioural outcomes in genetic syndromes is a concept that has been explored within the framework of *behavioural phenotype* research. This chapter will provide an overview of research in this field to date.

1.2 Overview of behavioural phenotype research

1.2.1 Defining behavioural phenotypes

The term behavioural phenotype was first used in relation to human behaviour by William Nyhan in 1971 (Nyhan, 1995). In an address to the Society for Pediatric Research, Nyhan presented his observation of children with two genetic syndromes, Lesch-Nyhan and Cornelia de Lange. He described the syndromes as having “a pattern of unusual behaviour that is unique to them... In these children, there are so many anatomic abnormalities...that it is a reasonable hypothesis that their behaviour is determined by an abnormal neuroanatomy...” (p. 4). Here Nyhan makes a clear link between the biological features of a genetic syndrome and behaviour. Use of ‘determined by’ when referring to the biological basis of behaviour alludes to an issue which is debated in the behavioural phenotype literature; the extent to which behaviours shown by those with genetic syndromes can be thought to be the direct result of the underlying genetic anomaly.

At a broad level, behavioural phenotypes have been defined as behaviours associated with syndromes (e.g. Deb, 1997). However, this definition fails to identify the types of behaviours, the syndromes for which this is the case and crucially the nature of the association between the syndrome and the behavioural outcome. Other definitions are more specific but as a result inconsistencies in definitions arise. Flint and Yule (1994) assert that “a behavioral phenotype should consist of a distinct behavior that occurs in almost every case of a genetic or chromosomal disorder, and rarely (if at all) in other conditions” (p. 666). This definition is similar, in terms of being deterministic, to Nyhan’s. A more probabilistic definition is proposed by Dykens (1995), who states that a behavioural phenotype involves “the heightened probability or likelihood that people with a given syndrome will exhibit certain behavioral and developmental sequelae relative to those without the syndrome” (p. 523). This

is a more flexible definition which addresses the limitations of the conservative nature of Flint and Yule's definition, where few syndromes would meet the criteria.

Few syndromes involve behaviours that occur in every case of those with the syndrome and none without. Syndromes and behaviours fitting these criteria have been suggested, including the cat like cry of infants with Cri du Chat syndrome or excessive eating (hyperphagia) shown in Prader Willi syndrome (PWS, Hodapp & Dykens, 2005). However, while Hodapp and Dykens (2005) describe hyperphagia in PWS as being an example of a behaviour that does not occur in other syndromes, subsequent research suggests hyperphagia is also found in monosomy 1p36 (D'Angelo *et al.*, 2006). It seems likely therefore that more than one syndrome will typically be connected to any given behavioural outcome. An example of this is presented by Hodapp & Dykens, (2005), whereby a specific pattern of simultaneous over-sequential processing has been found in three different syndromes; FXS, PWS and SMS.¹ Hodapp and Dykens (2005) emphasise the rarity of one-to-one correspondence between syndrome and behaviour, or total specificity (a single pathway between genes and behaviour) as it is termed by Hodapp (1997). Instead they highlight the much more common case of partial specificity where syndromes produce partially specific effects (such that there is a specific association between a small number of syndromes and a single outcome, as suggested by Hodapp, 1997).

¹ While cited by the authors as an example of a behavioural phenotype, over sequential processing may be considered a cognitive endophenotype. Cognitive endophenotypes have been studied particularly in neuropsychiatric disorders, such as schizophrenia (e.g. Saperstein *et al.*, 2006), where cognitive endophenotypes are cognitive traits associated with behaviours found in a disorder which mediate the link between biological characteristics and behavioural outcomes. The importance of including cognitive endophenotypes, together with biological factors, in models of the development of behaviour has been stressed by Morton (2004). Whilst this point is relevant for subsequent consideration of different levels in models of potential pathways from genetic difference to behaviour difference, the point remains that the behavioural *outcome* of the cognitive endophenotype is common to three different syndromes.

A final contrasting perspective is of no specificity, such that genetic syndromes have no effect on behaviour. This approach is reflected in studies using groups of individuals with a variety of differing genetic syndromes, rather than dividing them by aetiology. This approach fails to take into account the wealth of evidence that certain behaviours are more likely to be found in those with certain genetic syndromes. As such it ignores behavioural characteristics that may have implications for the well being of those with genetic syndromes. It may also lead to misleading results as in mixed ID samples inconsistent effects of behavioural phenotypes may effectively mask each other.

The probabilistic definition of behavioural phenotypes proposed by Dykens (1995) and partial specificity of behavioural outcomes (advocated by Hodapp, 1997, as the most commonly observed relationship between genotype and behavioural phenotype) together account for within syndrome variability in patterns of behaviour evident in many disorders. Partial specificity of behaviours in genetic syndromes has important theoretical implications for the aetiology of these behaviours. If there is not a direct link between the genetic basis of a disorder and behaviour, syndromes may share aetiological pathways between genetic abnormality and behaviour. Identifying these pathways has practical importance in addition to theoretical relevance, potentially informing intervention strategies. It also enables consideration of environmental influences on behaviours in terms of why behaviours may or may not be expressed by those with a genetic syndrome. Even behaviours that may be understood within a single pathway model, implicating inevitability of a behavioural outcome in those with a given genetic syndrome, can be affected by environmental changes. Self-injurious behaviour is shown by nearly all of those with Lesch-Nyhan syndrome (Christie *et al.*, 1982), however an effect of the environment on the rate at which this behaviour is shown has been demonstrated (Hall, Oliver & Murphy, 2001). This suggests that genetic difference can interact with the environment, even in highly genetically determined behaviours (a

perspective supported by Langthorne, McGill & MacLean, 2008 and Tunnicliffe & Oliver, 2011).

A recent systematic review of what were termed *phenotype-environment* interactions supported the importance of environmental influences, such as operant reinforcement, on phenotypic (challenging) behaviours in genetic syndromes (Tunnicliffe & Oliver, 2011). The term phenotype-environment interaction acknowledges the interaction of phenotypic behaviours with environmental variables. Additionally, as many of the genetic syndromes studied in behavioural phenotype research are caused by loss of genetic material, use of such disorders to model pathways from specific genes to behavioural outcomes is potentially problematic. Where a syndrome is caused by a loss of genetic material it is the *loss* of genes that is related to behavioural outcomes rather than the presence of a specific gene leading to behaviour. In this case models can map hypothetical pathways from genetic *characteristics* to behavioural outcomes but not genes per se. Therefore, when discussing what have previously been conceptualised as pathways from genes to behaviour and interactions between genes and environment, this should be reflected.

Given the flexibility of Dykens' (1995) definition in identifying syndromes with characteristic profiles of behaviour and its utility in enabling comparisons of behaviours across syndrome groups, use of the term behavioural phenotype will refer to this definition.

1.2.2 Background to behavioural phenotype research

The behavioural outcomes associated with genetic syndromes have become the focus of a vast amount of recent research. Hodapp and Dykens (2001) report a surge of interest in behavioural phenotype research, with an estimated 14 times as many articles published on this topic in the 1990's as there were in the 1980's. As technology for detecting genetic

syndromes improves², new syndromes are being identified at a rapid rate (Shaffer *et al.*, 2007). Potocki Lupski syndrome is one such example, caused by duplication of chromosome 17p11.2 and thus described as the reciprocal of SMS where material is lost from the same region (Potocki *et al.*, 2000). Contrasting behaviours found in these two syndromes to identify possible effects of genes in this region has thus become the focus of recent research (e.g. Crespi, Summers & Dorus, 2009).

The existence of disorders characterised by physical and behavioural features with a common biological cause was known well before the genetic difference underpinning the syndrome could be identified. The clinical presentation of Down syndrome (DS) was first described by John Langdon Down in 1866 but it was not until 1959 that Lejeune, Gautier & Turpin identified the chromosome 21 trisomy which is the genetic basis of the majority of cases of DS (1959, cited in Dykens, Hodapp & Finucane, 2000). This discovery came less than 10 years after the identification of the structure of the human chromosome in 1953 by Watson and Crick (cited in Dykens *et al.*, 2000). DS was the first of many genetic disorders associated with ID to be identified, there are now over 1000 such genetic disorders described (Walz & Benson, 2002), many of which are believed to be characterised by specific behavioural features.

Beliefs regarding biologically determined behaviour and abilities have had a chequered history. Beliefs that inheritance patterns could be used to direct human evolution to enhance the human race is the basis of the Eugenics movement, which abused principles of genetic inheritance to justify enforced sterilisation of those whom they felt were ‘feeble minded’ (Trent, 1994). This coloured research into human behaviour, remaining a contentious issue

² including use of microarray-based comparative genomic hybridization (array CGH), which does not require a specific chromosomal abnormality to be suspected, unlike older techniques such as Fluorescence in situ hybridization (FISH) testing.

today in behavioural phenotype research. Suggestions that behaviours may be genetically ‘determined’, implies they are inevitable and unchangeable, disregarding any impact of the environment. Concerns have been expressed that this premise could result in therapeutic nihilism; the belief that those with genetic disorders cannot be helped (Holland, 1999). Such concerns can be countered by arguments that increased awareness of features of genetic syndromes offers benefits likely to outweigh these risks, a perspective outlined in section 1.2.3.

In summary, the study of behaviours associated with genetic syndromes has evolved rapidly over the past two decades resulting in increased awareness of characteristic cognitive, social and emotional profiles evident in a number of genetic syndromes. These profiles make up the behavioural phenotype of those syndromes.

1.2.3 Benefits of studying behavioural phenotypes

Given concerns about a potential detrimental impact of associating genetic syndromes with behavioural phenotypes, including therapeutic nihilism and stigmatism, the potential benefits of behavioural phenotype research warrants explication. These benefits include development of appropriate interventions, theoretical advances relating to both typical and atypical development and provision of information and guidance for caregivers and professionals.

Understanding which behaviours are more likely to be shown by those with certain genetic syndromes has clear benefits for intervention, particularly for syndromes likely to require intervention for specific behaviour problems known to be highly prevalent. Awareness that, for example, SMS is associated with very high levels of self-injury (Arron, Oliver, Berg, Moss & Burbidge, 2011; Dykens & Smith, 1998; Finucane, Dirrigl, & Simon., 2001; Greenberg *et al.*, 1996; Martin, Wolters & Smith, 2006) or that Williams syndrome (WS) is

associated with anxiety (Udwin, Yule & Martin, 1987; Udwin & Yule, 1991), identifies that these syndromes are likely to benefit from aggressive early intervention to prevent behaviours becoming established.

As well as identifying syndromes where early intervention is likely to be beneficial, behavioural phenotype research may provide an understanding of where intervention should be targeted. Research by Woodcock, Oliver & Humphries (2009a, b) has illustrated how difficult behaviours found in a syndrome may be linked to a specific underlying cognitive deficit. This research demonstrated how repetitive questioning and temper outbursts shown by those with PWS (Woodcock *et al.*, 2009a) may be underpinned by reduced task switching capacity which results in situations where demand is placed on these abilities (e.g. unexpected change) being aversive if task switching capacity is exceeded (Woodcock *et al.*, 2009b). This suggests that in PWS, interventions targeting task switching deficits may be more beneficial than those solely addressing the behavioural outcome of the temper outbursts. Interventions aiming to target specific cognitive deficits linked to negative behavioural outcomes (e.g. working memory training in Attention Deficit Hyperactivity Disorder, ADHD) have been shown to be effective (Klingberg, Forssberg & Westerberg, 2002; Klingberg *et al.*, 2005).

Finally, understanding both commonalities and differences in behaviour profiles across syndromes may inform intervention choices such that the most appropriate intervention, given a syndrome's cognitive and behavioural features, is selected. Hodapp and Dykens (2001) cite the example of anxiety found in both FXS and WS. They note that other phenotypic features of the syndromes suggest different interventions may be effective despite the common behaviour problem. Social anxiety associated with FXS (Cornish, Turk & Levitas, 2007; Einfeld, Tonge, & Florio, 1994) suggests group based therapies may be less effective and

potentially aversive, whereas they may be suitable in WS, where high sociability is reported (Dykens & Rosner, 1999). Understanding that even highly genetically determined behaviours (e.g. self-injury in Lesch-Nyhan syndrome) can be influenced by environmental events (Hall *et al.*, 2001) supports the potential for environmental interventions to reduce rates of challenging behaviours shown in certain syndromes.

In addition to identifying syndromes where particular behavioural problems are likely to occur, behavioural phenotype research enables exploration of patterns of more general strengths and weaknesses across domains of cognitive development. This move from the 'no specificity' approach (where cognitive and behavioural profiles of ID are considered to be the same regardless of genetic aetiology of the disability), enables recognition of uneven and contrasting profiles. This is illustrated by findings that in SMS receptive language skills are stronger than expressive language skills (Chen, Potocki & Lupski, 1996, Greenberg *et al.*, 1996, Sarimski, 2004), a profile which contrasts with WS where aspects of expressive language are believed to be a relative strength (Mervis & John, 2008). In PWS an uneven cognitive profile has also been described with strengths in visual processing but weaknesses in auditory processing, short term memory and mathematics (Whittington, Holland, Webb, Butler, Clarke & Boer, 2004). It is evident that uneven profiles of cognitive development exist within and across genetic syndromes associated with ID, suggesting these outcomes result from different aetiological pathways. Identification of strengths in cognitive profiles has further implications for intervention. In conjunction with addressing deficits, identification of areas that are strengths can suggest areas that can be capitalised on in interventions (Oliver, Woodcock & Adams, 2010).

Further to practical benefits of informing intervention, links made in behavioural phenotype research between genetic characteristics, environmental influences and behaviour can inform

theories of development. At the most basic level, loss of genetic material which is associated with a specific behaviour can be taken to imply that the missing genes are directly responsible for the behaviour. Although the link is rarely (if ever) as direct as this, paths traced by Woodcock *et al.* (2009b) and Woodcock, Humphreys, Oliver & Hansen (2010) between the genetic basis of PWS (loss of material from chromosome 15), neural atypicalities and the cognitive endophenotype (reduced task switching capacity) and problem behaviours (temper outbursts) suggests how a pathway can be mapped from genetic characteristics to behaviour. This then informs theories of both atypical and typical development, including the trajectory of development. For example patterns of strengths and weaknesses in syndromes have been found to change with time. In older individuals with DS numerosity is better than that in WS. However, in infants this pattern is reversed (Paterson, Girelli, Butterworth & Karmiloff-Smith, 2006). Such detailed study of behavioural phenotypes emphasises the critical importance of considering the role of development in understanding behavioural outcomes (see Karmiloff-Smith, 1998).

A final benefit to elucidating behavioural phenotypes associated with genetic syndromes is the value of enhanced awareness of phenotypic behaviours, both for caregivers and professionals. This extends beyond identifying appropriate interventions and includes ability to plan for the individual across the lifespan, knowing the likely course of behaviours. Parents of children with disabilities experience higher levels of stress than those of non-disabled children (Hodapp, Fidler & Smith, 1998; Olsson & Hwang, 2001) and caregivers report that lack of information about what to ‘expect’ in terms of behaviour creates difficulties (Griffith *et al.*, 2011). Awareness of likely behavioural outcomes can therefore help with planning for service provision and early identification of emerging problems.

1.3 Themes in behavioural phenotype research

A number of themes are starting to emerge from the field of behavioural phenotype research, including how genetic difference may lead to behavioural difference, how environmental factors can interact with genetic difference and how patterns of behaviour change over development. These themes will be explored below.

1.3.1 Pathways from genetic characteristics to behaviour

Illustrating how genetic difference can lead to behaviour enables understanding of how genes can influence behaviour applicable not only to the study of atypical development but also mainstream developmental psychology. Research in PWS presented in section 1.2.3 by Woodcock *et al.* (2009 a, b) and Woodcock *et al.* (2010) represents one of the most comprehensively elucidated examples of a potential pathway from genetic characteristics to behaviour. A pathway was traced from genetic difference caused by loss of material from chromosome 15 to neural atypicalities³ hypothesised to result in cognitive deficits in task switching capacity to the end point of repetitive questioning and temper outbursts in situations where excess demand is put on the task switching system. This pathway was supported by evidence from a wide range of sources. Parent reports confirmed the behavioural outcome and provided information about the environmental contexts. Cognitive assessments identified difficulties in switching from one type of task to another and functional magnetic resonance imaging (fMRI) studies suggested that those with PWS were processing the tasks differently from controls at a neural level.

Use of such diverse research methodologies in research assessing behavioural phenotypes enabled Woodcock *et al.* (2009b) to build a model, based on principles proposed by Morton

³ Reduced activation in the posterior parietal and ventromedial prefrontal cortices in PWS when performing switching tasks.

(2004), which identified specific pathways from genetic characteristics to behaviour via a number of intermediary steps. This model considered not only the genetic basis of the syndrome and behavioural outcome but also interceding cognitive, physiological and environmental factors that are able to account for variable expression of behaviours. The interplay of these factors may explain why behaviours are not always shown in response to environmental change. For example Woodcock *et al.* suggest that even when there are similar impairments in task switching, some individuals have greater cognitive resources available enabling them to cope more effectively with increased cognitive demand.

Fully elucidating pathways from genetic characteristics to behaviour can also enable examination of how syndromes with different aetiologies may have similar behavioural outcomes. Woodcock *et al.* (2009b) suggest that the pathways hypothesised in PWS can also account for behaviour in FXS, suggesting that the syndromes have a shared deficit in task switching. Thus, it is the shared cognitive impairment in task switching that accounts for negative responses to unexpected change shown in FXS. This is an example of the partial specificity model of behavioural phenotypes suggested by Hodapp (1997) (see section 1.2.1). Importantly, Woodcock *et al.* (2009b) address the role of environmental events in eliciting difficult behaviours, where events such as unexpected change result in an increased demand on task switching, creating an aversive state which evokes escape behaviours and associated operant learning. This key role of the environment has been considered in detail in research, outlined below, aiming specifically to examine how environmental factors interact with genetic factors.

1.3.2 Phenotype - environment interactions

As noted in section 1.2.1 the interaction between genetic difference, environmental influences and phenotypic behaviours can be termed phenotype-environment interactions. The work of

Woodcock *et al.* (2009a, b) identified how the environmental trigger of unexpected change can interact with a genetic difference hypothesised to result in impaired task switching, resulting in an aversive physiological state and ultimately challenging behaviour. This type of interaction has also been suggested to occur in a number of other syndromes, including Lesch-Nyhan syndrome (see section 1.2.1) and Angelman syndrome (AS). Evidence for the role of genetic disorder and environmental influences on behavioural outcomes in AS is of particular importance for theories of development due to the role of imprinted genes in this syndrome. Imprinted genes are genes whose expression is determined by the parent from whom they are inherited. AS is the result of loss of material from the maternal copy of chromosome 15 (q11-13), whereas in PWS material is lost from the same region of the paternal copy of the chromosome (Donlon, 1988). The role of the ‘parent of origin’ of a chromosome has been the focus of much research as it has been hypothesised that genomic imprinting results in differential ‘investment’ of each parent’s genome in the child (Brown & Consedine, 2004). In this theoretical framework the paternal genome will ‘seek to’ minimise paternal resource use and maximise maternal investment, whereas the maternal genome will have the opposite effect (Haig & Wharton, 2003). Brown and Consedine (2004) suggest that in AS, the imbalance caused by the deletion of maternal material results in individuals with this syndrome showing behaviours that maximise maternal investment (thus minimising paternal demand), including positive affective behaviours (laughing, smiling) thought to have evolved to increase social resource provision from the person receiving these positive emotional signals.

Evidence supporting increased rates of this ‘emotion signalling’ has been found in a number of studies which found that children with AS smile more towards adults (Oliver, Demetriades & Hall, 2002) and that they also seem to approach adults more than contrast groups do (Oliver *et al.*, 2007). Both findings support the hypothesis that there is a strong drive to elicit

social resources from caregivers. Furthermore, it has been shown that laughing and smiling shown by those with AS then affect adult behaviour, resulting in positive responses from adults (Oliver *et al.*, 2007). Thus, there is an interaction between phenotypic behaviours and the environment whereby those with the syndrome demonstrate a strong drive to access attention and are likely to find adult attention particularly rewarding and are also more likely to elicit positive adult responses. Some attention-seeking behaviours can be challenging e.g. aggressive grabbing and hair pulling (Arron *et al.*, 2011; Summers *et al.*, 1995), thus understanding this drive is also of practical, in addition to theoretical, importance. Increased drive for attention can be considered in an operant model of challenging behaviour whereby a response to a difficult behaviour (i.e. provision of attention) which is highly rewarding is also highly reinforcing, resulting in increased likelihood of this behaviour being shown in future when an individual experiences periods of low attention. It is critical therefore to identify the role of the environment because if behaviour is influenced by environmental factors, manipulation of these factors may enable effective intervention strategies.

1.3.3 Developmental trajectories

The developmental trajectory approach (Thomas *et al.*, 2009) is an exciting and relatively recent development in behavioural phenotype research. The critical importance of considering development across the lifespan when describing behavioural phenotypes is illustrated by the findings of Paterson *et al.* (2006) outlined previously. Patterns of cognitive performance, specifically numerosity, in DS and WS were shown to change dramatically with age. The authors suggest that processing style influences the developmental trajectory of numerical skills in these syndromes. Crucially they state that “one cannot infer the infant starting state from the adult end state” (p. 190). Considering how development itself can influence the behavioural outcomes associated with a genetic syndrome is central to research examining developmental trajectories.

With a basis in growth curve modelling (e.g. Chapman, Hesketh, & Kistler, 2002; Rice, 2004), the developmental trajectory approach aims to evaluate task performance of individuals with a given genetic syndrome as a function of age, and then compares this function to a typically developing contrast group to identify differences in trajectories. It also aims to examine how performance on difference tasks is related, and whether task performance can be predicted based on performance on other tasks (Thomas *et al.*, 2009). Developmental trajectories can be developed based on either cross sectional data (collected at one point in time from individuals of various ages), longitudinal data (collected from individuals of the same age across multiple time points) or a combination of the two.

Benefits of this approach include a shift away from static representation of ability, which is unlikely to be representative. The trajectories derived from this approach enable much more detailed understanding of how behaviour of those with genetic syndromes may differ from typically developing individuals. Thomas and colleagues identify seven different ways in which trajectories may differ; delayed onset, slowed rate, delayed onset and slowed rate, nonlinear trajectory, premature asymptote, zero trajectory and no systematic relationship with age (Thomas *et al.*, 2009). This then becomes a much richer source of description than a simple dichotomy of delay versus deviance. In addition to increased theoretical understanding this approach also has practical advantages when the syndrome group being investigated has a wide age/ability range and thus task performance is likely to vary significantly. The developmental trajectory approach takes into account this variability, using it in the analysis to describe patterns of behaviour and ability in the syndrome. This alludes to a potential limitation of developmental trajectories which is that if the behaviour is not demonstrated across a wide age range (e.g. shown only by a certain age group) then this approach is not appropriate and more traditional matching methods may be appropriate.

1.4 Methodological issues in behavioural phenotype research

As research into behavioural phenotypes of genetic syndromes has evolved a number of important methodological considerations, presented below, have been identified.

1.4.1 Measurement of behaviour

Hodapp and Dykens (2005) outline a number of methodological concerns regarding how behaviours believed to characterise genetic syndromes are measured. They note that early research into behavioural phenotypes advocated use of a single scale assessing behaviours that could be used for all genetic syndromes to characterise behaviour (e.g. O'Brien, 1993), an approach supported by the Society for the Study of Behavioural Phenotypes. Despite this support from a leading group of researchers, the authors identify limitations including the inability of such measures to identify novel highly idiosyncratic behaviours and also relative lack of sensitivity to patterns of strengths and weaknesses that are likely to characterise many genetic syndromes (see section 1.2.3 for examples of these patterns). A further criticism is that lack of detail fails to identify subtle differences between apparently similar behavioural outcomes, for example anxiety reported in FXS is thought to be social anxiety (Cornish *et al.*, 2007; Einfeld *et al.*, 1994; Hessler, Glaser, Dyer-Friedman & Reiss, 2006) whereas in WS specific phobias are more common (Dykens, 2003).

An extension of more general behavioural questionnaire measures is use of specific psychiatric symptom questionnaires (Hodapp & Dykens, 2005), enabling determination of whether behaviours identified as problematic can be classified using diagnostic criteria for psychiatric disorders. For instance, the obsessive compulsive like behaviours observed in PWS such as hoarding, ordering and insistence on sameness (Dykens *et al.*, 1992) have subsequently been examined in detail using the Yale-Brown Obsessive-Compulsive scale (Goodman *et al.*, 1989) and compared to a group diagnosed with Obsessive Compulsive

Disorder by Dykens, Leckman & Cassidy (1996). This provided support for the existence of compulsive behaviours in this syndrome group and evaluation of severity. While informant reports have the strength that they can elicit information that individuals with ID may not be able to self-report they are subject to potential bias and limitation in accuracy (Hodapp & Dykens, 2005). A further concern regarding use of informant report measures is appropriateness of these for populations with ID, for example items may ask about behaviours that are less likely to be shown by those with disabilities and normative data may not be available for ID populations.

Examination of patterns of strengths and weaknesses (described in section 1.2.3), based on statistical comparison of different domains of functioning, is a further method of assessing characteristic profiles of behaviour associated with genetic syndromes. An extension of this is the recent use of cluster and factor analysis that enable examination of whether the underlying relationships between behaviours are similar in those with a given genetic syndrome to those in the general population. For example the compulsive behaviours in PWS appear to show different patterns of interrelation compared to those in typically developing populations, with skin picking in PWS being a factor unrelated to other behaviours (Feurer *et al.*, 1998).

While the use of informant report measures has been advocated as a first step to understanding behaviours in genetic syndromes (Hodapp & Dykens, 2005), limitations outlined above mean that additional methods of describing behaviour may be valuable. Observations of behaviour can inform understanding of disorders during the early stages of description. Observation of highly prosocial behaviour in WS (Jones *et al.*, 2000) has informed research aiming to explore the neurological basis of this behaviour (e.g. Järvinen-Pasley *et al.*, 2008). While observational methods may be criticised for being informal, use of

methods that operationalise and quantify naturally occurring behaviours, e.g. the smiling in AS described in section 1.3.2, can enable reliable and valid evaluation of behaviour. It is evident therefore that each available method for assessing behaviour has advantages and limitations. Hodapp and Dykens (2005) conclude that use of multiple methodologies is likely to provide the most useful approach to describing behaviour in genetic syndromes.

1.4.2 Use of contrast groups

A critical aspect of the behavioural phenotype definition is the increased probability that those with the syndrome will show a behaviour in comparison to those without the syndrome (Dykens, 1995). To evaluate whether a behaviour can be considered phenotypic, a contrast group without the syndrome is therefore required. What constitutes an appropriate contrast group is the topic of much debate. Hodapp & Dykens (2001) summarise the main types of groups used as follows: typically developing individuals (matched on mental or chronological age), heterogeneous ID, DS, different syndrome but similar aetiology and finally no syndrome but similarities on behaviours of interest. Choice of these differing options determines the type of comparison that can be made.

Comparison of individuals with genetic syndromes to typically developing children enables researchers to establish strengths and weaknesses present in a syndrome. Conversely, comparison against individuals with a different source of ID (either a mixed group or those with DS) enables examination of specificity of behaviour to that syndrome versus the effects of ID per se. Fine grained comparison of groups which either have similar aetiology or similar behaviours enable identification of particular aetiology specific behaviours (Dykens *et al.*, 2000).

Contrasting behaviour to chronologically age matched groups enables researchers to identify areas where children are absolutely delayed, whereas mental age matches enable determination of whether there is specific delay relative to overall level of development. Where children do not differ from chronological age matches it has been suggested this may represent 'intact' functioning. The most commonly cited example of this is language ability in WS. However, fine grained analysis of underlying domains of language indicates impairment in a wide range of language abilities (see Karmiloff-Smith *et al.*, 1997). If a syndrome group is found to differ on a measure of behaviour from chronological age matched groups, but not from mental age matches, it suggests that their behaviour may reflect their developmental age rather than a specific aspect of their syndrome. Alternatively, individuals with a syndrome may perform better than mental age matched controls which indicates that they may have a *relative* strength in that behaviour, such is likely to be the case for language in WS (Mervis, Morris, Bertrand & Robinson, 1999) and also aspects of social functioning in DS (Serafica, 1990).

Use of typically developing contrast groups, both chronological and mental age matches, can aid conclusions regarding whether development is delayed or 'deviant'. If a syndrome group performs less well than a chronological age matched group but the same as a mental age matched group then they are considered to be developmentally delayed, showing the same pattern of development as typically developing individuals but at a slower rate. Conversely if they are impaired when compared to both contrast groups then they are considered to be developing atypically, or to be 'deviant' (Hodapp, Burack & Zigler, 1990). Matching to typically developing groups to infer delay or deviance has specific theoretical limitations, particularly that if it is determined that a genetic syndrome is associated with delay, it would be expected that they would eventually reach the same level of development as typically developing individuals, which is often not the case (Paterson *et al.*, 2006). Furthermore, while

this strategy enables evaluation of strengths and weaknesses, it does not enable evaluation of behavioural specificity for any given syndrome group.

Use of contrast groups with ID enables evaluation of whether a behaviour characterises that particular genetic syndrome or whether it is a feature of those with ID in general. While this is an important consideration, concerns exist regarding how representative individuals recruited into these groups are of the general population of individuals with ID. A further concern is that in a mixed ID group there are likely to be a number of individuals who have genetic syndromes which may have their own behavioural phenotype and inclusion of these individuals may mask differences. Hodapp and Dykens (2001) also note that non-specific ID may be associated with a familial cause and as such may involve different environmental influences e.g. lower socio-economic status.⁴

An alternative to using mixed groups is to make comparisons to one specific genetic syndrome; the most common group used for this type of comparison is DS. While DS enables the effects of ID to be accounted for, the syndrome has its own behavioural phenotype (Chapman & Hesketh, 2000) and as such differences between the syndrome of interest and a DS contrast group may be attributable to atypicality in the behaviour of those with DS. This is a significant limitation suggesting that DS should only be used as a contrast group if guided by theoretical principles. These principles are outlined by Hodapp and Dykens (2001) in terms of selecting groups that are “same but different” (p. 5), suggesting that this enables more precise characterisation of the behaviours related to specific disorders. This approach compares behaviours that are similar across groups, e.g. anxiety in FXS and WS described in

⁴ It should be noted, in the context of the various causes of ID (see section 1.1), that the suggestion that non-specific ID can have a familial cause related to polygenetic inheritance (where multiple genes, with small individual effects, combine to contribute to an outcome) is contentious. Identification of specific genes that contribute significantly to intelligence has been very limited (Butcher, Davis, Craig & Plomin, 2008) although recent developments in mapping the human genome have resulted in the discovery of a single gene (HMGA2) that has the biggest effect on IQ scores, but even this increases IQ by only 1.29 points (Stein *et al.*, 2012).

section 1.2.3. Subtle difference between syndromes may then enable greater understanding of the behaviours and their specificity to that syndrome. Where behaviours are represented in the general population, for example obsessive compulsive behaviours, groups of non-intellectually disabled people with this diagnosis may also be compared to syndromes where this is a problem behaviour (e.g. PWS, Hodapp & Dykens, 2001)

Finally, using no control group may also be an option. This can identify within syndrome profiles of strengths and weaknesses however it is not then possible to evaluate the extent to which this profile is specific to that syndrome and restricts the number of domains across which comparisons can be made (as comparisons should only be made across standardised scores from the same measure, Hodapp & Dykens, 2001). It is evident that researchers investigating behavioural phenotypes need to consider the differing nature of conclusions that can be reached and evaluate what question they are trying to answer in their research about the nature of the behaviour of interest.

1.5 Summary

An increasing amount of research examining genetic syndromes has focussed on behavioural phenotypes. While there is debate over the extent to which the link between a genetic disorder and patterns of behaviour can be considered direct and/or unique, there is consensus that those with specific genetic syndromes may show characteristic profiles of behaviour which differ from those without the syndrome. Studying behavioural phenotypes enables identification of likely behavioural outcomes, valuable for parents and professionals in terms of managing expectations and intervention for difficult behaviours. The existence of behavioural phenotypes also has implications for theories regarding the links between genetic difference and behaviour.

Theories regarding this link have been developed as part of behavioural phenotype research and include pathways from genetic difference to behaviour and potential interactions between phenotypes and the environment. Current theories also emphasise the way genetically influenced behaviours can be influenced by development. To effectively explore both the theoretical and practical applications of behavioural phenotypes, research in this field needs to take into account a number of methodological concerns including selecting appropriate measures and contrast groups to describe behavioural profiles and determine their specificity. Research examining the behavioural phenotype associated with a given syndrome should take into account these contextual factors.

CHAPTER 2

Smith-Magenis syndrome

2.1 Preface

Smith-Magenis syndrome (SMS) is a genetic neurodevelopmental disorder which has a particularly striking behavioural phenotype, including behaviours described as ‘unique’ and a range of difficult behaviours which present challenges both for those with the syndrome and their carers. These behaviours may fit within the theoretical frameworks identified in chapter one, specifically identification of pathways from genetic difference in SMS and behavioural outcomes and potential phenotype-environment interactions. Describing and understanding the SMS behavioural phenotype is therefore of both clinical and theoretical importance. This chapter will present an overview of research examining key features of SMS, focussing on the behavioural phenotype. This literature will then be synthesised to develop a hypothetical model of behaviour in SMS.

2.2 Aetiology and prevalence of Smith-Magenis syndrome

SMS is a rare genetic disorder with an estimated prevalence of around 1 in 25,000 births (Greenberg *et al.*, 1991), although prevalence estimates vary up to 1 in 15,000 cases (Smith, Magenis, & Elsea, 2005). Smith, Dykens and Greenberg (1998) also cite the 1 in 25,000 prevalence rate but indicate this is likely to be an underestimate. The disorder was first described in 1982 by Smith and colleagues and has subsequently been found to be associated with a de novo deletion on chromosome 17p11.2 (Greenberg *et al.*, 1991; Smith *et al.*, 1986). More recently, individuals demonstrating features of SMS caused by a mutation of the retinoic acid-induced 1 (RAI1) gene located on chromosome 17p11.2, have been described (Slager, Newton, Vlangos, Finucane, & Elsea, 2003) leading researchers to suggest that this gene is implicated in most of the features of the syndrome. Mutation of gene RAI1 is responsible for less than 10% of cases (Elsea & Girirajan, 2008).

2.3 The physical phenotype of Smith-Magenis syndrome

2.3.1 Facial and physical characteristics

Common facial features include brachycephaly (flat head shape), heavy brows with a prominent forehead, broad face, mid face hypoplasia, broad nasal bridge, downturned corners of the mouth, upward slanting eyes and a heavy jaw (Allanson *et al.*, 1999; Greenberg *et al.*, 1991). The facial appearance changes with age; in infancy it is described as 'doll like' or cherubic (Smith, Dykens and Greenberg, 1998) but it is described as coarsening with age (Allanson, Greenberg & Smith, 1999). Other physical features include short, broad hands, short stature and a hoarse, deep voice (Greenberg *et al.*, 1996).

2.3.2 Health problems

A range of health difficulties is reported. Vision (including myopia both with and without retinal detachment, Finucane, Jaeger, Kurtz, Weinstein & Scott 1993; Chen *et al.*, 1996) and hearing problems are frequently noted and infantile hypotonia and scoliosis are also common (Greenberg *et al.*, 1996). Signs of peripheral neuropathy have also been found in over 55 -75% of individuals with SMS (Greenberg *et al.*, 1991, 1996). Smith *et al.*, (1998) summarise other health problems, based on the findings of Greenberg *et al.*, (1996), that are more variable in nature, including cardiac defects (37%), renal abnormalities (35%), thyroid abnormalities (29%), low immunoglobulins (23%), seizures (11-30%), abnormal EEG without seizures (21%), forearm abnormalities (16%) and facial clefts (9%).

2.4 The behavioural phenotype of Smith-Magenis syndrome

2.4.1 An overview the behavioural phenotype of Smith-Magenis syndrome

In addition to the physical features associated with SMS, researchers have identified a characteristic profile of cognitive and behavioural features which suggest that there is a behavioural phenotype associated with the syndrome.

2.4.2 Cognitive ability and adaptive behaviour in Smith-Magenis syndrome

2.4.2.1 Cognitive ability

Studies of cognitive functioning in SMS indicate the majority of individuals fall into the moderate intellectual disability (ID) range⁵ (de Rijk-van Andel, Catsman-Berrevoets & Hamers, 1991; Greenberg *et al.*, 1996; Moncla *et al.*, 1991; Udwin *et al.*, 2001). Dykens *et al.*, (1997) reported relative weaknesses in short term memory and strengths in long term memory. Further weakness in sequential processing was identified, with strengths in visual attention and reading. Reading strengths were not supported by Udwin, Webber and Horn (2001) who found that adults with SMS failed to progress beyond the six to seven year-old level on the Wechsler Reading Dimensions assessment (WORD, Wechsler, 1993). However, the strengths in perceptual skills and long-term memory and weaknesses in sequential processing were supported.

A small number of individuals with SMS without ID have been described. Greenberg *et al.* (1996) found the majority of their sample of 25 individuals with SMS had moderate ID but one participant (a 30 year old) was in the borderline range of ID. Similarly, Martin *et al.*

⁵ 40-50 IQ points.

(2006) found one participant in their study fell in the low average range of cognitive ability and a further 28% (five individuals) fell in the borderline range. While no one has studied samples of those with SMS with IQ in the normal range, Crumley (1998) described a twelve year old female with SMS, noting that despite not having ID she still showed the characteristic behavioural patterns (which will be described in detail subsequently).

Children with SMS and normal range IQs may fail to maintain this level of achievement. Elsea and Giriraja (unpublished data, cited in Elsea & Giriraja, 2008) note while school-age children with low normal IQs have been identified, IQ decreases with age and by adulthood they fall into the mild ID range. Despite possible IQ decline with development, it is evident that there are a number of individuals with SMS reported to have no cognitive impairment. Furthermore, it is likely that with increasing professional awareness and improved testing, less severely affected individuals with SMS will be increasingly identified.

Only one study has directly evaluated developmental changes in cognitive ability. Udwin *et al.* (2001) compared attainment of children and adults with SMS. Children were found to have IQs in the moderate range of ID (≤ 50) whereas adults had IQs in the mild range (50 - 69). This slight increase in IQ scores in adults was attributed to non-equivalent adult/child IQ tests⁶ (a trend found in the general population) and also a potential cohort effect. The authors suggest therefore that, although it does not actually increase, IQ does not decline with age in SMS, unlike other genetic syndromes such as fragile X syndrome (FXS, Hagerman *et al.*, 1989) and Down syndrome (DS, Brown, Greer, Aylward & Hunt, 1990). This is inconsistent with the possible decreases in IQ suggested by Elsea and Giriraja (2008), indicating that cognitive functioning across the lifespan requires further examination in SMS.

⁶ Wechsler Adult Intelligence Scale versus Wechsler Intelligence Scale for Children.

2.4.2.2 Communication

Communication deficits have been reported, with speech delay being greater than motor delay. Several studies have found weaknesses in expressive language when compared to receptive language (Chen *et al.*, 1996; Crumley, 1998; Greenberg *et al.*, 1996; Sarimski, 2004). Despite potential communication deficits it has been noted that children with SMS are less impaired in their communicative abilities than one might expect for example from autistic children (Greenberg *et al.*, 1996).

2.4.2.3 Adaptive functioning

Adaptive functioning in SMS is reported to be less than might be predicted from either age or cognitive ability (Potocki, Shaw, Stankiewicz & Lupski, 2003; Dykens, Finucane & Gayley, 1997; Udwin *et al.*, 2001). Udwin *et al.* (2001) found that adults with SMS were more dependent on carers than suggested by their overall level of cognitive ability. The majority (over 70%) of adults studied could not dress, cook a meal or complete household chores independently and over 50% could only be 'left alone' for minutes. Most adults were described by caregivers as dependent on staff and requiring high levels of support. None lived independently or had achieved formal educational qualifications and only one adult was described as being employed. Udwin *et al.* hypothesise that divergence in cognitive ability and adaptive behaviour results from the challenging behaviour, attention deficits, impulsive behaviour, 'attention-seeking' and autistic behaviours⁷ found in SMS.

Similarly, Whittington *et al.* (2004) have suggested academic underachievement in Prader-Willi syndrome (PWS), another genetic syndrome associated with challenging behaviour,

⁷ While this is an imprecise term it has utility here in highlighting the overlap in phenomenology of behaviours in ASD and SMS.

may be associated with difficult behaviours. In addition to finding that achievement was lower than that predicted by IQ scores, they also suggest that placement of those with PWS in special schools may be the result of their behaviour rather than cognitive impairments. This led to the proposal that immature social behaviour, challenging behaviour, attention deficits/hyperactivity and autistic features may obscure cognitive ability. The similarities between this suggestion and that of Udwin *et al.*, (2001) in relation to SMS is striking and lends weight to the argument that it is the challenging behaviours found in SMS rather than impairments in cognitive ability that result in reduced adaptive functioning.

Whilst Udwin *et al.*'s study (2001) provides a detailed examination of adaptive behaviour in SMS, information on adaptive functioning was not obtained using a standardised instrument therefore findings cannot be evaluated systematically. Other studies which have used the Vineland Adaptive Behavior Scales (VABS, Sparrow, Balla & Chicchetti, 1984, Sparrow, Chicchetti & Balla, 2005) indicate that adaptive function is generally low (Dykens *et al.*, 1997, Dykens *et al.*, 2003) but some aspects of adaptive behaviour may be less impaired than others. While Dykens *et al.* (1997) found no differences across domains of communication, daily-living skills and socialisation, more recent studies have found relative strengths in socialisation compared to other domains (Martin *et al.*, 2006; Taylor & Oliver, 2008; Wolters *et al.*, 2009). Martin *et al.* (2006) found as age increased, scores on the daily-living skills domain decreased, suggesting some aspects of adaptive function may plateau in SMS while they continue to progress in typically developing children. Martin *et al.*'s study is the only one which examined VABS subscales and links to cognitive ability. IQ was unrelated to any subdomains of daily-living skills (supporting Udwin *et al.*'s suggestion that attainment in daily-living may not reflect cognitive ability), whereas a number of communication and socialisation subdomains did correlate positively with IQ.

2.4.3 Challenging behaviour in Smith-Magenis syndrome

Comparisons with other genetic syndromes with similar level of intellectual disability, such as PWS and Cri du Chat syndrome, indicate higher scores on measures of challenging behaviour in SMS (Clarke & Boer, 1998). Furthermore, Smith *et al.* (1998) estimate that these behaviours are present in over 60-80% of those with the syndrome. These difficult behaviours are likely to be related to elevated levels of caregiver stress. Hodapp *et al.* (1998) report that caregivers of people with SMS report higher stress levels than a comparison group of children with ID of heterogeneous origin. Challenging behaviour was also the single best predictor of caregiver stress in SMS. These challenging behaviours include self-injury and aggression and also other behaviours reported to be problematic, including impulsive behaviour, repetitive behaviour and attention-seeking. These behaviours can therefore be considered to be of clinical significance and will be discussed in terms of how common they are, what forms they take and what may cause them.

2.4.4 Self-injury in Smith-Magenis syndrome

2.4.4.1 Prevalence of self-injury

Estimates of prevalence of self-injury are generally very high, varying between 67-96% (Dykens & Smith, 1998; Finucane *et al.*, 2001; Greenberg *et al.*, 1996; Martin *et al.*, 2006). This is considerably higher than estimates of prevalence in individuals with ID of a heterogeneous origin, which generally range from 4-10% (Kiernan & Kiernen, 1994; Oliver, Murphy & Corbett, 1987). A recent study comparing rates of challenging behaviour across seven genetic syndromes and a heterogeneous ID contrast group, found individuals with SMS showed the most self-injury, with approximately 93% showing self-injury, in contrast to 64.3% for the next highest group (Lowe syndrome). Furthermore those with SMS were at

least 6.32 times more likely to show self-injury compared to the heterogeneous ID contrast group (Arron *et al.*, 2011).

2.4.4.2 Phenomenology of self-injury

Phenomenology of self-injurious behaviours is highly varied. A wide range of topographies have been reported, including common behaviours e.g. self hitting and rarer behaviours e.g. pulling out of finger and toe nails (onychotillomania) and insertion of objects into bodily orifices (polyembolokoilomania). The most common self-injurious behaviours are self-hitting and self-biting (Arron *et al.*, 2011; Dykens & Smith, 1998; Finucane *et al.*, 2001; Martin *et al.*, 2006). Estimates of prevalence of self hitting range from 71% (Dykens & Smith, 1998) - 93% (Martin *et al.*, 2006) and self biting from 77% (Dykens & Smith, 1998) - 80% (Martin *et al.*, 2006). Finucane *et al.* (2001) conducted the only detailed and specific study of self-injury in SMS and found the most common behaviour shown was hand-biting (displayed by nearly all participants). Slapping self, head-banging, skin-picking and onychotillomania were shown by approximately half of their sample. On average individuals in this study showed 4.45 different types of self-injury, a figure between the averages of 5.4 derived by Martin *et al.* (2006) and 3.69 reported by Dykens & Smith (1998), supporting claims that those with SMS who show self-injury tend to show a variety of behaviours. Finucane *et al.* (2001) report that the number of types of self-injurious behaviours shown increases with age.

The wide range of self-injurious behaviours was also reported by Arron *et al.* (2011), who found that those with SMS were more likely than a contrast group of individuals with

heterogeneous ID⁸ to show self-hitting, hitting self with or against an object, self-biting and pulling self. Unlike previous studies those with SMS were not more likely to insert objects than the contrast group. These more unusual behaviours of inserting objects and nail-pulling have varying prevalence estimates, with insertion of objects ranging from 18.2% (Finucane *et al.*, 2001) - 47% (Martin *et al.*, 2006; although this includes insertion of fingers not just objects) and nail pulling varying from 13% (Martin *et al.*, 2006) - 55.2% (Finucane *et al.*, 2001). Variation in prevalence of nail-pulling may depend on age. When Finucane *et al.* (2001) split participants by age, 26.7% of younger participants showed the behaviour whereas 85.7% of their older sample had shown the behaviour at some point in their life, thus it may be a behaviour that is first demonstrated in older individuals as opposed to early in childhood.

2.4.4.3 Aetiology of self-injury

Likely explanations for high rates of self-injury include biological factors, environmental influences and interactions between the two. Biological explanations for self-injury primarily relate to signs of peripheral neuropathy found in SMS, which has been linked to genes that play a role in peripheral nerve functioning located on chromosome 17 near the region deleted in SMS (Chen *et al.*, 1996). Finucane *et al.* (2001) suggest peripheral neuropathy may have two roles: it may cause an unpleasant sensation in extremities (potentially accounting for the unique nail pulling behaviour) and it may reduce pain perception. Smith *et al.* (1998) note that individuals with SMS have a relative lack of sensitivity to pain, reducing the pain caused by self-injurious behaviour during temper outbursts. Reduced pain perception may be a moderating variable that reduces the response cost of self-injury (Petty & Oliver, 2005).

⁸ This is *all* of the contrast group of children with heterogeneous ID, not just those with heterogeneous ID who showed self-injurious behaviour.

Links between discomfort and challenging behaviours are supported by evidence from informant reports indicating that physical discomfort is the primary function of challenging behaviour in SMS (Langthorne & McGill, 2012). Langthorne and McGill (2012) found that more SMS participants met criteria for physical discomfort-related challenging behaviour than contrast groups (FXS and non-specific ID) for all topographies of challenging behaviour. They also had higher scores on the attention subscale of the Questions About Behavioral Function measure (Matson & Vollmer, 1995) than children with FXS but *within* the SMS sample there was little difference shown in types of function, suggesting that challenging behaviour, including self-injury, in SMS is likely to have multiple functions, including responses to pain and accessing attention. The authors also describe results of direct functional analysis of challenging behaviour in SMS, which found four of six participants met criteria for attention maintained problem behaviour.

Finucane *et al.* (2001) suggest that operant control of behaviour may account for increases in certain types of self-injury with age (see section 2.4.4.2) such that a self-injurious behaviour is maintained by environmental contingencies, for example increased attention or removal of a demand. The role of environmental factors is also supported by Langthorne and McGill's (2012) assessments of the function of challenging behaviour in SMS, which include social communicative functions such as seeking attention and access to tangibles. Social communicative functions were also found for aggressive behaviour by Sloneem, Oliver, Udwin & Woodcock (2011), a finding discussed in more detail in section 2.4.5.1.

A potential interaction between the genetic characteristics of SMS and the environment is described by Finucane *et al.* (2001) whereby increased prevalence of nail pulling in older participants may reflect in part an age dependent gene expression. They hypothesise that after

this behaviour starts to be manifested (possibly in response to discomfort), people with SMS learn that those around them respond to these behaviours both immediately and in a highly reinforcing manner, e.g. by quickly providing attention. Thus, the genetic difference involved in the syndrome interacts with environmental events resulting in increased rates of behaviour.

2.4.5 Aggression in Smith-Magenis syndrome

2.4.5.1 Prevalence of aggression

Prevalence estimates of physical aggression vary widely, from 38% (Madduri, Turcich, Lupski & Potocki, 2002) - 93% (Webber, 1999). Estimates from published research include rates of 70% (Dykens *et al.*, 1997), based on a small sample of 10 individuals and a recent larger study (42 individuals) found aggression was significantly heightened in SMS compared to a comparison group with ID of a heterogeneous origin, with 73% of individuals with SMS showing aggressive behaviour (Arron *et al.*, 2011). In another recent study of aggression in SMS by Sloneem *et al.* (2011), 87.5% of their sample of 32 children and adults with SMS showed physical aggression and they were more likely to show this behaviour than those with ID of mixed aetiology. Variation in prevalence estimates is due in part to differing definitions of aggression, depending on topography of aggressive behaviour (for instance, Madduri *et al.*'s definition included self-injury as well as physical aggression) and consequences of aggressive behaviour (e.g. whether tissue damage was caused). This latter difference reduces one estimate from 93% to 59%, Webber, 1999). While estimates of aggression do vary, they are generally high and contrast with estimates of physical aggression in people with ID of mixed aetiology, which vary from 2.1% (Borthwick-Duffy, 1994) - 54% (Davidson *et al.*, 1996).

2.4.5.2 Phenomenology of aggression

There has been limited examination of the topographies of aggression. Case reports indicate types of physical aggression are varied and include topographies commonly reported in other groups such as hitting (Hagerman, 1999) and punching (Colley, Leversha, Voullaire & Rogers, 1990). Other less common behaviours have been reported, including biting (Colley *et al.*, 1990), poking at other people's eyes (Finucane, Konar, Haas-Givler, Kurtz & Scott, 1994) and strong hugging (Smith *et al.*, 1998). As these originate from anecdotal reports it is not possible to determine whether these behaviours are seen more commonly in SMS than other groups. In general, evidence indicates the phenomenology of aggressive behaviours in SMS is similar to that of others with intellectual disability and includes hitting, punching, and property destruction (Colley *et al.*, 1990; Crumley, 1998; Finucane *et al.*, 1993, 1994, 2001; Greenberg *et al.*, 1991; Hagerman, 1999; Smith *et al.*, 1986; Stratton *et al.*, 1986).

Only one study has specifically examined aggressive behaviour in SMS. Reporting on 32 individuals Sloneem *et al.* (2011) examined topography and function of aggressive behaviour and characteristics associated with aggression. A mean of seven different topographies were shown, while hitting and grabbing were most common (>80%), biting, kicking and pinching were also shown by more than half of individuals. Comparisons with individuals without SMS showed biting and hitting were significantly more common in SMS. No differences in severity of aggression in SMS versus a contrast group (ID of mixed origin) were found.

2.4.5.3 Aetiology of aggression

Aggression was found by Sloneem *et al.* (2011) to serve social communicative functions such as obtaining attention, escape from demands and access to tangibles to a significantly greater

extent than self stimulation or pain/discomfort (assessed using the QABF, Matson & Vollmer, 2005). Severity of aggressive behaviour was moderately associated with hyperactivity and autistic type behaviours and strongly associated with impulsivity, suggesting that impulsivity is a specific risk factor for aggression in SMS. Additionally, factors identified as being related to challenging behaviour more broadly, found by Langthorne and McGill (2012) and Taylor and Oliver (2008) which include pain/physical discomfort, attention-seeking and access to tangibles are likely to apply to aggression.

2.4.6 Stereotyped and repetitive behaviours in Smith-Magenis syndrome

2.4.6.1 Prevalence of stereotyped and repetitive behaviours

Stereotyped and repetitive behaviours are reported to be near universal in SMS; both Dykens & Smith (1998) and Martin *et al.* (2006) found that all children with SMS that they studied were reported to show at least one stereotypy, measured using the Stereotypy checklist (Bodfish *et al.*, 1995). In addition, children who show stereotyped behaviours tend to show more than one (Dykens & Smith, 1998; Martin *et al.*, 2006).

2.4.6.2 Phenomenology of stereotyped and repetitive behaviours

The repetitive behaviours that are reported are diverse, with mean totals of over 10 topographies (Dykens & Smith, 1998; Martin *et al.*, 2006). Most common behaviours are teeth grinding and inserting hands or objects in mouth (Dykens & Smith, 1998; Hildenbrand & Smith, 2012; Martin *et al.*, 2006). These repetitive behaviours (mouthing objects and hands and teeth grinding) are reported to interfere at least moderately with individuals' lives (Martin *et al.*, 2006). While teeth grinding and mouthing are relatively common in individuals with intellectual disability (Cocchi & Lamma, 1999; Matson, Dempsey & Wilkins, 2008; Matson

& Rivet, 2008), other repetitive behaviours reported are highly specific to SMS. One such behaviour is uniquely high levels of what has been termed ‘attachment to people’⁹, characterised by continually asking to see, speak to or contact a particular favourite person, assessed using the Repetitive Behaviour Questionnaire (Moss, Oliver, Arron, Burbidge & Berg, 2009). This targeted social drive was elevated both in relation to other syndrome groups and in relation to scores of those with SMS on items assessing other types of repetitive behaviour.

Two other behaviours are described as ‘unique’ to SMS. An unusual ‘self-hugging’ stereotype has been described (Finucane *et al.*, 1994) which appears to be involuntary, occurring primarily in response to pleasure (Dykens *et al.*, 1997; Willekens, Cock & Fryns, 2000). Finucane *et al.* (1994) noted the behaviour was seen to a varying extent in all of their participants, whereby they either crossed their arms tightly across their chests and tensed their upper bodies or clasped their hands together in front of them and squeezed their arms to their sides. Dykens and Smith (1998) cite self hugging as occurring in 46% of their sample. They also found repetitive page-turning (‘lick and flip’ behaviour where children lick their hands and then use it to rapidly flip over pages) as a common stereotype ‘unique’ to SMS (51% of their sample).

2.4.6.3 Aetiology of stereotyped and repetitive behaviours

Of theories accounting for repetitive behaviours found in ID populations, theories relating to impaired executive function and neurotransmitters seem to have greatest potential for understanding the very high rates shown in SMS. Lewis, Baumeister & Mailman (1987)

⁹ The use of the term ‘attachment’ is taken directly from the measure of behaviour used (the Repetitive Behaviour Questionnaire, Moss *et al.*, 2009) and is not considered to be synonymous with attachment as used in mainstream developmental psychology. Rather it signifies behaviours that reflect motivation to access social resources from a particular person. The term ‘targeted social drive’ will be used throughout the thesis to avoid ambiguity in relation to the use of the term attachment and potential confusion with ‘attachment’ as understood within the mainstream child development literature.

suggest repetitive behaviour is “the behavioural output of dysregulated neuronal systems” (p.254). The neurotransmitter serotonin is implicated in this model, with drugs that increase serotonergic functioning reducing repetitive, compulsive and obsessive behaviours in individuals with neurodevelopmental disorders (McDougle, Kresch & Posey, 2000). Similarly, drugs which inhibit serotonin reuptake used by individuals with SMS have anecdotally been suggested to reduce repetitive behaviours (Hagerman, 1999), supporting a potential role of neurotransmitter dysfunction.

Deficits in executive functioning may also account for repetitive behaviour in SMS. Turner (1997) states that part of the role of the executive functioning system is to inhibit undesirable ongoing action, suggesting that disruption of the process of generating and inhibiting actions results in repetitive behaviour. This is supported by findings that deficits in executive function are observed in other neurodevelopmental disorders with high levels of repetitive behaviour, e.g. autism (see Ozonoff, 1997 for a review). Impairments in executive function in SMS appear to be likely, given the high levels of impulsivity (see section 2.4.7.1) which has been suggested to be underpinned, in part, by deficits in inhibition (Schachar & Logan, 1990).

The more unusual repetitive behaviour relating to targeted social drive (characterised by continually asking to see, speak to or contact a particular favourite person) in SMS may be linked to high levels of attention-seeking behaviour and drive to interact with adults described as being a problematic part of the behavioural phenotype of SMS (see section 2.4.8 below).

2.4.7 Impulsivity in Smith-Magenis syndrome

2.4.7.1 Prevalence of impulsivity

Many descriptions of SMS allude to impulsivity being a key feature of the behavioural phenotype (Allanson *et al.*, 1999; Chen *et al.*, 1996; Clarke & Boer, 1998; Dykens & Smith, 1998; Dykens *et al.*, 2000; Gropman, Duncan & Smith, 2006; Haas-Givler & Finucane, 1996; Hagerman, 1999; Smith, Dykens & Greenberg, 1998; Smith & Gropman, 2001). An early description of the SMS behavioural phenotype, using the Reiss Screen for Maladaptive Behavior (Reiss, 1988) found a rate of impulsivity in SMS of 80% (Dykens *et al.*, 1997) and Dykens *et al.* (2000) reported that 86% of their sample showed impulsive behaviours, assessed using the Child Behavior Checklist (Achenbach, 1991).

More detailed research into impulsive behaviour has been carried out recently by Oliver, Berg, Moss, Arron & Burbidge (2011), who found SMS was associated with an elevated impulsivity score (on the Activity Questionnaire, Burbidge *et al.*, 2010) compared to four of seven other syndromes examined (heterogeneous ID, Cornelia de Lange syndrome, PWS and Lowe syndrome) and high proportions of clinically elevated impulsivity scores were found in SMS for both children and adults (40 and 58.3%, respectively). Horn (1999, cited in Udwin, 2002) also reported persistence into adulthood of behavioural problems, including impulsivity, using a longitudinal follow up study. While overactivity reduced through adolescence and into adulthood, adults continued to show high levels of impulsivity and distractibility.

While use of informant report measures such as the Reiss Screen and Child Behavior Checklist can give an initial indication of the prevalence of a behaviour such as impulsivity, as noted in section 1.4.1, as they are reliant on caregiver reports of behaviour they are subject to possible bias and reduced accuracy (Hodapp & Dykens, 2005). Therefore, while they are useful as the first step in identifying behaviours associated with SMS, use of multiple

methods, including direct observation and testing is the next step in understanding impulsive behaviour in SMS.

2.4.7.2 Phenomenology of impulsivity

As little research has undertaken direct examination of impulsivity is it difficult to establish the forms it takes. Webber (1999) used the Parental Accounts of Children's Symptoms measure and found that 69% of her sample had difficulty waiting their turn and 52% were reported to 'Butt into conversations or games'. Similarly, together with being impulsive and easily distractible, one of the 10 most problematic behaviours in SMS was described by caregivers as 'demands being needed to be met immediately' (Clarke & Boer, 1998). Caregiver endorsement of such items suggests impulsive behaviour may in part be related to problems waiting for things (e.g. a demand to be met or for their turn).

A recent study which specifically considered impulsivity in individuals with SMS, found it was strongly associated with severity of challenging behaviour (Sloneem *et al.*, 2011), more strongly than other well known risk-markers such as hyperactivity and autistic type behaviour (Arron *et al.*, 2011). It was suggested in discussion of these results that impulsivity may be a risk-marker for aggressive behaviour in SMS.

Whatever form of behaviour impulsivity takes in SMS, it seems to be problematic, both in terms of its high prevalence but also its severity. Caregivers in the study of children and adults with SMS by Clarke and Boer (1998) reported impulsivity to be the primary problem behaviour associated with the syndrome. As this appears to be an issue of such clinical significance, reliance on informant report checklist measures of impulsivity (due to lack of

detailed descriptions or direct observations of impulsive behaviour) is an issue which requires addressing.

2.4.7.3 Aetiology of impulsivity

While no research has directly examined the aetiology of impulsive behaviour in SMS, examining what underpins impulsivity in other groups may offer insight. Approaches to understanding impulsivity have conceptualised it as involving deficits in inhibitory control, where impulsive individuals cannot control their behaviour (e.g. Schachar & Logan, 1990) and also being a result of an inability to delay gratification, where this inability is driven by an emotional aversion to waiting, related to atypical motivational reward systems (e.g. Sonuga-Barke & Taylor, 1992; Sonuga-Barke, Taylor, Sembi & Smith, 1992). These two accounts do not necessarily conflict in terms of explaining impulsivity. Indeed, Sonuga-Barke incorporates both inhibition and delay of gratification deficits in a dual pathway model accounting for impulsive behaviour in ADHD (Sonuga-Barke, 2002). Individuals with SMS may therefore have specific deficits in response inhibition and/or ability to delay gratification, resulting in high levels of impulsive behaviour.

Accounts of the biological aetiology for impulsive behaviour link inhibition deficits to prefrontal areas and interconnections with the basal ganglia and striatum, whereas delay aversion may be associated more with the ventral striatum (Sonuga-Barke, 2002). Given high rates of aspects of behaviour associated with deficits in inhibition such as repetitive behaviours (see section 2.4.6.1) and neuroanatomical findings that frontal lobe development

may be atypical in the syndrome (Smith *et al.*, 1986)¹⁰, inhibition deficits are a strong candidate function underpinning impulsive behaviour in SMS.

2.4.8 ‘Attention-seeking’ in SMS in Smith-Magenis syndrome

2.4.8.1 Defining attention-seeking

Attention-seeking is a poorly defined construct. A review by Mellor (2005) of the attention-seeking literature found 78% of articles studying this construct did not define it. However, in the behavioural phenotype literature it is commonly included in behaviour checklists e.g. Reiss Screen for Maladaptive Behavior (Reiss, 1988), Child Behavior Checklist (Achenbach, 1991). These measures have been used with a variety of genetic syndromes including Angleman syndrome (Clarke & Marston, 2000) and PWS (Hartley, MacLean, Butler, Zarcone & Thompson, 2005) but fail to provide detail regarding the form of attention-seeking behaviours. Evaluation of attention-seeking in SMS in terms of phenomenology should provide insight into what behaviours these reports represent.

2.4.8.2 Prevalence of attention-seeking

Research by Dykens and colleagues (1997, 1998) identified high levels of attention-seeking in individuals with SMS, based on caregiver reports. Using the Reiss Screen for Maladaptive Behavior to examine problem behaviours, attention-seeking was found to be problematic for 80% of the SMS sample (Dykens *et al.*, 1997). A subsequent study examined distinctiveness and correlates of challenging behaviours in SMS, comparing individuals with SMS, PWS and mixed ID. Child Behavior Checklist scores indicated 94-100% of those with SMS were

¹⁰ This finding was from neuropathological study of a patient with a more severe deletion than typical, with deletion of the whole 17p11.2 band.

reported to “demand a lot of attention” and they had significantly higher scores on the social problems subdomain than the mixed ID group (Dykens *et al.*, 1998). Further links between maladaptive behaviour and social functioning were made by Sarimski (2004) who examined parental descriptions of the context of aggressive and self-injurious behaviour, finding that aggressive behaviours were reported to be motivated by desire for social attention. However, the parental reports of behaviour used as the basis of this functional analysis were not subject to inferential testing and thus validity of these findings is uncertain.

2.4.8.3 Phenomenology of attention-seeking

As the majority of accounts of attention-seeking derive from studies employing informant report measures, where caregivers validate single items from checklists of many behaviours e.g. Dykens *et al.*, 1997, 1998), there is a lack of detail about the behaviours ‘attention-seeking’ represents. However, evidence from Moss *et al.*'s (2009) study of repetitive behaviour in genetic syndromes alludes to the phenomenology of attention-seeking in SMS. As described in section 2.4.6.2, SMS was associated with a strong targeted social drive, characterised by continually wanting to see, speak to or contact a particular favourite person. Preference for interacting with particular people is reflected in anecdotal accounts of social behaviour in SMS. Haas-Givler (1994) describes students with SMS as attention-seeking and ‘very adult-oriented’ with little interest in interacting with peers. They are described as demanding an ‘inordinate amount of’ and as having a ‘sometimes insatiable’ need for individualised attention from adults with aggression resulting if availability of attention from teachers is restricted.

Empirical research into social behaviour in SMS is limited. One study which did directly observe social behaviour involved examination of self-injury and aggression during varying levels of available attention (Taylor & Oliver, 2008). For three of four children studied it was shown problem behaviours were preceded by low levels of adult social contact, supporting suggestions of a role for low attention in evoking challenging behaviour in SMS. Thus, there is support for suggestions of an unusually strong drive for social contact in SMS. However, while the natural observation methods enabled direct observation of social behaviour, lack of experimental manipulation precluded examination of causal relationships.

2.4.8.4 Aetiology of attention-seeking

The aetiology of apparently elevated attention-seeking behaviour is unclear. In mainstream child development literature, strong drive for adult interaction may be considered in the context of attachment processes, where drive to interact with a caregiver is an adaptive biologically determined process (Bowlby, 1969). In this context it is possible that strong drive in SMS represents aberrant attachment, possibly similar to insecure attachment (Ainsworth, Blehar, Waters & Wall, 1978; Bowlby, 1969). However, no research has investigated this so this proposal cannot be evaluated.

In Angelman syndrome (AS), a genetic syndrome associated with a strong drive to interact with adults (Horsler & Oliver, 2006), a biological cause of this drive has been proposed. As described in full in section 1.3.2, Brown & Considine (2004) have suggested that elevated rates of prosocial behaviours shown by those with AS such as laughing and smiling, (Horsler & Oliver, 2006) are the phenotypic effects of genomic imprinting, resulting from conflict between genes inherited from the mother and father. Loss of information from a maternally

imprinted gene causes an imbalance in AS, thus the effects of the paternally derived gene are manifested as increased drive to access maternal resources such as attention (thus decreasing access to paternal resources).

In addition to a biological drive, attention-seeking and specificity of this to adults, might be considered in an operant model, such as that proposed by Oliver (1995). It is possible that children with SMS find adults particularly reinforcing and learn to associate them with positive outcomes and so ultimately express a preference for their attention. Similarly, adults may be more responsive to some of the challenging behaviours shown by those with SMS, with a greater appreciation of potential costs of challenging behaviour (injury, damage to property). Hence, they may respond more readily, thus making them more reinforcing.

2.4.9 Autism Spectrum Disorder (ASD) in Smith-Magenis syndrome

2.4.9.1 ASD in genetic syndromes

ASDs are pervasive developmental disorders currently defined by a triad of impairments in social interaction, communication and repetitive behaviour (DSM-IV-TR; APA 2000; ICD-10; WHO 1992). In the general population, ASD has a prevalence of around .008 % (77.2 per 10,000, Baird *et al.*, 2006). This prevalence is greatly elevated in ID populations, nearing 40% (La Malfa, Lassi, Bertelli, Salvini, & Placidi, 2004). In genetic syndromes autism is most commonly associated with FXS, Rett Syndrome and Tuberous Sclerosis Complex (Moss & Howlin, 2009). There is debate about whether autistic characteristics shown in genetic syndromes have the same presentation as those in idiopathic autism (see Moss & Howlin, 2009 for a review). For example atypical gaze is associated with both FXS and ASD, however differences in these gaze atypicalities have been suggested, characterised as gaze *avoidance* in

FXS versus gaze *indifference* in ASD (Cornish *et al.*, 2007). Males with FXS have been found to show more eye contact avoidance than those with idiopathic ID (despite FXS showing less autism than this contrast group), whereas more children with idiopathic ID showed other abnormal eye contact (Turk & Graham, 1997). Atypical eye contact in FXS has been attributed to over-arousal, contrasting with broader social impairments, including lack of motivation, underpinning similar behaviour in ASD (Cornish *et al.*, 2007). Examination of prevalence and phenomenology of ASD in SMS could provide insight into its presentation in this syndrome.

2.4.9.2 Prevalence of ASD

Individuals with SMS often receive diagnoses of ASD (Gropman *et al.*, 2006) and high rates of autism have been reported (e.g. 93%, Webber, 1999). However, overall findings regarding ASD in SMS are mixed. Laje *et al.*, (2010b) indicate 90% of their sample of 62 participants met criteria for ASD assessed using the Social Responsiveness Scale (SRS, Constantino & Gruber, 2005). Analysis of Social Communication Questionnaire (Rutter, Bailey, Berument, Lord & Pickles, 2003) data gathered in addition to SRS data, indicated that while group means were actually below the cut off for ASD, just over 50% of individuals met the criteria for ASD at some point in their lives. Oliver *et al.* (2011) reported 68.4% percentage of their sample scored above the cut off for ASD (and 36.8% for autism) using the Autism Screening Questionnaire¹¹. These rates were not notably different from the seven other genetic syndromes studied and are notably lower than estimates using the SRS (Laje *et al.*, 2010b), indicating the measure of ASD used is likely to impact upon prevalence estimates.

¹¹ Berument, Rutter, Lord, Pickles & Bailey (1999) - the predecessor to the widely used Social Communication Questionnaire.

2.4.9.3 Phenomenology of ASD

Oliver *et al.* (2011) found that SMS only differed from one group (PWS) on the social interaction subscale of the autism screening measure used¹² and did not differ from any groups on the communication or repetitive behaviour subscales. While this study has the advantage of contrast groups of other genetic syndromes in identifying the specificity of behaviours to SMS, in common with other studies reporting on ASD assessments in SMS there was no comparison group of individuals with idiopathic autism, precluding direct comparisons of this area of interest.

Estimates of severity of ASD symptomology vary. Studies have reported mean ratings of ASD in SMS ranging from the non-autistic range (Wolters *et al.*, 2003) to the low end of mild (Martin *et al.*, 2006) to severe for the majority of a sample (Laje *et al.*, 2010b). This may be due to the different measures used (Laje *et al.* used the SRS, Wolters *et al.* and Martin *et al.* used the Childhood Autism Rating Scales, CARS, Schopler, Reichler, & Renner, 1988) and age of participants is also likely to affect results. Martin *et al.*'s sample had a mean age of 5.7 years and all of Wolters *et al.*'s sample was under the age of three, whereas Laje *et al.*'s sample had a mean age of 14.4 years. Symptoms may therefore become more severe with age. Supporting this Wolters *et al.* reported mild to moderate autistic behaviours began to emerge in older children in their sample. Examination of ASD in across the lifespan therefore needed to establish severity.

¹² The ASQ.

2.4.9.4 Aetiology of ASD

Given lack of differences between rates of ASD in SMS and those of a range of other genetic disorders associated with ID (Oliver *et al.*, 2011) high scores on ASD measures may be a function ID rather than SMS specifically. It has also been suggested children with SMS may receive ASD diagnoses mainly attributable to language abnormalities and repetitive behaviours and, as such, the profile of behaviour is different from idiopathic ASD (Gropman *et al.*, 2006). This is not supported by the findings of Moss *et al.* (2009), who found no association between repetitive behaviour and ASD in SMS, suggesting repetitive behaviours may not actually be strongly associated with ASD in this syndrome.

A number of studies have found socialisation is a relative strength in SMS. This is inconsistent with diagnoses of ASD, where lowest scores are typically found on the socialisation subscale and higher scores on daily-living skills (Kraijer, 2000). Martin *et al.* (2006) report that children aged between two - 12 years had higher socialisation scores on the VABS than communication and daily-living skills scores and also that socialisation scores were significantly higher than predicted from IQ scores. Similarly, Gropman *et al.* (2006) describe the infant behavioural phenotype of SMS as including near or age-appropriate social skills for 16 of 19 children, but this declines with age, suggesting potential strengths in social functioning are subject to developmental influences. Aetiology of autistic behaviours in SMS remains unclear therefore, with indications that some ASD diagnoses may be misplaced (a suggestion supported by evidence of social strengths in the syndrome).

2.4.10 Sleep disturbance in Smith-Magenis syndrome

2.4.10.1 Prevalence of sleep disturbance

While sleep disturbance is common in individuals with ID (with prevalence rates of over 80%, Quine, 1991; Wiggs & Stores, 1996), it is particularly prevalent and problematic in SMS. Sleep disturbance, measured using polysomnography, is an almost universal phenomenon in SMS (De Leersnyder *et al.*, 2003; Greenberg *et al.*, 1996; Potocki *et al.*, 2000), and is described as one of the cardinal features of the disorder (Gropman, Elsea, Duncan & Smith, 2007). Greenberg *et al.* (1996) estimated that around 75% of their sample experienced sleep disturbance in terms of sleep behaviours such as settling difficulties, night-time waking and daytime sleepiness. Additionally, high rates (over 50%) of sleep abnormalities in underlying functions such as REM sleep have been reported (Greenberg *et al.*, 1996, 1991). Parental reports of sleep problems indicate prevalence rates of 94% (Dykens & Smith, 1998). However, prevalence rates may vary depending on assessment methods used, e.g. parents may not be aware of night time waking, which methods such as actigraphy may detect (Gropman *et al.*, 2007).

2.4.10.2 Phenomenology of sleep disturbance

Sleep disturbance is believed to manifest in infancy (Greenberg *et al.*, 1996) and persist into adulthood. Gropman *et al.* (2007) describe a pattern of developmental change in sleep disturbance in SMS. In infancy reduced 24 hour sleep is reported (Duncan, Gropman, Morse, Krasnewich & Smith, 2003) despite parental beliefs that their babies are ‘good sleepers’ (Gropman *et al.*, 2006). In childhood, night-time and early morning waking, together with shortened sleep cycles are noted, as is daytime fatigue (Duncan *et al.*, 2003).

In older children, adolescents and adults activity appears to be elevated early in the night, suggesting difficulty initiating sleep (Gropman *et al.*, 2007). Smith *et al.* (1998) also found a relationship between age and sleep, with increased age associated with reduced night-time sleep and increased but shorter naps. These naps have been described as ‘sleep attacks’ (de Leersnyder, Claustrat, Munnich & Verloes, 2006), alluding to the sudden and irresistible nature of the urge for sleep. Despite this apparent reduction in sleep quality with age, caregivers report decreases in sleep problems with age (Horn, 1999, cited by Udwin, 2002), a finding attributed to reduced disruptive night-time behaviours with age rather than improved sleep.

Gropman *et al.* (2007) suggest that daytime sleepiness may account for some disruptive behaviours shown by those with SMS. This suggestion is supported by research reporting a relationship between tantrums and increased melatonin (De Leersnyder *et al.*, 2001b). Based on this, the authors suggest a number of the behavioural problems associated with the syndrome, e.g. hyperactivity, attention deficit and challenging behaviour, may be attributed to a response to fatigue due to increased daytime melatonin. Sleep related behaviours, specifically morning behaviours, have been found to be related to elevated stress in carers and parent-family problems (Hodapp *et al.*, 1998).

2.4.10.3 Aetiology of sleep disturbance

Sleep disorder in SMS has been primarily ascribed to inverted melatonin release pattern which disrupts circadian rhythm (De Leersnyder *et al.*, 2001a; Potocki *et al.*, 2000). This inversion leads to elevated daytime levels of melatonin release and reduced night-time melatonin release, the opposite pattern to typically developing individuals, resulting in

daytime sleepiness and night-time waking. Inversion of the melatonin release cycle is not thought to represent inversion of the central clock in the suprachiasmatic nucleus because not all 24 hour patterns are inverted¹³ as they would be if the central clock were inverted. It is hypothesised instead that regulatory features which control the release of melatonin by the pineal gland are inverted. De Leersnyder *et al.* (2006) suggest that haploinsufficiency of a ‘clock gene’ which controls circadian rhythms, may therefore account for sleep problems in SMS.

If inverted melatonin release is the primary cause of sleep disorder in SMS, then treatment providing evening melatonin (as released in typically developing individuals) or suppressing its daytime release (e.g. beta blockers) should be efficacious. A review of the literature on use of melatonin for sleep disturbance in young people has suggested it results in improvements even of severe sleep problems and sleep problems in those with genetic disorders, although the evidence base is variable (Turk, 2003). In SMS use of melatonin has primarily been reported as being effective in combination with a second drug which acts as a melatonin antagonist (blocking the effect of abnormal daytime melatonin release). De Leersnyder *et al.* (2001b, 2003, 2006) evaluated the impact of acebutolol, a beta-1 adrenergic blocker and night-time melatonin to induce sleep in a sample of children with SMS. Results indicated improvement in sleep behaviours (increased total sleep time, reduced early morning waking). Analysis of melatonin levels indicated that this drug treatment suppressed daytime release of melatonin, improving sleep behaviours. Reduced hyperactivity and improved cognitive performance were also reported.

¹³ Body temperature and cortisol follow a typical 24 hour cycle (Boudreau, 2009)

However, as Turk (2003) states, evidence regarding improvements in hyperactivity and cognitive performance is unclear; apart from reported reductions in number of temper-outbursts the specific outcome measure for behavioural improvements was not reported. Furthermore, Laje, Bernert, Morse, Pao & Smith (2010a) found that while sleep aides (of which melatonin was the most frequently used) were the most common pharmacological treatment used and the earliest started treatment, their use did not affect caregiver ratings of disruptive behavioural outcomes.

2.5 Summary

In addition to a characteristic physical phenotype of SMS, there is now clear evidence for a distinct behavioural phenotype characterised by intellectual disability, low adaptive functioning and a range of behaviours that are challenging for those with the syndrome and their caregivers. As SMS is a relatively recently identified syndrome, initial work has focussed on describing the behaviours found. As a result, some features of the behavioural phenotype are beginning to be well defined. For instance the prevalence and phenomenology of self-injurious and aggressive behaviours have been delineated relatively clearly. However, even for behaviours that have been the focus of much research, key aspects, such as aetiology, are little understood.

Literature presented in chapter one identified how aspects of behavioural phenotypes can be considered in the context of explanatory models of behaviour. These models represent potential interactions between a syndrome's genetic characteristics and behavioural outcomes, taking into account cognitive underpinnings and environmental influences. The behavioural phenotype of SMS has a number of features that may be understood within such a framework. Furthermore, throughout this review of the key aspects of the behavioural phenotype, links have been made between the behavioural outcomes in SMS, e.g. between impulsive behaviour and aggression, attention-seeking and challenging behaviour and sleep problems and challenging behaviours. Given such links it is important to move on from describing the behaviours found in SMS to understanding their aetiology. Key aspects of the behavioural phenotype of SMS studied to date, and potential links between these, are presented in figure 2.1, in a hypothetical model of the pathway from the genetic characteristics of SMS to behaviour in this syndrome based on the conventions of Morton (2004) and following the approach of Woodcock *et al.* (2009b) outlined in section 1.3.1.

2.6 Presenting a hypothetical model of behaviour in SMS

At the biological level the model presented in figure 2.1 identifies how genetic difference in SMS (loss of genetic information located on chromosome 17p11.2, specifically gene RAI1) may affect development of the brain, central nervous system, endocrine system and structural characteristics such as the mouth and ear. Atypicalities in each of these areas may then affect behaviour either directly or indirectly.

Direct pathways from biological difference to behaviour are illustrated in the effect of oral motor dysfunction on expressive communication deficits. Indirect pathways include those which affect another function, either cognitive functions which then are then hypothesised to impact on behaviour or physiological states which may then act as setting events for subsequent challenging behaviour such as self-injury and aggression. Pathways through cognitive functions may suggest that in addition to the behavioural phenotype of SMS, a cognitive endophenotype (see footnote in section 1.2.1) can be identified in the syndrome. Indirect pathways may also affect cognitive functions which then, in turn, alter physiological processes which then cause behavioural responses, such as the pathway from cognitive demand to physiological arousal to difficult behaviours illustrated in Woodcock *et al*'s (2009b) model of behaviour in PWS.

In addition to pathways from biological characteristics to behaviour, the model incorporates reciprocal environmental influences on behaviour, as advocated by Tunnicliffe and Oliver (2011) and Woodcock *et al.* (2009). This enables conceptualisations of phenotype-environment interactions, such as the social reinforcement of challenging behaviour, through caregiver behaviour. These environmental influences on behaviour in the current model may

include positive reinforcement of behaviour via the provision of attention (Oliver, Hall & Murphy, 2005) or negative reinforcement through the removal of a demand (e.g. Vollmer, Marcus, Ringdhal, 1995). The model also reflects how child characteristics may affect environmental factors. Finally, links between behaviours identified in previous research (e.g. between impulsivity and aggression, see section 2.4.5.3) are represented at the behavioural level of the model.

Smith-Magenis syndrome

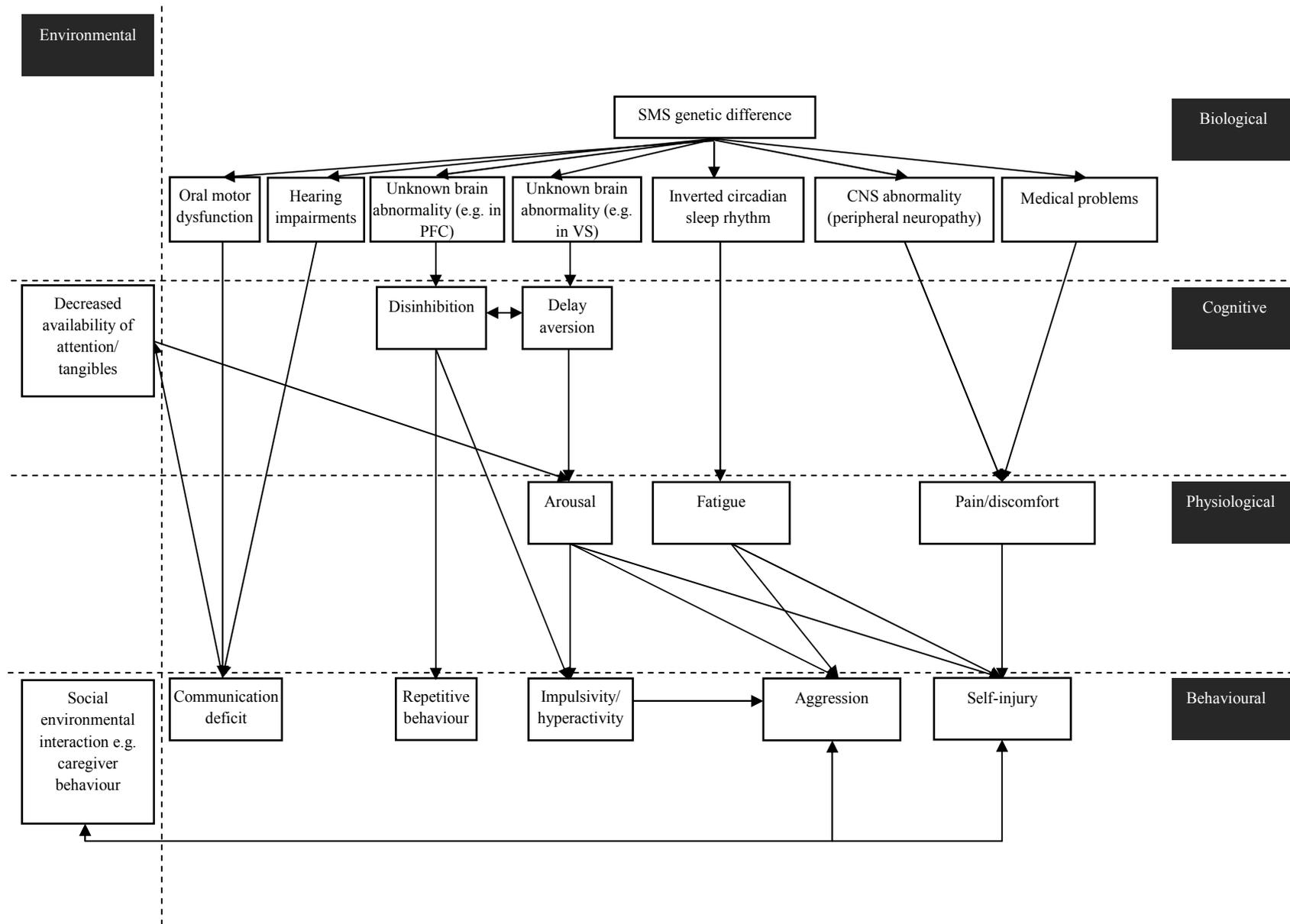


Figure 2.1 Hypothetical model of pathways from genetic difference to behaviour in Smith-Magenis syndrome

2.6.1 Extending the hypothetical model of pathways from genetic difference to behaviour in Smith-Magenis Syndrome

Impulsivity and drive for adult attention are two aspects of the SMS behavioural phenotype that have received limited attention in terms of research examining their nature, how they may relate to challenging behaviour and interact with other key aspects of behaviour in SMS. Inclusion of pathways to impulsivity and drive for adult attention in a model of behaviour such as that outlined in figure 2.1 may facilitate understanding of the development of these difficult behaviours within an established theoretical framework, potentially identifying critical points of intervention. Focussed investigation of such under-examined features of the syndrome is needed to progress current knowledge which is based primarily on informant reports using behavioural checklists.

Hodapp & Dykens (2005) emphasise the need to move towards a theory driven approach in research examining behaviour in genetic syndromes. In SMS this is possible for some aspects of behaviour, including impulsivity which can be understood in the context of literature from other syndromes and typical development. As such a theory driven approach to understanding impulsive behaviour in SMS, considering the role of the prefrontal cortex and associated executive functions including inhibition, is possible. Other behaviours, such as attention-seeking are not well understood in either typical development or genetic syndromes and are poorly characterised. Thus research examining this is in the early stages, requiring description of phenomenology (derived from observations) which may then lead to theory driven examination of aetiology, where more controlled studies to examine behaviours can be carried out (Hodapp & Dykens, 2005).

It is evident therefore that there is a need to carry out direct, empirical research of both attention-seeking and impulsive behaviour in SMS. Detailed informant reports of behaviour are required as a first step in identifying specific atypicalities in social functioning. Subsequent direct observations of behaviour in social situations can then focus on these atypicalities, describing how they manifest behaviourally and what factors may influence this. Gaining an understanding of ‘attention-seeking’ in SMS at these different levels may enable identification of pathways to this behavioural outcome, suggesting potential targets for intervention. Similarly direct examination of whether response inhibition may be a potential cognitive underpinning of impulsive behaviour is now required, given strong evidence linking response inhibition to impulsivity. Identifying what deficit may lead to impulsive behaviour again suggests a clear target for intervention.

2.7 **Conclusion and aims of the thesis**

Many aspects of the SMS behavioural phenotype cause potential harm and distress to individuals with the syndrome and stress for their caregivers (Hodapp *et al.*, 1998). Improved understanding of factors affecting these behavioural outcomes may, ultimately, improve quality of life of those with SMS and their caregivers. This thesis will examine aspects of the behavioural phenotype of SMS that have, to date, received little focussed investigation but may prove critical in understanding problematic aspects of the behavioural phenotype; social functioning and behavioural inhibition.

The broad aims of this thesis are to:

1) Describe and examine reported unusual social behaviour in Smith-Magenis syndrome, characterised as attention-seeking and preference for adult attention.

Diverse methods of evaluating social behaviour will be employed to achieve this aim. These are:

- i) Assessments of caregiver accounts of social behaviour, using a number of standardised indices of social functioning, to provide novel detailed description of social functioning in SMS. Contrasting these descriptions to other syndrome groups will identify characteristic profiles of behaviour and refine descriptions of atypical social behaviour in SMS.
- ii) Direct observations of individuals with SMS in naturalistic social situations to provide objective, reliable and ecologically valid quantification of social behaviour. Observing and recording key social variables (rate and enjoyment of social initiations of interaction with adults and peers) will enable

examination of social preference. Contrasting findings with another syndrome group will enable evaluation of the extent to which SMS can be considered to be characterised by unusual attention-seeking and preference for adult attention.

- iii) Experimental methods to directly examine the effect of manipulating levels of attention and familiarity of adults in order to make causal inferences regarding the drive for attention and preference for interaction with specific people shown by those with SMS.

Using these methods further insight will be gained into phenomenology of unusual social behaviour in SMS, evaluating accounts of attention-seeking directed toward specific adults and potentially validating its addition as a behavioural outcome in SMS to the model above (figure 2.1). Identification of effects of key social variables will provide insight into the aetiology of unusual social behaviour in SMS, implicating causal pathways.

2) Examine impaired inhibition as a potential explanatory mechanism of elevated impulsivity in Smith-Magenis syndrome.

- i) Caregiver reports of impulsive and associated behaviour will be gathered with the aim of evaluating existing reports of elevated impulsive behaviour in SMS.
- ii) Use of a battery of assessments of response inhibition will directly evaluate compromised behavioural inhibition as explanatory of impulsive behaviour in SMS. Associations between inhibition deficits and reports of impulsive behaviour would implicate a relationship between these two factors.

Replication of findings of elevated impulsive behaviour in SMS will support its place as a behavioural outcome in a model of behaviour in the syndrome (see section 2.5). Further understanding of the cognitive underpinnings of impulsive behaviour, specifically behavioural inhibition, will support the pathway identified in this model from dysfunction in the prefrontal cortex, through disinhibition to impulsivity.

In the context of findings of studies designed to achieve the aims outlined above (presented in the following four chapters), the model presented in figure 2.1 will be re-evaluated in the general discussion presented in the closing chapter of the thesis.

CHAPTER 3

Refining the description of atypical social behaviour in Smith-Magenis syndrome

3.1 Preface

The previous chapter reviewed research describing the behavioural phenotype of Smith-Magenis syndrome (SMS) and presented a hypothetical model of behaviour in the syndrome. Two aspects of behaviour were identified where further research was needed to understand pathways from genetic difference to behavioural outcomes within such a model. One area is what has been described as ‘attention-seeking’ behaviour. Therefore, this chapter aims to refine the description of atypical social behaviour in SMS to further understand the phenomenology of social functioning with specific reference to behaviours that might be described as ‘attention-seeking’. Standardised survey methods will be used to gain reliable, valid data which can be compared across syndrome groups to identify atypicality in aspects of social behaviour in SMS.

3.2 Introduction

While an increasing amount of research into behavioural phenotypes has focussed on characteristic social behaviours found in neurodevelopmental disorders (for example sociability in autism and Williams syndrome, WS, has now been extensively researched) there has been limited investigation of social functioning in SMS. This is surprising as overviews of the behavioural phenotype of the syndrome have identified difficult behaviours that seem likely to be related to social behaviour, for example widely reported attention-seeking (e.g. Dykens *et al.*, 1997, see section 2.4.8.2) and self-injurious behaviour and aggression associated with decreases in social attention (e.g. Sarimski, 2004; Taylor & Oliver, 2008, see sections 2.4.8.2 and 2.4.8.3). Other syndromes have been found to be characterised by specific patterns of social behaviour, for example broad social deficits in Autism Spectrum Disorder (ASD) have been extensively investigated (Carter, Davis, Klin, & Volkmar, 2005; Constantino *et al.*, 2003). Similarly low levels of sociability and increased social anxiety have been found in fragile X syndrome (FXS, Cornish *et al.*, 2005; Lesniak-Karpiak, Mazzocco & Ross, 2003; Turk & Graham, 1997). This contrasts with WS where excessive sociability, manifested by those with WS being unusually sociable, friendly and empathic (Jones *et al.*, 2000; Tager-Flusberg, Sullivan, Boshart, Guttman, & Levine, 1996) has been reported, leading to individuals with WS being labelled as ‘hypersociable’ (Jones *et al.*, 2000).

In Down syndrome (DS) strengths in sociability have traditionally been considered as part of the behavioural phenotype, with stereotypes of individuals with DS describing them as “outgoing and “affectionate” (Wishart & Johnston, 1990). There has been debate regarding whether sociability in DS is elevated compared to typically developing individuals, preserved or just higher than those with similar levels of cognitive impairment. There is now broad

agreement that strengths in sociability in DS are relative rather than absolute (Serafica, 1990). Studies indicate individuals with DS do tend to have good social functioning across a range of domains; they are reported to have good social skills, better social understanding and more appropriate social behaviour than others of similar age and cognitive and communicative development (Dykens & Kasari, 1997; Kasari, Mundy, Yirmiya & Sigman, 1990; Kasari & Freeman, 2001), they seek out social contact and have been found to be more socially orientated than those without DS (Kasari & Freeman, 2001; Kasari & Sigman, 1996). However, in contrast, weaknesses in emotion recognition have also been found in the syndrome implicating problems with socio-cognitive understanding (Wishart & Pitcairn, 2000).

As illustrated above with regard to DS, social functioning is not a unitary construct thus cross syndrome comparisons are potentially problematic. The preceding descriptions of different syndromes illustrate the multiple domains of social functioning across which syndrome specific patterns of strengths and weaknesses may be evident. The term ‘sociability’ is often used as an umbrella term for aspects of social functioning. However, this term is poorly defined in the literature. For instance, Rapin and Katzman (1998) state “impaired sociability” is one of the defining features of autism. However, a distinction needs to be made as to which domain of social functioning ‘sociability’ refers to - some individuals with ASD report having the desire to interact with others (social motivation) but not the social skills needed to interact effectively (Bauminger & Kasari, 2000). In addition to motivation and skills, other features of social functioning include social cognition, social competence and social behaviour (see Cook & Oliver, 2011 for a review of definitions of social functioning). The current study will focus on social behaviour, operationalising sociability in terms of behaviours shown during

episodes of social interaction e.g. approach behaviours and positive affect, which facilitate social interaction.

As noted in section 2.4.8.3 descriptions of social functioning in SMS derive primarily from informant report measures (e.g. Dykens *et al.*, 1997, 1998; Sarimski, 2004) and anecdotal accounts (e.g. Feinstein & Singh, 2007; Haas-Givler 1994); there has been limited empirical investigation of this to date. Research by Dykens *et al.* (1997, 1998) found attention-seeking was commonly reported (see section 2.4.8.2 for further details) and preference for interacting with particular types of people appears to be a highly specific feature of social behaviour in SMS. As described in detail in section 2.4.6.2, Moss *et al.* (2009) found high levels of targeted social drive in SMS (characterised by continually asking to see, speak to or contact a particular favourite person). Preference also features in commonly cited anecdotal descriptions of those with SMS as attention-seeking and ‘very adult-oriented’ with limited interest in peers (Haas-Givler, 1994).

The link between periods of low attention and episodes of challenging behaviour reported by Sarimski (2004) is also supported in Haas-Givler’s (1994) anecdotal account, with aggression described as resulting if attention from teachers is unavailable. The sole empirical study of social behaviour to date (Taylor & Oliver, 2008) further supported a link between unavailability of attention and challenging behaviour, where reduced attention from adults reliably preceded episodes of self-injury and aggression (see section 2.4.8.3 for more detail).

In terms of broad social deficits related to autism spectrum disorders individuals with SMS are frequently diagnosed as having ASD (Gropman *et al.*, 2006, see section 2.4.9.4) but when directly contrasted to other genetic syndrome groups rates of ASD have not been found to be elevated (Oliver *et al.*, 2011). The extent to which phenomenology of ASD behaviours in SMS resembles that of idiopathic autism is also unclear. As noted in section 2.4.9.4 it has been suggested that ASD diagnoses may result from language abnormalities and high rates of repetitive behaviour (Gropman *et al.*, 2006). This proposal is supported by relative strengths in socialisation found in SMS, contrasting with weaknesses in this domain in ASD (Kraijer, 2000; Sparrow, Chichetti & Balla, 2005). It is unclear therefore to what extent there is overlap between aspects of unusual social behaviour in SMS and impairments in social functioning seen in ASD.

Whilst the majority of descriptions of the behavioural phenotype of SMS do not focus explicitly on social functioning, a profile of atypical social behaviour seems to be emerging, including strong drive to interact with particular individuals and preference for adult social interaction, high levels of attention-seeking and challenging behaviour associated with low levels of attention. Given the socially demanding nature of attention-seeking behaviour and links with challenging behaviour outlined above, social behaviour is clearly of clinical significance for those with SMS and those who care for them.

Further delineation of the behavioural phenotype of SMS with specific focus on indices of social functioning is therefore required. As noted previously, the majority of past research has focussed on identifying ASD like differences between groups, however other differences including in sociability and social preferences are likely to be of particular relevance in SMS

(given reports of ‘attention-seeking’ behaviours suggesting strong social drive). There is a lack of clarity regarding phenomenology of autism-type behaviours in SMS which implicates a need to examine further this specific feature of the behavioural phenotype, particularly in the context of possible strong social drive, not considered to be characteristic of ASD. Examination of ASD phenomenology together with sociability and social preference will enable evaluation of whether any atypicalities in the latter two aspects of social functioning are likely to be attributable to the more fundamental and common atypicalities associated with ASD. This may provide more specific insight into the nature of the unusual profile of social behaviour and enable consideration of potential aetiological pathways to attention-seeking behaviour which is reported, thus expanding the model of behaviour in SMS presented in section 2.5. Examination of to what extent unusual aspects of social functioning can be considered phenotypic in SMS, requires comparisons with appropriate contrast groups.

To address the areas of interest outlined above, in the current study data in an existing database was analysed, comparing aspects of social functioning in SMS using two contrast groups: DS and ASD. These contrast groups were selected as they evidence divergent levels of social functioning, relatively high and low respectively in terms of broad indices of social functioning e.g. social understanding, social skills and social behaviour (ASD, Travis, Sigman & Ruskin, 2001; see above for description in DS) and so provide well documented points of reference for findings in SMS. Behaviours indicative of autism spectrum disorder (ASD) in SMS were assessed and compared across the three syndromes to identify broad social deficits associated with ASD. Levels of sociability with caregivers, familiar adults, unfamiliar adults, familiar peers and unfamiliar peers were also compared across groups to examine sociability with various types of people who can be considered ‘targets’ of social interaction. Targeted

social drive (characterised by requesting to see speak to or contact a particular favourite person) was compared across groups to identify any differences in social preference.

Hypothesised findings and areas for exploration are outlined below.

Autism Spectrum Disorder phenomenology

It was hypothesised that those with a diagnosis of ASD would show greater impairments related to Autism Spectrum Disorder phenomenology than those with DS and SMS, scoring higher on each of the measure's subscales. It was further hypothesised that those with SMS would show higher levels of Autism Spectrum Disorder phenomenology than those with DS, based on reports of increased autism diagnoses in this syndrome group.

Sociability

It was hypothesised that the ASD group would show fewer behaviours associated with sociability so would be rated by caregivers as less sociable than those with both SMS and DS. As those with SMS have been reported to show elevated levels of targeted social drive it was also hypothesised that this group would be rated as being more sociable than those with DS.

Targeted social drive

Findings of previous research indicate that individuals with SMS show elevated levels of targeted social drive, it was thus hypothesised:

- i) The SMS group would have higher levels of targeted social drive than both contrast groups, who would not differ from each other.

- ii) Elevated targeted social drive specifically, as opposed to generally restricted preferences, would be unique to SMS, thus this pattern of results would not be found for the two other related items from the restricted preferences subscale of the measure used.

3.3 Methods

3.3.1 Participants

The current study was part of a larger postal questionnaire study comparing aspects of behavioural phenotypes of genetic syndromes (see Oliver *et al.*, 2011, for details). Families of those with SMS who had participated in a previous postal survey and expressed interest in taking part in future research (n = 42) were approached by a letter sent by the Cerebra Centre for Neurodevelopmental Disorders. This letter invited them to participate in the current research project and was sent together with a pack containing the measures used in the current study. Of the 42 families approached, 28 questionnaires were returned, representing a relatively strong return rate of over 65%. Efforts were made in line with recommendations to maximise response rates including attaching a cover letter and enclosing pre paid, addressed return envelopes (Wilkinson & Birmingham, 2003). While the final sample is not large, SMS is a rare disorder and as such recruiting large samples presents a challenge. Given the significant behavioural difficulties associated with the syndrome there is an evident clinical need to study behaviour in this group even in small samples. Furthermore the striking behavioural phenotype of SMS suggests that effect sizes are likely to be large for key behaviours of interest potentially reducing sample sizes required to achieve sufficient power.

While this return rate was felt to be acceptable, the reasons for non return of questionnaires should be considered. It is possible that those with SMS for whom questionnaire packs were not returned may differ from those who did not take part in the study. It is expected however that this bias would be consistent across the contrast syndrome groups thus limiting the effect of this in terms of the contrasts made in this type of study (Arron *et al.*, 2011).

Participants with SMS were included in the study if they had a confirmed diagnosis of the syndrome from a professional, were reported to be verbal (the measure of targeted social drive required participants to be verbal) and were over four years old (minimum age for the autism screening measure). Individuals who did not provide age or date of birth information were excluded. Consequently one individual was excluded because they were under four years old, four because they were nonverbal and a further individual was excluded due to non completion of the sociability questionnaire.

The remaining 22 participants were matched with individuals from two other syndrome groups; DS and ASD (from a total sample of 126 and 220 respectively). The DS group were recruited via the Down's Syndrome Association and the ASD group were recruited via the National Autistic Society. Individuals with DS were considered for matching if they met the inclusion criteria outlined above, individuals with ASD were additionally required to score above the cut off for ASD on the autism screening measure (22) and to have no diagnosis of an additional genetic syndrome. Participants were matched on estimates of adaptive behaviour as a proxy measure of intellectual disability (based on scores on the self help subscale of the Wessex Scale, see appendix F2) and age. Table 3.1 describes participant demographics (participants with SMS were assessed using the ASQ, participants with DS and ASD received the more recent version, the SCQ¹⁴, see appendix F3). As shown in table 3.1 there were a larger number of male in the ASD sample compared to the other two syndrome groups. This reflects the increased ratio of males to females with ASD (Rapin, 1999).

¹⁴ The ASQ and SCQ are considered equivalent measures, differences in scoring between the measures affect non verbal individuals only, who were not included in the current study. For clarity this assessment is referred to as the SCQ throughout.

Table 3.1 Mean age (standard deviation) and range, gender (percent male), mean adaptive functioning scores (standard deviation) and ‘autism’ scores (standard deviation) in each syndrome

		SMS	DS	ASD
N		22	22	22
Age	Mean	16.37	15.77	14.21
(Years)	(SD)	(8.48)	(8.37)	(7.66)
	Range	5-38	5-36	4-39
Gender	Number of males	11	9	19
	(%)	(50.00)	(40.91)	(86.36)
Adaptive functioning ^a	Mean	6.86	6.86	6.77
	(SD)	(1.21)	(1.21)	(1.11)
SCQ score	Mean	19.35	12.25	27.00
	(SD)	(5.61)	(8.51)	(5.32)

^a Assessed using the self help subscale of the Wessex scale, as a proxy measure of intellectual disability (see section 3.3.2.2).

3.3.2 Measures

3.3.2.1 Demographic information

A demographic questionnaire (see appendix F1) provided information on date of birth, gender, mobility, verbal ability and diagnostic status (whether and which diagnosis was made, when and by whom it was given).

3.3.2.2 Estimate of intellectual disability

The Wessex scale (Kushlick, Blunden & Cox, 1973)

Estimates of adaptive behaviour, as a proxy measure of intellectual disability, were obtained using the Wessex scale (see appendix F2), an informant based measure of adaptive behaviour in children and adults with intellectual disability. It comprises five subscales; continence, mobility, self help skills, speech and literacy. Vision and hearing items are also included. Estimates of adaptive functioning were based on the self help subscale, with a maximum score of nine. Both item and subscale level inter reliability have been found to be good (Kushlick *et al.*, 1973; Palmer & Jenkins, 1982). This measure of adaptive behaviour was selected in preference to other measures such as the Vineland Adaptive Behavior Scales (Sparrow, Chicchetti & Balla, 2005) as it is a questionnaire measure and thus can be completed by respondents as part of a postal survey such as the current study. Its concise format provides an overview of key areas of adaptive functioning while ensuring participants are able to complete the questionnaire pack in an acceptable timeframe.

3.3.2.3 Measure of ASD phenomenology

Autism Screening Questionnaire (ASQ, Berument et al., 1999); Social Communication Questionnaire (SCQ, Rutter et al., 2003).

The SCQ, previously known as the ASQ, is an informant questionnaire based on the Autism Diagnostic Interview–Revised (ADI–R: Lord *et al.*, 1994) used to screen for presence of autism in individuals over the age of four years (see appendix F3). It contains 40 items, using a yes/no response format, forming three subscales; communication, social interaction and repetitive and stereotyped behaviour. Cut off points are 15 for ASD and 22 for autism. Very

good agreement has been found between diagnostic classification obtained using this measure and that found using the ADI-R (Berument *et al.*, 1999; Bishop & Norbury, 2002).

3.3.2.4 Measures of sociability and targeted social drive

Sociability Questionnaire for people with Intellectual Disabilities (SQID, Nelson, 2010)

Sociability was assessed using the Sociability Questionnaire for people with Intellectual Disabilities (see appendix F5), a 24 item informant based questionnaire designed to examine behaviours indicative of sociability and social anxiety in children and adults with intellectual disabilities. The measure comprises two subscales; social interaction (sociability in one to one settings) and social performance (sociability in groups). Twenty items are rated on a seven point Likert scale from 'very shy' to 'very sociable', four further items use a yes/no response format. In this study 10 items from the questionnaire were used, these items were those enabling consistent sociability comparisons to be made across the five targets for social interaction included in the scale (caregiver, familiar adult, familiar peer, unfamiliar adult, and unfamiliar peer). This therefore comprised items from the 'Social interaction' subscale only and resulted in a composite one to one social interaction score for each of the five targets. Preliminary analyses found both the social interaction and social performance scales had good inter-rater reliability (.87 and .87 respectively, Nelson, 2010).

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

To examine targeted social drive the Repetitive Behaviour Questionnaire was used (see appendix F7). This is an informant report measure consisting of five subscales; stereotyped behaviour, compulsive behaviour, insistence on sameness, restricted preferences and

repetitive speech. Informants rate the frequency of 17 behaviours on a four point scale from 'never' to 'more than 'once a day'. The RBQ has been found to have good item level inter-rater reliability and test-retest reliability (.46 - .80 and .61-.93 respectively, Moss *et al.*, 2009). Only the restricted preferences subscale was used in the current study.

3.3.3 Procedure

Questionnaire packs were distributed directly to families and carers of individuals with SMS and to families and carers of those with DS and ASD via the relevant support groups. Carers received a cover letter, an information sheet, questionnaire pack and consent form. To address effects of priming the study was presented as an investigation of behaviours associated with genetic syndromes. Carers returned completed questionnaires and consent forms in a prepaid envelope.

3.3.4 Data Analysis

Data were tested for normality using Kolmogorov-Smirnov tests. Where data were not normally distributed ($p < .05$), non-parametric techniques were employed.

ASD phenomenology was investigated by carrying out between groups comparisons of scores on each SCQ subscale (Communication, Social interaction, and Repetitive Behaviour). Kruskal Wallis tests (alpha $p < .05$) were used to identify differences between groups, with Mann-Whitney non-parametric post hoc tests, with an alpha level of .01, used for items where a significant difference between groups was found.

To assess levels of sociability, one to one sociability scores with each 'target person'; (caregivers, familiar and unfamiliar adults and peers) were calculated for the three syndrome groups. It was not possible to analyse data in a mixed design 'syndrome group' by 'target person' analysis of variance (ANOVA), as data were not normally distributed and could not be transformed to normality. Therefore, interactions between syndrome group and target for social interaction were explored using a series of post hoc between and within group comparisons. Sociability with each target person was therefore compared in Kruskal Wallis analyses to assess patterns of sociability between groups (alpha $p < .05$). Mann-Whitney post hoc tests were employed for items for which a significant difference between groups was identified, using an alpha level of .01. Freidmans tests with post hoc Wilcoxon analyses, with an alpha level of .01 were used to examine differences within each syndrome group.

To investigate specificity of targeted social drive within the subdomain of restricted preferences, scores for each of the three items in this subscale of the RBQ ('attachment to people' measuring targeted social drive, attachment to objects and restricted preferences) were compared across groups, using the analyses described for SCQ data above.

3.4 Results

3.4.1 Autism spectrum disorder phenomenology

To explore the profile of ASD phenomenology shown by individuals with SMS and its relation to that of idiopathic ASD, scores on the SCQ were analysed, comparing syndrome group scores on each subscale. Figure 3.1 shows the profile of scores on the Communication, Repetitive Behaviour and Social Interaction subscales¹⁵, illustrating how the ASD group have elevated scores (indicative of more impairments) compared to DS (as expected) and SMS on all domains, and the somewhat higher scores of SMS compared to DS on each domain.

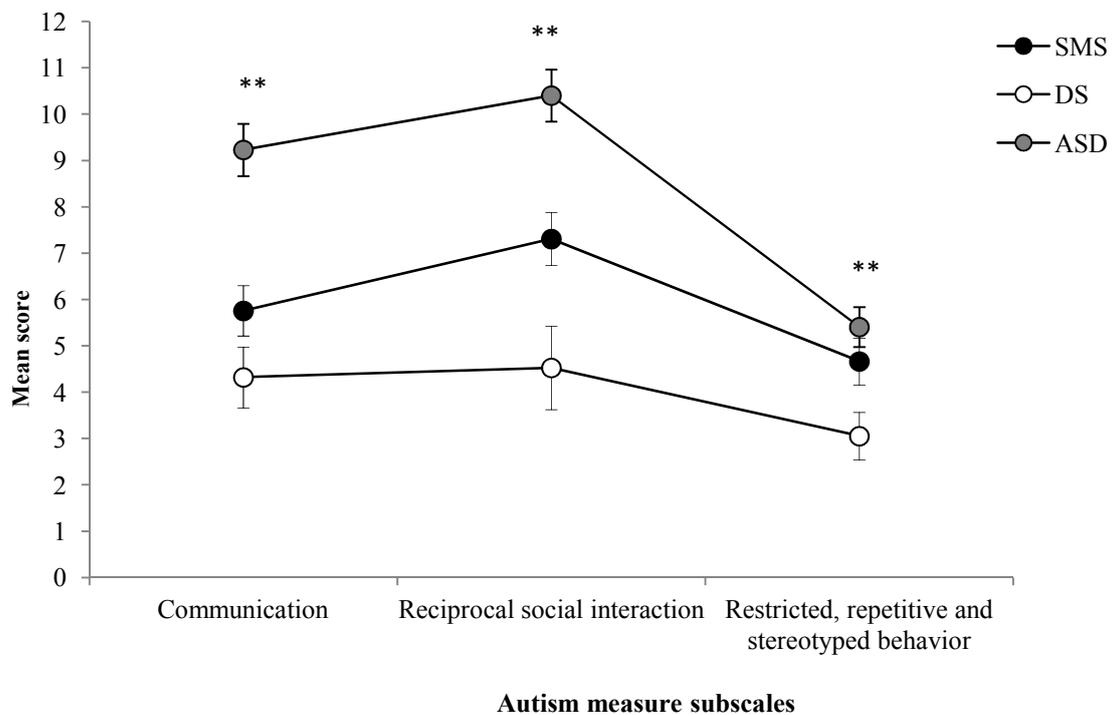


Figure 3.1 Mean and standard error of autism screening measure subscale scores for syndrome groups (significant between syndrome differences * $p \leq .01$, ** $p \leq .001$)

Significant differences between the syndrome groups were found for each subscale; Communication ($\chi^2 = 22.99$, $p < .001$), Repetitive Behaviour ($\chi^2 = 13.73$, $p = .001$) and Social

¹⁵ Means and standard errors are shown as they illustrate the distinctive profiles of scores across domains more effectively than the median values and associated measures of dispersion

Interaction ($\chi^2 = 22.21, p < .001$). Post hoc comparisons for Communication scores showed the ASD group had significantly higher scores (greater impairment) than both the SMS and DS groups ($U = 66.5, p < .001$ and $U = 43, p < .001$ respectively) but no difference was found between SMS and DS ($U = 106, p > .01$). Analysis of Repetitive Behaviour scores found ASD had significantly higher scores than DS ($U = 88, p < .001$). Neither DS and SMS groups nor SMS and ASD groups differed significantly on this subscale ($U = 130.5, p > .01$ and $U = 178.5, p > .01$ respectively). On the Social Interaction subscale comparisons indicated the ASD group scored significantly higher than both SMS and DS ($U = 73.5, p = .001$ and $U = 49.5, p < .001$ respectively). SMS and DS did not differ on this subscale ($U = 86.5, p > .01$).

3.4.2 Sociability

Differences in levels of sociability between syndrome groups were tested by comparing each syndrome group's sociability scores for each of the five targets for social interaction (caregiver, familiar and unfamiliar adults and peers). Separate analyses were performed for each target person. Patterns of sociability within-groups were also analysed to explore preferences for interaction with different target people within each syndrome. Figure 3.2 illustrates the lower overall sociability of those with ASD compared to those with SMS and DS¹⁶, who showed very similar levels of sociability with each target for interaction. The figure also demonstrates similarity of patterns of differences across the various target people, with greatest sociability with caregivers followed by familiar adults and familiar peers. Overall lowest sociability was with unfamiliar adults, followed by unfamiliar peers.

¹⁶ Again, means and standard errors are shown as they illustrate the distinctive profiles of scores across domains more clearly than the median values and associated measures of dispersion

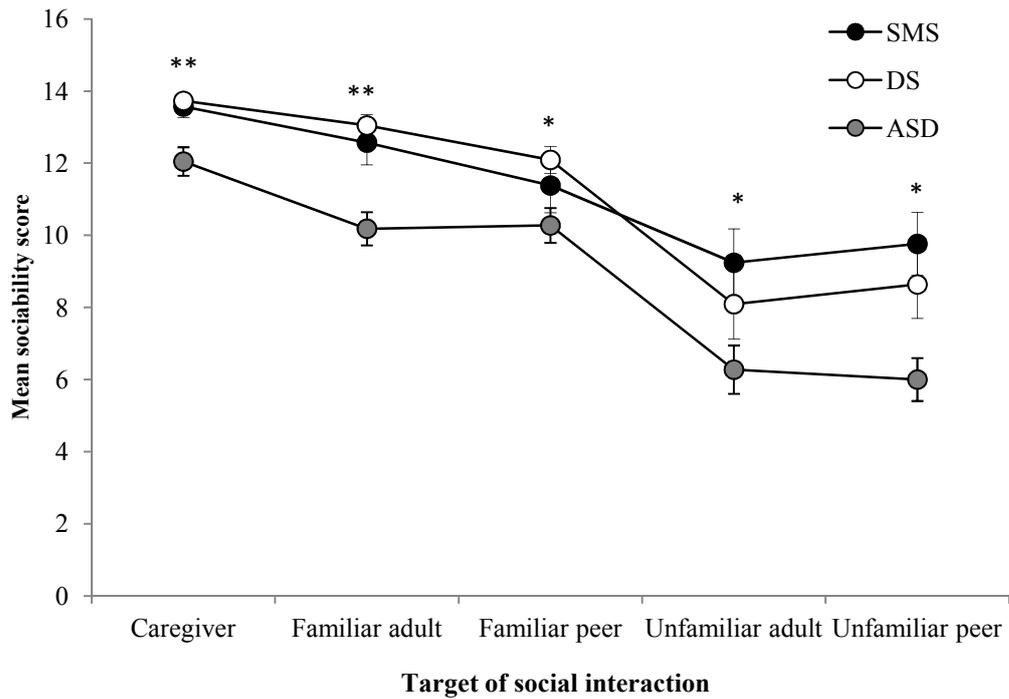


Figure 3.2 Mean and standard error of sociability scores for each target person on the Sociability Questionnaire for Individuals with Intellectual (significant between syndrome differences * $p \leq .01$, ** $p \leq .001$)

Kruskall-Wallis tests found significant differences between syndrome groups for each of the targets for one to one interaction; caregivers ($\chi^2 = 16.643$, $p < .001$), familiar adults ($\chi^2 = 22.832$, $p < .001$), familiar peers ($\chi^2 = 8.314$, $p = .016$), unfamiliar adults ($\chi^2 = 6.24$, $p = .044$) and unfamiliar peers ($\chi^2 = 12.31$, $p = .002$). Post hoc tests were used to further examine significant differences found between groups. No significant differences were found between SMS and DS groups for any targets of social interaction. The ASD group were reported to be less sociable than SMS when interacting with caregivers ($U = 115$, $p = .001$), familiar adults ($U = 84$, $p < .001$) and unfamiliar peers ($U = 89.5$, $p < .001$) but no differences were found for interactions with familiar peers and unfamiliar adults. The ASD group were also found to be less sociable than the DS group with caregivers ($U = 114$, $p = .001$), familiar adults ($U = 63$, $p < .001$) and familiar peers ($U = 115$, $p = .004$) interactions but, as expected, no differences were found for interactions with unfamiliar adults and unfamiliar peers.

Data in figure 3.2 also suggest differences in sociability were shown across interactions with different targets for social interaction. While patterns appear broadly similar for each syndrome, it was not possible to directly compare whether they differed according to syndrome as data did not meet assumptions of parametric analyses and there is no non-parametric alternative available to perform this analysis. Therefore, non-parametric Friedman analyses assessed whether levels of sociability differed across each of the targets for social interaction for each syndrome group individually. Table 3.2 shows significant differences in sociability across targets were found for each syndrome.

Table 3.2 Median scores, interquartile range, statistical analyses and post hoc analyses on sociability scores across targets for social interaction, for each syndrome group

Group	Targets for social interaction					df	χ^2	p value	Post hoc analyses
	Caregiver (CG) Median (Interquartile range)	Familiar Adult	Familiar Peer	Unfamiliar Adult	Unfamiliar Peer				
SMS	14 (0)	14 (1.5)	12 (4)	10 (9)	11 (4)	4	45.79	< .001	CG, FA > FP, UA, UP
DS	14 (0)	14 (2)	12 (2.5)	9.5 (8.25)	10.5 (8.25)	4	62.39	< .001	CG, FA > FP > UA, UP
ASD	12 (4)	10 (3)	10 (2.25)	6 (5.25)	6 (5)	4	64.66	< .001	CG > FA, FP > UA, UP

For both SMS and DS post hoc tests found no difference between caregivers and familiar adults, for ASD sociability was higher with caregivers than familiar adults. Other than this, sociability was higher with caregivers than with all other target people for all syndrome groups. For SMS and DS sociability was higher with familiar adults than with familiar peers, no difference between these two targets was found for ASD. Sociability with familiar peers

was not different from sociability with unfamiliar adults or unfamiliar peers in SMS, whereas in DS and ASD sociability was higher with familiar adults than with unfamiliar adults and unfamiliar peers. Finally, there was no difference found between sociability with unfamiliar adults and unfamiliar peers in any syndrome group.

3.4.3 Restricted preferences

To test the hypothesis that individuals with SMS would have higher levels of targeted social drive than those with DS and ASD, scores on the item assessing targeted social drive of the Repetitive Behaviour Questionnaire were analysed. To examine whether any differences found were specific to this behaviour the two other items in the restricted preferences subscale were analysed. Figure 3.3 shows the profile of restricted preferences across the syndromes¹⁷, highlighting the uniquely elevated average score for SMS on the targeted social drive item compared to both other syndromes and also other subscale items.

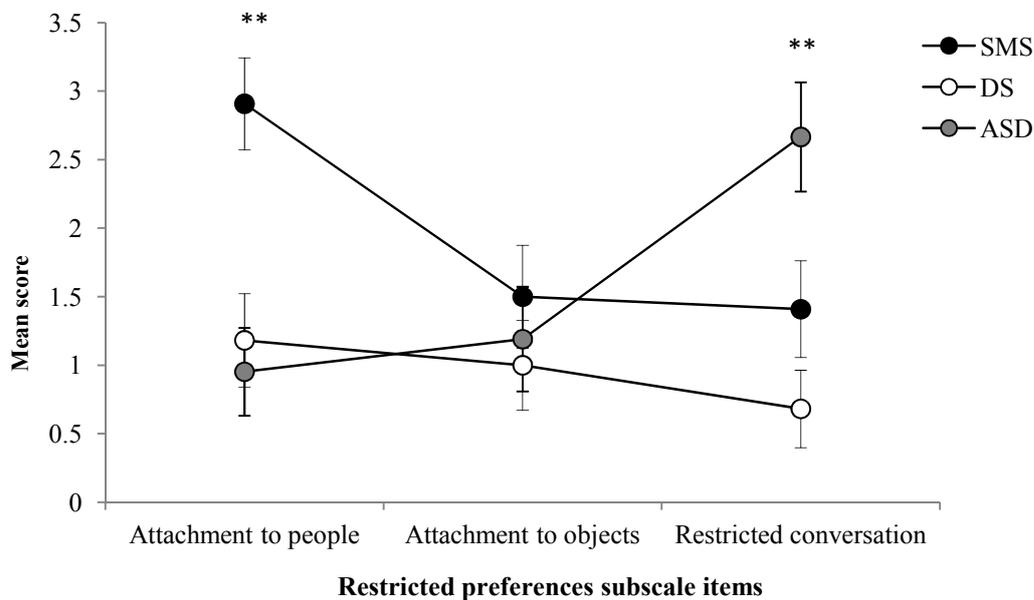


Figure 3.3 Mean and standard error of ‘Restricted Preferences’ Repetitive Behaviour Questionnaire subscale scores for syndrome groups (significant between syndrome differences * $p \leq .01$, ** $p \leq .001$)

¹⁷ As for the previous two figures means and standard errors are shown as they illustrate the distinctive profiles of scores across domains more clearly than the median values and associated measures of dispersion

Significant differences between the syndrome groups were found on two items within the restricted preferences subscale; targeted social drive ($\chi^2 = 15.54, p < .001$) and restricted conversation ($\chi^2 = 13.163, p = .001$). There was no difference between groups on the attachment to objects item. Results for targeted social drive indicated that SMS had significantly higher scores than both the DS and ASD groups ($U = 119, p = .002$ and $U = 95, p < .001$ respectively), but no difference was found between DS and ASD. Post hoc analysis of restricted conversation scores found that ASD had significantly higher scores than DS ($U = 109, p = .001$). Neither DS and SMS nor SMS and ASD differed significantly on this item.

3.4.4 Summary of results

In summary, on the measure of autism spectrum disorders, SMS did not differ from DS any subscales. Those with ASD had higher scores (greater impairments) than DS on all subscales and higher scores than SMS on the communication and social interaction subscales. No difference was found between the SMS and ASD groups on the repetitive behaviour subscale.

Differences in sociability between syndromes were found for interactions with all target people (caregivers, familiar and unfamiliar adults and peers); follow up analyses found no differences in sociability between SMS and DS for any target people. As expected, ASD had significantly lower sociability than both SMS and DS with the majority of target people (caregivers, familiar adults and unfamiliar peers in SMS, caregivers, familiar adults and familiar peers in DS). Within each syndrome differences were found in levels of sociability shown with the different target people, patterns of these differences were broadly similar, although there were some differences between the syndrome groups. Sociability with caregivers was only higher than with familiar adults in ASD and while those with DS and

ASD were more sociable with familiar peers than unfamiliar adults and peers there was no difference found in SMS.

Those with SMS had significantly higher levels of targeted social drive than DS or ASD, who did not differ from each other. This pattern of results was not replicated for other items within the same Restricted Preferences subscale of the RBQ.

3.5 Discussion

Profiles of social functioning in SMS, in comparison to those with DS and ASD, were examined in this study. ASD phenomenology, sociability and presence and specificity of elevated preferences towards particular people in SMS were assessed. This is the first study to focus specifically on social functioning in SMS and inclusion of matched DS and ASD comparison groups enables SMS results to be anchored against groups which have relatively well researched social behaviour. Profile of ASD phenomenology differed from those with idiopathic ASD, suggesting that identification of any atypicalities on other measures of social functioning are unlikely to be attributable to ASD in SMS. Sociability of individuals with SMS and DS with a range of targets for social interaction did not differ, and were generally higher in these groups than in ASD. Within syndrome patterns of sociability with each of the targets for social interaction were broadly similar across the syndrome, with higher sociability with caregivers and familiar adults and reduced sociability with unfamiliar peers and unfamiliar adults (more mixed results were found for familiar peers). Uniquely elevated levels of targeted social drive, reflecting preferences for specific people, were found in SMS.

ASD phenomenology profiles indicated that individuals with SMS did not show a profile of behaviours associated with ASD. Consistent in part with the hypothesis that those with SMS would show lower levels of ASD phenomenology compared to the idiopathic ASD group, those with SMS differed from those with a diagnosis of ASD on two of the three subscales of autism screening measure used. They showed fewer impairments in communication and, critically for the current study, social interaction. Additionally, neither communication nor social interaction was impaired in those with SMS when compared to those with DS. This is contrary to the hypothesis which anticipated that those with SMS would show deficits in these

areas as they have elevated levels of autism diagnoses. This may support the previous suggestion that those with SMS do not show a profile of behaviour consistent with ASD. Those with DS have been found to have relatively low levels of ASD when compared overall rates in individuals with intellectual disability. For example Kent, Evans, Paul & Sharp (1999) found a prevalence of 7% in individuals with DS, notably lower than the 16.7% incidence of ASD in those with an IQ of 70 and below found in previous research (de Bildt, Sytema, Kraijer & Minderaa, 2005). However, a recent study by Moss, Richards, Nelson and Oliver (2012) found that 8% of those with DS in their sample reached the cut off for autism and 19% reached the cut off for ASD (assessed using the SCQ). In subsequent comparisons with a matched group with idiopathic autism, those with DS and ASD were similar in terms of repetitive and stereotyped behaviours and self-injury, however those with ASD and DS were rated as being less 'withdrawn from their surroundings'. This suggests caution should be employed when using DS as a 'typical' contrast group in terms of ASD. However, differences between the ASD sample and both DS and SMS samples support the suggestion that both of these groups differ from idiopathic ASD in terms of autism-like behaviours.

One aspect of ASD phenomenology where individuals with SMS do seem to demonstrate impairments is in repetitive behaviour. In contrast to the hypothesis that those with SMS would show fewer impairments in ASD phenomenology than those with ASD, those with SMS did not differ from those with ASD on this subscale.. This finding adds further credence to suggestions by Gropman *et al.* (2006) that while individuals with SMS may receive diagnoses of ASD, these may be due primarily to high levels of repetitive behaviour and language impairments. Repetitive behaviours have been associated with impairments in executive function, as discussed in section 2.4.6.3. Given these links between executive function and repetitive behaviour and specificity of this deficit in the profile of behaviour

shown in SMS, further investigation of executive function (for example inhibition, identified previously as a possible explanatory mechanism for repetitive behaviour, see section 2.4.6.3), in SMS seems warranted. Need for further research of executive function in SMS is further reinforced by high levels of behavioural difficulties in SMS such as impulsive behaviour that are also indicative of executive function deficits, specifically behavioural inhibition (see section 2.4.7.3).

Lack of differences in levels of sociability between DS and SMS, which contradict the hypothesis that those with SMS would show elevated sociability related to their high levels of targeted social drive, suggests that on a gross level sociability does not appear either excessive or impaired in SMS, as individuals with DS have been proposed to have relatively ‘intact’ sociability (Chapman & Hesketh, 2000; Kasari & Freeman, 2001). Lack of elevated sociability in SMS can be contrasted with WS, which is associated with hypersociability and individuals with the syndrome have been found to show higher sociability than DS controls (Jones *et al.*, 2000). That individuals with SMS did not have lower sociability than the DS group and had significantly higher levels of sociability than the ASD group (as hypothesised because they may be expected to have reduced sociability) for the majority of targets for social interaction, further suggests individuals with SMS do not have impaired sociability (and is in line with findings described above regarding ASD phenomenology and lack of this type of social deficit).

Indications of a relatively typical profile of sociability in SMS are perhaps surprising in the context of research describing the behavioural phenotype of SMS as characterised by very strong drive for social contact, with high levels of attention-seeking reported (Dykens *et al.*,

1997, 1998) particularly with adults (Haas-Givler, 1994). It might be expected that strong drive for social contact and desire for attention would be manifested by higher levels of sociability when interacting with social targets in SMS compared to other syndrome groups. Target specific high sociability might also be anticipated, with cross syndrome differences in sociability found specifically for interactions with caregivers and/or familiar adult targets, for whom the literature describes a strong preference for social interaction. Again this pattern of findings was not present in the current study. However, high levels of attention-seeking and drive for social contact with adults may not be demonstrated in SMS by the type of positive behaviours typically associated with high sociability. Instead it may manifest in challenging behaviours such as aggression and self-injury, which are highly prevalent in SMS (Dykens *et al.*, 1998). This suggestion is supported by the findings of Sarimski (2004) and Taylor and Oliver (2008) who found low attention evoked self-injurious and aggressive behaviours in children with SMS. Despite the lack of between-syndrome differences for SMS and DS described previously, it is of note that SMS was the only group for whom sociability with familiar peers was not rated as higher than sociability with unfamiliar adults and unfamiliar peers. This finding is consistent with the lack of interest in peers described by Haas-Givler (1994).

In summary the current findings, both relating to ASD phenomenology and sociability, suggest impaired sociability typically found in ASD¹⁸ is not characteristic of the overall sample of those with SMS, indicating the behavioural phenotypes of the two disorders may be divergent in this respect. While levels of sociability have not been specifically examined in studies of behaviour in SMS to date, previous research has suggested socialisation is a relative strength in the syndrome (Crespi *et al.*, 2009; Martin *et al.*, 2006), further supporting the

¹⁸ For example the lack of social reciprocity identified as one of the diagnostic criteria in the DSM IV (APA 2000).

suggestion that individuals with SMS may have aspects of social functioning that are relatively intact and that sociability may be one of these.

In contrast to the overall lack of atypical patterns of sociability found in SMS in this study (with the caveat noted above), analysis of levels of targeted social drive identified uniquely high levels of this targeted social drive in SMS. This was found to be highly specific as it was not found in either the DS or ASD groups, who did not differ from each other. Furthermore, this pattern of findings was not replicated for either of the other two items in the restricted preferences subscale of the repetitive behaviour measure used, indicating this restricted preference is specific to people. These findings converge with those of Moss *et al.* (2009) who identified SMS as having a specific profile of repetitive behaviour characterised by very high levels of targeted social drive, not found in any of other genetic syndromes examined. Aetiology of this preference for particular people is unclear. Strong drive to interact with particular people and distress when their attention is unavailable shown in SMS, has some parallels with early attachment behaviour (Bowlby, 1969). It is possible therefore that this behaviour may be the result of biologically driven attachment processes aimed at eliciting social resources from a target person. This model of social behaviour has been suggested in Angelman syndrome (AS), a genetic disorder characterised by high levels of socially oriented behaviour which can include aggressive grabbing to make social contact with caregivers (Oliver *et al.*, 2007; Strachan, Shaw, Burrow, Horsler, Allen & Oliver, 2009) (see section 2.4.8.4) Unlike AS however, there is currently no clear evidence that implicates the specific genetic aetiology of SMS as being linked to the resulting hypothesised social differences.

Findings of high levels of targeted social drive to people are particularly interesting considered alongside the earlier findings regarding sociability. Despite no differences being found between SMS and DS in sociability with a wide range of people there are striking differences in the extent to which these two groups are reported to have a drive to interact with particular people. As discussed previously, drive to interact with particular people might be expected to be associated with increased levels of sociability with those people, yet elevated sociability was not found in this study. Again, it is possible that this discrepancy occurs because drive to interact is manifested in SMS by self-injurious or aggressive behaviours rather than behaviours typically considered to reflect sociability. Alternatively, it is possible that high levels of sociability are associated with the targeted social drive identified but that this drive is more circumscribed than the subgroups of people identified on the sociability measure. It may relate to only one particular person in the subcategory and this may then be missed if there is not elevated sociability with others in that subgroup.

A caveat that should be applied to the interpretation of the results of this study is use of DS as a comparison group. Many studies have suggested individuals with SMS have good functioning across a range of domains e.g. social skills, empathy and social competence (Kasari *et al.*, 1990; Kasari & Freeman, 2001). Despite this, care should be taken in use of this group as a comparison group of a genetic syndrome with relatively 'intact' social functioning (Hodapp & Dykens, 2001). DS has its own behavioural phenotype and there is continuing debate about how far social skills are intact relative to other syndrome groups and about the evenness of the profile of social functioning in the syndrome (Dykens & Kasari, 1997; Freeman & Hodapp, 2000; Kasari & Freeman, 2001).

However, DS is the most common genetic syndrome and thus social functioning in the syndrome has been widely researched (Kasari & Freeman, 2001). Use of a well researched comparison group enables inferences to be made about social functioning in the context of existing research findings, which would not be possible using comparison groups with other genetic syndromes about which little is known in terms of social functioning. DS also has a similar level of intellectual disability to SMS (both with IQs in the 40-50 range, Greenberg *et al.*, 1996; Melyn & White, 1973) enabling more effective matching, resulting in more closely comparable groups and greater confidence that the differences identified in the study are not artefacts of differences in ability.

Sociability was determined by scores on a subset of items from the sociability measure¹⁹. Reliability and validity data are only available for the complete subscales, thus it is possible that this measurement does not provide a true reflection of sociability across the target individuals. However, between-syndrome analyses revealed differences in the direction expected for the two syndromes known to have high and low sociability (DS and ASD respectively). This indicates items discriminated different levels of sociability across syndromes, thus supporting the validity of this set of items within the measure. Similarly, within syndrome analyses identified differences between levels of sociability across the targets. Results indicated higher sociability with caregivers, familiar adults and peers as expected, suggesting the measure discriminated effectively between different types of people.

Additionally, use of a single item from the RBQ to infer targeted social drive is not robust as it provides limited information about the types of behaviour this ‘attachment’ reflects or

¹⁹ Composite scores for each person were calculated using two items for each target person from the social interaction subscale.

situations in which this behaviour is shown. However, item level analysis of the scale has been carried out previously (Moss *et al.*, 2009) supporting the use of this item, together with the other restricted interest subscale items, as early pilot data for investigating unusual social preferences in SMS.

Finally it is possible that the larger number of males in the ASD sample may have affected results relating to sociability. There is some evidence to suggest that sociability as a trait is more developed in females. For example females have been found to orient more to faces than males, make more eye contact than males, pass theory of mind tests earlier and show greater social sensitivity (Lutchmaya & Baron-Cohen, 2003). This is somewhat controversial however as others have found that gender does not affect sociability as a temperamental trait (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006). The findings of Else-Quest *et al.*, based on a meta analysis of studies examining effects of gender on temperament, are consistent with other past research such as Maccoby and Jacklin (1974). Furthermore even if gender had affected sociability in the ASD group the gender imbalance in the ASD sample reflects that found in the population of those with ASD. As such this sample is representative of those with this disorder which was an important factor in the current study. Furthermore this would not have affected results for the DS and SMS comparison which indicated relatively typical sociability in SMS, as gender was relatively well matched.

Understanding social functioning in genetic syndromes has important clinical implications as self-injurious and aggressive behaviour reinforced by social attention are common in those with intellectual disability (Fisher, Deleon, Rodriguez-Catter & Keeney, 2004; Iwata, Dorsey, Slifer, Bauman & Richman, 1982). Furthermore, attention-seeking behaviour is likely to be

directed towards specific familiar people and while this has implications for safety (as it is unlikely to increase likelihood of approaching strangers), it may increase the burden felt by those who care for individuals with SMS. Caring for a child with SMS is associated with high levels of caregiver stress compared to carers of children with mixed or non-specific developmental disabilities (Hodapp *et al.*, 1998), and stress is strongly associated with the challenging behaviours shown by those with the syndrome (Hodapp *et al.*, 1998). This stress is likely to be exacerbated by high levels of attention-seeking behaviour directed towards caregivers (Isles, 2011), particularly given associations between reduced availability of attention and challenging behaviour (see sections 2.4.8.2 and 2.4.8.3). In addition to having a negative impact on caregivers, in a classroom context the strong drive for individualised adult attention, lack of interest in peers and the challenging behaviour which can result when attention is unavailable impacts both on the child's well being, their learning and the learning of those around them (Haas-Givler, 1994; Haas-Givler & Finucane, 1996).

There is a clear need for more empirical research into social functioning in SMS. A consensus is emerging from parental report studies and anecdotal accounts of an atypical pattern of social behaviour in SMS, characterised by a strong drive to interact with particular people. Future research should include direct observations of behaviour to evaluate the specificity of this drive for social attention. Examination of the role of different targets of social interaction may ascertain whether attention-seeking behaviours in SMS are underpinned by a generally excessive desire for social interaction or a specific drive to access social resources from a primary caregiver, potentially indicative of attachment processes.

CHAPTER 4

The nature of social preference and interactions in Smith-Magenis syndrome

4.1 Preface

Research presented in chapter three, which examined caregiver reports of aspects of social functioning in Smith-Magenis syndrome (SMS), supported past reports that social behaviour is atypical in SMS. A specific drive to interact with particular people, characterised by continually asking to see, speak to or contact a particular favourite person was found. However, more generalised excessive sociability was not found suggesting that this drive for interaction and attention may be restricted to circumscribed types of people. It is unclear what form this unusually strong social preference takes. There is a need therefore for research examining the phenomenology of social behaviour in SMS directly to further evaluate reports of an unusual profile of social behaviour, characterised by a drive to gain attention from particular people and sensitivity to low attention.

Methodologies used to research other genetic syndromes associated with strong social drive, for example Angelman syndrome (AS), can provide guidance on studying this in a novel syndrome such as SMS. Such methods, including natural observations and experimental manipulations of social situations, of assessing behaviour may have utility in examining social behaviour in SMS. Therefore the current study will utilise natural observation

methodologies of behaviour in every day contexts to derive more detailed initial descriptions of social behaviour in SMS.

4.2 Introduction

The anecdotal descriptions of socially demanding behaviour in SMS in the classroom provided by Haas-Givler and Finucane (1996) and Haas-Givler (1994) (see section 2.4.8.3) have formed the basis of influential descriptions of the behavioural phenotype of SMS (e.g. Smith & Gropman, 2001; Udwin, 2002). However, these descriptions are limited by their anecdotal nature. They are not the result of systematic, objective study of behaviour and are subject to potential bias in terms of type of individuals the authors encountered and limited scope for reliably assessing behaviours. More systematic sampling is important to increase the extent that results can be generalised. Similarly, objective assessments of behaviours would provide a more robust description of behaviours shown by individuals with SMS towards adults and peers in their school environment.

To date only one study has directly assessed behaviour of children with SMS in the school environment. Taylor and Oliver (2008) observed five children to examine environmental influences on challenging behaviour. They coded child and adult behaviours in real time, enabling objective evaluation of level of attention given to children and their responses to changes in attention. Challenging behaviour was found to be reliably preceded by reduced availability of adult attention and resulted in increased attention from adults. The authors note this was in the context of each child having one-to-one adult support throughout the school day (thus they were already experiencing high levels of attention) suggesting particular sensitivity to reduced attention. Use of operationally defined behaviours and real time coding enabled objective recording of behaviour, providing empirical support for reports of ‘attention-seeking’ behaviours in SMS. However, the role of peers, a key aspect of school environments, was not examined. Attention from peers may be an important influence on

behaviour in SMS, although this may be attenuated by reported lack of interest in peers (Haas-Givler, 1994). Additionally, lack of a contrast group limits the extent that this behaviour can be considered specific to SMS.

It is evident that more empirical research directly examining strong social preference in SMS is required. Excessive social drive in genetic syndromes is relatively rarely reported, in contrast to social deficits which are widely studied in Autism Spectrum Disorder (ASD) for example (Carter *et al.*, 2005; Constantino *et al.*, 2003) and fragile X syndrome (FXS, Bailey *et al.*, 1998; Cohen *et al.*, 1988; Cornish *et al.*, 2007; Turk & Graham, 1997). However, there is a gradually increasing body of research examining strong social drive in genetic syndromes, the most commonly studied of which are AS (Brown & Consedine, 2004; Oliver *et al.*, 2002; Oliver *et al.*, 2007; Strachan *et al.*, 2009) and Williams syndrome (WS, Jones *et al.*, 2000; Tager-Flusberg *et al.*, 1996).

Individuals with AS (the result of the loss of genetic information on the maternal chromosome 15) are described as being highly sociable, actively seeking interaction and maintaining adult interaction more successfully than comparable individuals without the syndrome (Oliver *et al.*, 2007). They also demonstrate a range of pro-social behaviours including excessive laughing and smiling (Horsler & Oliver, 2006). This is of significant theoretical interest as these behaviours provide support for theories that genomic imprinting can explain these phenotypic behaviours (Brown & Consedine, 2004, see section 1.3.2).

Natural observation studies have been used to examine social behaviour in genetic syndromes reported to have unusual social drive, such as AS. Oliver *et al.* (2007) observed children with AS at school over a number of hours, recording whether children were experiencing one-to-one attention, shared attention (adult attention is given to the participant and another child) or free-play (the participant receiving no adult attention). Child and adult social behaviours, such as smiling, looking and giving attention, were also recorded. Analyses indicated children with AS smiled more when receiving adult attention and initiated interaction more than the contrast group. Adult behaviour was also examined, enabling insight into the reciprocal nature of social interactions. Adult smiling also increased during interaction with children with AS. Examination of sequential analyses of interactions revealed that the child smiled first during interactions and that adult attention, adult smiling and eye contact were all more likely to occur after a child with AS smiled than by chance, a pattern not found in the contrast group. This supported assertions in the literature that children with AS are more likely to initiate social interactions with 'pro social' behaviours in order to solicit attentional resources from caregivers (Brown & Consedine, 2004), in line with predictions made from kinship theory (see section 1.3.2).

This methodology and the theoretical context is of interest when examining social functioning in SMS as it demonstrates a method for examining sequences of behaviour, which could enable identification of who initiates behaviour. In SMS children are reported to *seek* attention, thus in sequential analysis of behaviour it would be anticipated that they would initiate interactions more. Therefore natural observation methodologies and associated analyses have potential for application to a novel study of social behaviour of children in SMS in a similar setting.

In summary, problematic attention-seeking and difficult behaviour in conditions of reduced attention are purported to be features of the behavioural phenotype of SMS demonstrated particularly in the school environment. Such findings implicate a need to further investigate behaviour of children with SMS in this context in order to evaluate reports of atypical social behaviour, using objective and reliable assessments of behaviour.

The current study will examine social behaviour of children with SMS at school. Levels of attention and other socially relevant behaviours (looking, an index of attentional bias towards adults and affective responses, an index of enjoyment) directed towards adults and peers, will be examined to evaluate reports of increased preference for adult attention. Examination of sequences of behaviour will also be performed, using lag sequential analyses to enable evaluation of the nature of reciprocal interactions between adult and child²⁰ and also the association between adult attention and child behaviours such as looking and affective responses. These analyses are generally independent of factors such as overall amount of attention received from adults, which may differ as a function of schooling (special versus mainstream). Social behaviour of children with SMS will be contrasted to those with Down syndrome (DS). As discussed in section 3.5, DS is an appropriate contrast group for SMS given the similar profile of intellectual disability and expressive language deficits. In the context of reports of relatively strong functioning across a range of indices of social functioning contrasting social behaviour of these two superficially similar groups may provide insights into atypical social behaviour in SMS.

²⁰ How likely it is for adult directed attention from the child to be occurring when there is also child directed attention from the adult taking place, and vice-versa, and who initiates the interaction.

Given existing accounts of social behaviour in SMS the following hypotheses were developed:

- i) **Social preference:** Children with SMS will have greater preference for interacting with adults versus peers, therefore differences between adult directed attention from the child and peer directed attention from the child, and adult directed looking from the child and peer directed looking from the child, will be greater in SMS than in DS.
- ii) **Affect:** Children with SMS will show more positive affect when higher levels of attention are available and more negative affect when lower levels of attention are available. Therefore, more positive affect will be shown in one-to-one attention compared to shared attention and free play, and the effect of these conditions will be greater than in DS. Greater negative affect is expected in free-play and shared attention versus one-to-one attention, and again the effect of condition will be greater than in DS.
- iii) **Adult-child interactions:** Children with SMS will initiate and maintain interaction to a greater extent than those with DS. This will be reflected by adult directed attention from the child being shown earlier in sequences of interaction (i.e. before child directed attention from the adult occurs) and adult directed attention from the child being shown longer after child directed attention from the adult has ceased, than in DS. When analysing lags, before, during and after child directed attention from the adult occurs, this would result in an interaction between syndromes and lag, reflecting different patterns across time for the groups. As an exploratory complimentary analysis, sequence of interactions between adults and

children will examine how adults behave prior to, during and after child directed attention to the adult occurring.

- iv) Attentional bias: Children with SMS will show greater vigilance for adult attention. Thus they will look at adults with adults earlier in the sequence (i.e. before child directed attention from the adult occurs) than DS and will continue to look at the adult after child directed attention from the adult has occurred (thus maintaining interaction) than DS. This would result in an interaction between syndrome and lag.
- v) Affect: Children with SMS will show more positive affect during child directed attention from the adult than those with DS and will show increased negative affect after child directed attention from the adult has ceased, resulting in interactions between syndrome and lag for these analyses.

4.3 Methods

4.3.1 Recruitment

Participants were recruited from a sample involved in an existing research project (see section 5.3.2 for full details of this sample). Appendix G details the full recruitment process for the current study.

4.3.2 Participants

4.3.2.1 Demographic information

Ten participants with SMS and 10 with DS participated. Demographic details are shown in table 4.1. All participants with DS were reported to have confirmed diagnosis of trisomy 21, nine participants with SMS had chromosome 17p11.2 deletions, one had a gene RAI1 mutation.

Table 4.1 Gender (percent male) and mean chronological (standard deviation and range) and mental age (standard deviation) in each group

		SMS	DS
N		10	10
Gender	Number of males	4	5
	(%)	(40)	(50)
Age (Years)	Mean	9.98	9.10
	(SD)	(3.11)	(2.99)
	Range	5-15	4-13
Mental age ^b (Months)	Mean	48.13	52.32
	(SD)	(21.91)	(20.00)

^b Mental age estimates obtained from participation in previous study using either the *Wechsler Abbreviated Scale of Intelligence, WASI* (Wechsler, 1999) or the *Mullen Scales of Early Learning* (Mullen, 1995) depending on ability (see section 6.3.2)

Participants were comparable based on estimates of mental age derived from their participation in a previous study (see section 6.3.2 for full details). No significant differences in estimates of mental age or chronological age were found. Subsequent assessments of ability (using the Vineland Adaptive Behavior Scale II: classroom edition, Sparrow, Cicchetti & Balla, 2005) found no between-groups difference in raw scores on any subdomains.

4.3.2.2 Type of school

Nine of 10 children with DS attended mainstream schools, the remaining child attended a special school. In the SMS sample eight children attended special schools, one was at a mainstream school and one had a mixed placement²¹.

4.3.3 Measures

4.3.3.1 Measure of ability

Vineland Adaptive Behavior Scale II - Classroom Edition (VABS, Sparrow et al., 2005)

The Vineland Adaptive Behavior Scale - Classroom Edition is an informant report rating measure completed by teachers. It assesses four domains of adaptive behaviours; communication, daily-living skills, socialization, and motor skills. Scores for each of the four domains are combined to provide an adaptive behaviour composite score. The rating form is suitable for use with children aged over 3 years.

²¹ Attending special school in the morning and mainstream school in the afternoon.

4.3.4 Procedure

4.3.4.1 Testing and ethical considerations

The study was reviewed and approved by the ethics committee of the University of Birmingham.

Children were observed at school for the duration of one school day, typically from 9am to 3pm. The overall observation period ranged from 3.5 - 5 hours. Observations were carried out during the full range of school activities including classroom teaching (group and one-to-one sessions), outside classroom activities, transition periods and break times. Observations were carried out in 10 minute blocks and were stopped if there was potential for intrusion into children's privacy (e.g. during toileting). Teachers and support staff were asked to interact with children as they would typically. Researchers aimed to be as unobtrusive as possible, not interacting with the child.

Live coding was used to address concerns about privacy of other children in the classroom regarding the use of video. Researchers coded behaviour on a Hewlett Packard Jornada model 720 palm-held notebook, using the ObsWin32 software (Martin, Oliver & Hall, 2001), which enables real time coding of frequency and duration of operationally defined behaviours and environmental events. Researchers also recorded ratio of adults to children in the observational environment for each 10 minute observation block.

4.3.4.2 Real time coding procedure

Participant responses included child speech (words and utterances e.g. umm), non verbal gestures (e.g. pointing, nodding) and child initiated touching²². These behaviours were subsequently combined during analysis resulting in variables reflecting peer or adult directed attention from the child. Additional child variables included affect (positive and negative) and child looking (at adults or peers). Operational definitions of all coded behaviours and their inter-rater reliability Kappa coefficients (see section 4.2.5.3 below) are presented in appendix H.

Environmental events included child directed behaviours from the adult including speech, non verbal gestures and adult initiated touching. These were combined during analysis resulting in the variable of child directed attention from the adult. Adult directed attention from peers was not recorded as consent for direct observation had not been obtained.

Three settings were also recorded and are shown in table 4.2 below.

Table 4.2 Settings recorded in natural observations

Setting	Description
One-to-one attention	The child is receiving attention from an adult with no other child present
Shared attention	The child is receiving adult attention within a group setting where other children are present and also receiving attention
Free play	The child is not receiving direct attention from adult and is free to play without expectations from adults

²² Each behaviour was coded separately depending on whether the behaviour was directed towards the adult or peers.

4.3.5 Data analysis

Real time coding methods provide interval level data, appropriate for parametric analysis. The majority of data met parametric assumptions of normality of distribution and homogeneity of variance. A small number of Kolmogorov-Smirnov tests indicated that data deviated from assumptions of normality, however this test is believed to be a conservative estimate of normality and ANOVA is generally considered robust to violations of parametric assumptions (Maxwell & Delaney, 2004). Use of parametric analysis enables procedures such as analysis of covariance (ANCOVA) to be employed in order to control for potential confounds, thus parametric analysis, where possible, was deemed appropriate.

4.3.5.1 Between-groups comparisons of attention, looking and affect

Percentages of time that target behaviours and events occurred were calculated using ObsWin software. Difference scores were calculated for adult directed attention and looking from the child versus those directed towards peers²³ in order to obtain a single score representing preference (higher scores denoting greater preference towards adults). This score was expected to be linearly and positively related to ratios of adults to children present in the classroom, as increased ratio means more adults were available in the environment for interaction.

Difference scores for attention and looking were then analysed using 3 x 2 mixed ANCOVAs, with setting (one-to-one attention, shared attention and free play) and syndrome (SMS and

²³ By subtracting percentage of time a behaviour is directed towards a peer from percentage time directed towards adults.

DS) as independent variables and adult: child ratio as the covariate, to control for variability in adult child ratios.

Two further mixed 3 x 2 ANCOVAs for positive and negative affect (not directed towards a particular type of person, adult or peer) were also performed, with setting as the repeated variable and syndrome as the between-groups factor.

4.3.5.2 Adult-child interactions

Data were analysed to assess associations between child and adult behaviour. Yule's Q values, which describe strength of association between a criterion and target event, were calculated using ObsWin (Martin *et al.*, 2001). Yule's Q is analogous to a correlation coefficient, a value of 0 denotes no relationship between the criterion and target behaviours, +1 a strong positive relationship and -1 a strong negative relationship²⁴. Yule's Q values therefore represent the extent to which two variables (a criterion behaviour and a target behaviour) co-occur within a given time window (lag). Lags can be initiated from different points in the occurrence of the criterion variable. All variables were lagged from presence (where every interval that the criterion variable occurs is used to initiate lagging, Martin *et al.*, 2001) except for looking which was lagged from onset (when only the onset of the criterion variable is used to initiate lagging, Martin *et al.*, 2001) in order to clarify at what point it started given it is by nature an ongoing variable.

²⁴ As Yule's Q is measure of association, rather than statistical difference, its magnitude is independent of overall rates of the behaviours shown (unlike conditional and unconditional probabilities) which is crucial as those with SMS showed much higher levels of some behaviour overall therefore the unconditional probability is much higher (and so comparing the conditional probabilities of the two groups would be misleading).

Time based lag sequential analysis was used (Bakeman & Gottman, 1997), analysing sequential relationships for each participant by calculating probability of an environmental event (e.g. child directed attention from the adult occurring) within a 20 second epoch²⁵ for a child behaviour (e.g. adult directed attention from the child) for 60 before and 60 seconds after each event of interest (lag -3 to +3 respectively). Lag 0 represents the point at which the criterion variable occurs (for example the point at which child directed attention from the adult occurs). Mean Yule's Q values for all participants were calculated at each 20 second epoch and compared in mixed ANOVAs between-groups and across lags to evaluate effect of lag during the sequence, effect of syndrome and assess whether pattern of associations between target and criterion variables across lags differs between-groups (indicated by interactions). Analyses split sequences into three stages, *before* (-60s to -20s; lag -3 to -1), *during* (-lag 0) and *after* (+20 to +60s; lag +1 to +3) the criterion variable occurrence. Where assumptions of sphericity²⁶ (equality of variance between all possible pairs of groups in a repeated measures design), were violated Greenhouse-Geisser corrections (and associated corrected degrees of freedom) were used to address this violation.

Considering adult directed attention from the child as the target variable and child directed attention from the adult as the criterion variable, and vice versa, enables examination of reciprocal interactions between adult and child, i.e. how likely it is for a child to be giving attention to an adult when the child is receiving attention from the adult, and vice-versa.

²⁵ Twenty second epochs were chosen based on visual inspection of graphs of data at 5 second epochs which identified changes at these points.

²⁶ One of the assumptions of a repeated measures or mixed design with more than two levels of the within subjects variable

4.3.5.3 Inter-rater reliability

Inter-rater reliability was calculated for approximately 30% of the observations (24 hours in total). A second researcher was present for 6 of 20 visits and reliability observation periods were conducted live. Cohen's Kappa (Cohen, 1960) was calculated to control for influence of chance levels of agreement. Agreement was calculated using 10 sec epochs for presence of the target variable. Mean reliability of all variables was over .6, thus was 'good' according to Fleiss's definition (1981). Appendix H gives mean and range of Kappa for variables used in the analysis.

4.4 Results

4.4.1 Differences in schooling

As noted in section 4.3.2.2 more children with DS attended mainstream schools than those with SMS, potentially affecting the extent to which samples can be considered comparable.

Time children from each group spent in each condition is presented in table 4.3.

Table 4.3 Percentage time spent by children with SMS and DS in one-to-one attention, shared attention and free-play conditions

		One-to-one attention	Shared attention	Free play
SMS	Mean	24.423	49.639	27.206
	(SD)	(16.327)	(20.034)	(14.407)
DS	Mean	24.568	40.831	34.817
	(SD)	(10.977)	(11.035)	(13.769)

A 2 x 2 chi square analyses confirmed type of schooling (mainstream and special) was significantly different between groups ($\chi^2(2) = 12.80, p < .001$). Further analyses of ratios of adults to children throughout the school day suggested significantly smaller overall ratio of adults to children for SMS compared to DS ($t(18) = 5.525, p = .002$).²⁷

There were no between-group differences in amount of time spent in one-to-one attention ($t(18) = -1.208, p = .243$), shared attention ($t(18) = -.184, p = .856$) and free-play ($t(18) = 1.218, p = .239$), suggesting groups were comparable despite differences in schooling identified above.

²⁷ SMS had a mean adult child ratio of .5411, compared to .2336 in DS

4.4.2 Between-groups differences in child attention, looking and affect

4.4.2.1 Attention and looking

SMS and DS were compared in terms of differences between adult and peer directed attention and looking in each condition (one-to-one attention, shared attention and free play). Figure 4.1 below demonstrates the similarities of patterns of results for attention and looking preferences.

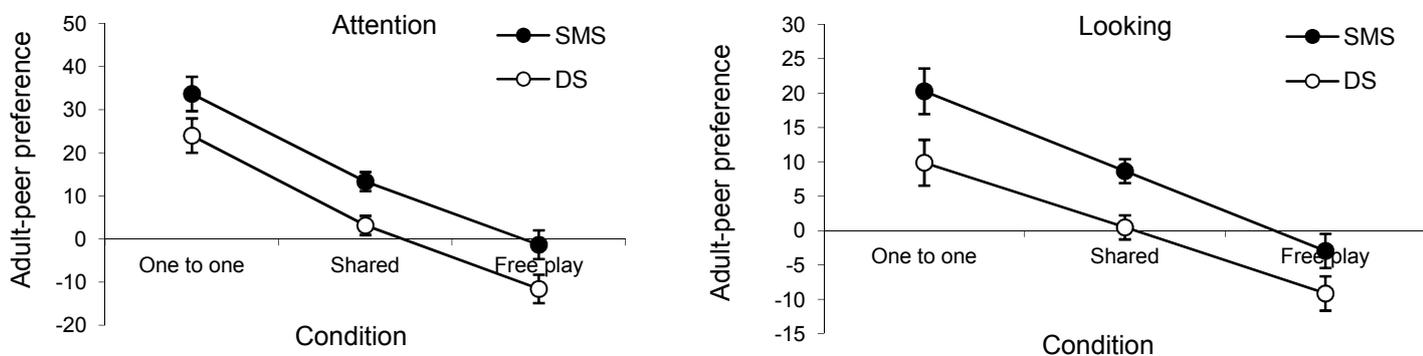


Figure 4.1 Preference values for adult and peer directed attention and looking from the child across conditions for the two syndromes (positive values represent adult preference, negative values indicate peer preference)

For attention a main effect of condition was found ($F(2, 16) = 25.617, p < .001$). Contrasts indicated that, as expected, preferential attention directed towards adults was greater in one-to-one attention than shared attention ($F(1, 17) = 24.707, p < .001$) and greater in shared attention than in free-play ($F(1, 17) = 5.836, p = .027$). There was also a main effect of syndrome ($F(1, 16) = 8.870, p = .008$), whereby SMS values were consistently higher, denoting greater preferential attention directed towards adults compared to DS, when overall adult:child ratio is partialled out. There was no interaction between syndrome and condition ($F(2, 17) = .004, p = .996$), thus pattern of differences between SMS and DS did not differ depending on setting.

For looking a main effect of condition was found ($F(2, 16) = 23.681, p < .001$), again contrasts showed preferential looking towards adults was greater in one-to-one attention than shared attention ($F(1, 17) = 21.315, p < .001$) and greater in shared attention than in free play ($F(1, 17) = 7.074, p = .017$). There was also a main effect of syndrome ($F(1, 16) = 7.583, p = .014$), with SMS having consistently higher scores, denoting greater preferential attention to adults, compared to DS. Lack of interaction between syndrome and condition ($F(2, 17) = 12.977, p = .698$) suggests pattern of differences between SMS and DS did not differ depending on setting.

These analyses therefore indicate that those with SMS showed greater preference for both directing attention and looking towards adults (over peers) across different conditions than those with DS did. For both syndromes preference towards adults was greatest in one to one attention and least in shared attention.

4.4.2.2 Affect

Children's affective responses in each condition were analysed (one-to-one attention, shared attention and free play), comparing those with SMS to those with DS.

Figure 4.2 illustrates the lack of effects for both positive and negative affect, with clearly overlapping error bars and also very similar patterns of negative affect for syndromes.

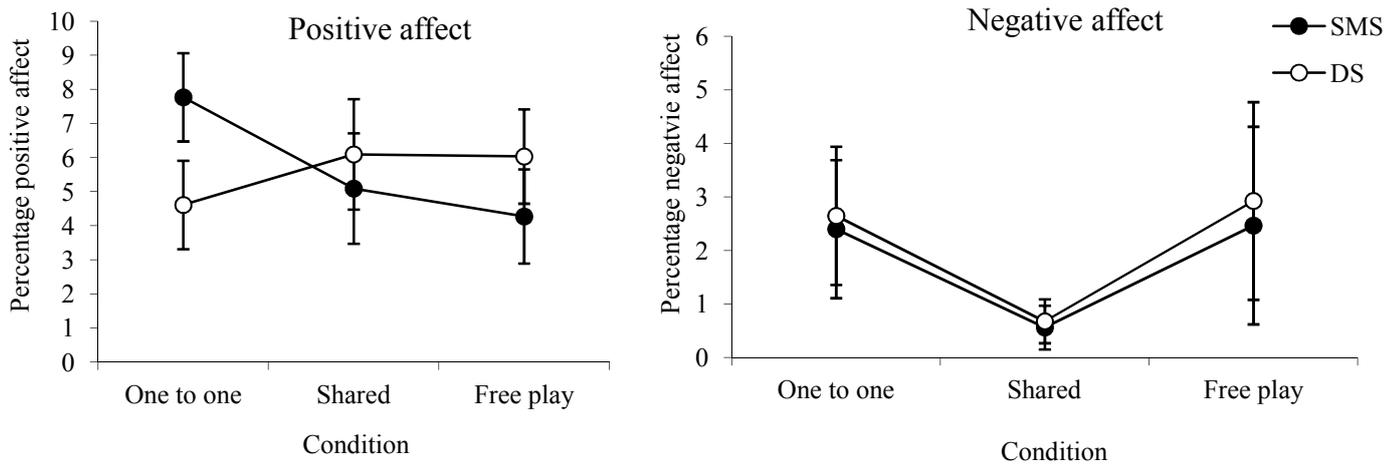


Figure 4.2 Between-groups differences in percentage time children showed positive affect and negative affect

No main effects of condition ($F(2, 17) = .143, p = .453$) or syndrome ($F(1, 18) = .007, p = .933$) were found for positive affect and there was no interaction between condition and syndrome ($F(2, 17) = 1.667, p = .204$). No main effects of condition ($F(2, 17) = 2.183, p = .128$) or syndrome ($F(1, 18) = .031, p = .863$) were found for negative affect and there was no interaction between condition and syndrome ($F(2, 17) = .0100, p = .990$).

Therefore, these analyses indicate lack of effects of either syndrome or condition on children's affective responses.

4.4.3 Adult-Child interactions

Two 3 X 2 ANOVAs were used for epochs before (lag -3 to lag -1) and after (lag 1 to lag 3) the criterion variable occurring, assessing whether groups show similar patterns of association between the variables of interest (interactions suggest different patterns) and also the effect of

time (differences across lags) and of group (differences in strength of association across syndromes). Differences in strength of association between the variables of interest at the point at which the criterion variable was occurring were assessed using t tests at lag 0.

4.4.3.1 Association between child directed attention from the adult and adult directed attention from the child

For both syndromes the association between child directed attention from the adult and adult directed attention from the child increased leading up to when the adult gave the child attention and then decreased following this point. There appears to be a consistently stronger association for the DS group compared to the SMS group, as illustrated in figure 4.3 below.

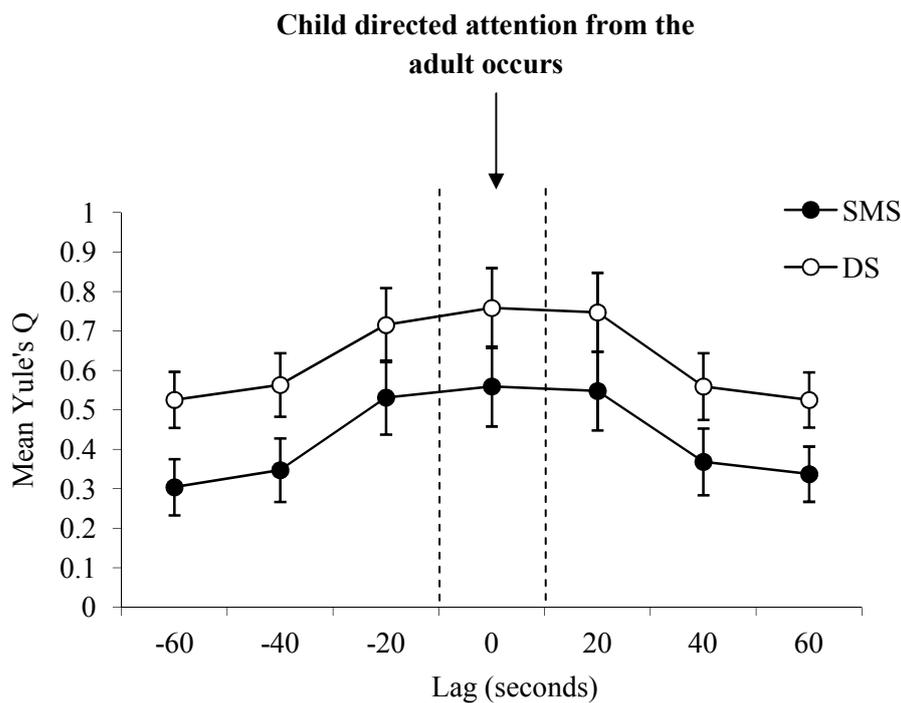


Figure 4.3 Association between child directed attention from the adult and adult directed attention from the child for the syndromes

Before child directed attention from the adult occurred there was a significantly stronger association overall for DS than SMS ($F(1, 18) = 5.458, p = .031$) and across syndromes the

association increased as occurrence of adult attention being given to the child approached ($F(1.246, 22.429) = 83.035, p < .001$). Syndromes groups did not show different patterns of association, only magnitude, denoted by lack of interaction ($F(1.246, 22.429) = .699, p = .443$). At the point when child directed attention from the adult occurred groups did not differ in strength of association, $t(10.855) = -1.870, p = .089$, equal variances not assumed), however after it occurred there was again a stronger association overall for DS than SMS ($F(1, 18) = 4.406, p = .05$) and across syndromes the association decreased the further away from occurrence of adults giving the child attention ($F(1.236, 22.257) = 57.066, p < .001$). Lack of interaction ($F(1.236, 22.257) = .035, p = .897$) again suggests that groups showed similar patterns of results.

The key findings from this analysis show that when child directed attention from the adult occurred the association between this and adult directed attention from the child did not differ between groups. However, both leading up to and after the point it occurred those with SMS showed a weaker association between the two variables than those with DS did. For both groups the association increased leading up to the point that child directed attention from the adult occurred and decreased afterwards, with these changes occurring at a similar rate for both groups.

4.4.3.2 Association between adult directed attention from the child and child directed attention from the adult

The association between adult directed attention from the child and child directed attention from the adult was consistently stronger for DS compared to SMS, as illustrated in figure 4.4.

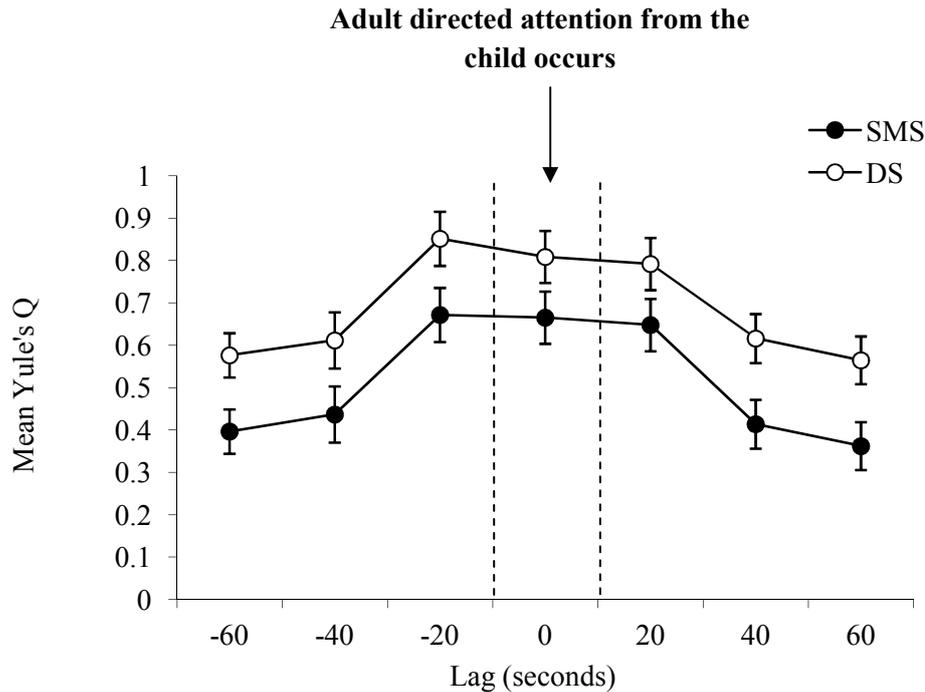


Figure 4.4 Association between adult directed attention from the child and child directed attention from the adult for the syndromes

Prior to the occurrence of adult directed attention from the child, the association between adult directed attention from the child and child directed attention from the adult was stronger for DS than SMS ($F(1, 18) = 4.871, p = .041$). Across groups this association increased as the point of adult directed attention from the child approached ($F(1.526, 27.462) = 61.332, p < .001$) and lack of interaction between lag and syndrome indicates patterns of increase did not differ between-groups ($F(1.526, 27.462) = .006, p = .995$). When adult directed attention from the child occurred no difference in strength of association was found between-groups ($t(18) = -1.649, p = .117$). After the occurrence of adult directed attention from the child the association between adult directed attention from the child and child directed attention from the adult decreased across groups ($F(1.325, 23.850) = 96.900, p < .001$) and this association was stronger overall for DS than SMS, ($F(1, 18) = 5.238, p = .034$). Rate of decrease was the same across syndromes, indicated by lack of interaction ($F(1.325, 23.850) = 1.493, p = .241$).

The main findings of this analysis therefore indicate that when adult directed attention from the child was occurring the association between this and child directed attention from the adult was the same for SMS and DS. However, both prior to and after its occurrence the association between the two variables was weaker in SMS than in DS. For both SMS and DS the association increased leading up to the point that adult directed attention from the child was given and decreased after, with no differences in the patterns of these changes found between groups.

4.4.3.3 Association between child directed attention from the adult and adult directed looking from the child

Overall there was a stronger association between child directed attention from the adult and adult directed looking from the child in DS than in SMS, as shown in figure 4.5, although overlapping error bars suggest variability in associations.

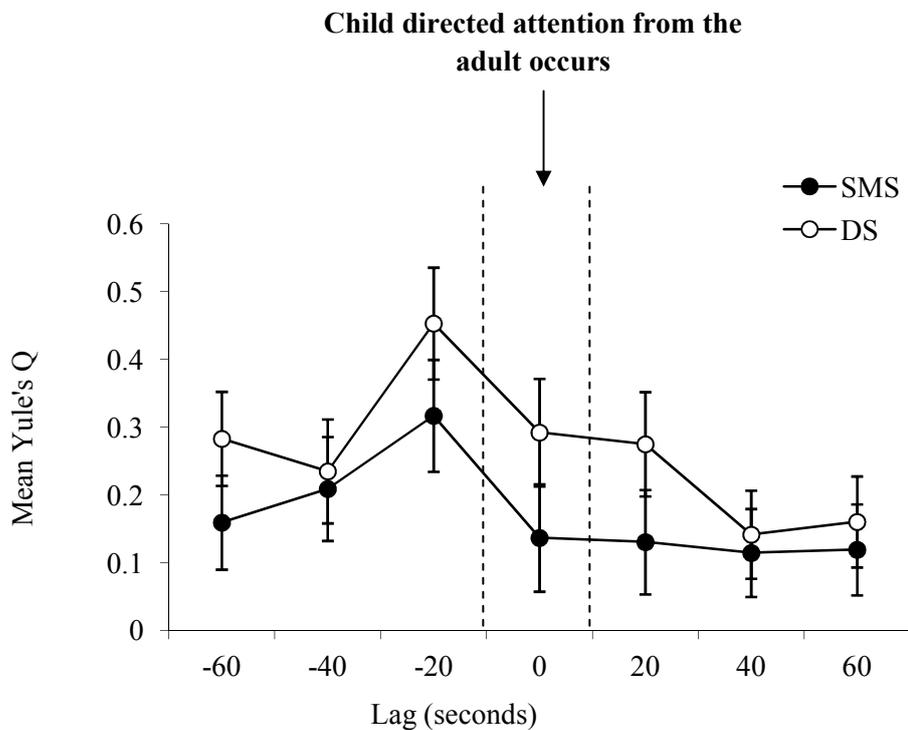


Figure 4.5 Association between child directed attention from the adult and onset of adult directed looking from the child for the syndromes

Before child directed attention from the adult occurred increases strength of association between onset of adult direct looking from the child at adult and child directed attention from the adult were shown across the groups ($F(2, 36) = 23.158, p < .001$). Groups did not differ in magnitude of this association ($F(1, 18) = .852, p = .368$) and a non significant interaction suggests pattern of associations did not differ between syndromes ($F(2, 36) = 2.369, p = .108$). At the point when child directed attention from the adult occurred the groups did not differ in strength of association ($t(18) = -1.387, p = .182$), however after it occurred DS showed decreases in strength of association not reflected by SMS. This difference in patterns is supported by a significant interaction ($F(2, 36) = 3.520, p = 0.040$).

Post hoc analysis of simple effects found no significant difference between groups at any lags; lag 1 ($t(18) = -1.327, p = .201$), lag 2 ($t(18) = -.294, p = .772$) or lag 3 ($t(18) = -.433, p = .670$). Within-groups analysis showed a significant decrease in DS between lags 1 and 2 ($t(9) = 4.207, p = .002$), but no difference between lags 2-3 ($t(9) = -.816, p = .435$). For SMS no significant differences were found between lags 1-2 ($t(9) = .498, p = .631$) or 2-3 ($t(9) = -.156, p = .880$).

No main effect of syndrome was found ($F(1, 18) = .559, p = .464$). A main effect of lag suggested that across groups the association decreases over time ($F(2, 36) = 5.532, p = 0.008$).

Overall this analysis suggests that both prior to and at the point that child directed attention from the adult occurred the association between this and adult directed looking did not differ

between SMS and DS, with the association becoming stronger leading up to the point attention was given. However, after its occurrence those with DS showed a decrease in association between the two variables which was not shown by those with SMS.

4.4.3.4 Association between child directed attention from the adult and affect

Positive affect

The syndromes showed similar magnitude and overall pattern of association between child directed attention from the adult and positive affect, as illustrated in figure 4.6.

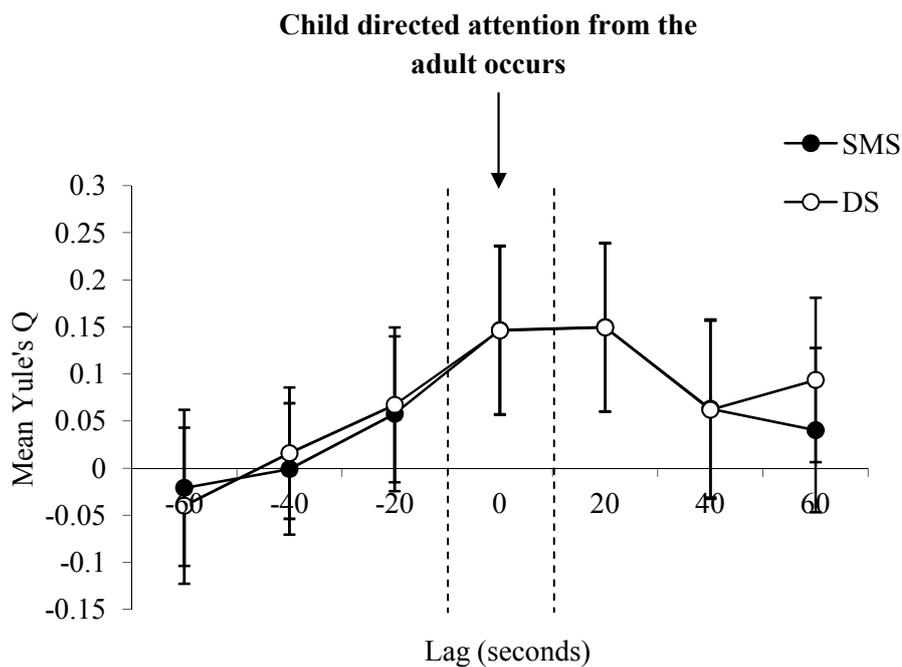


Figure 4.6 Association between child directed attention from the adult and child positive affect for the syndromes

Prior to child directed attention from the adult occurring an increase in strength of association between child directed attention from the adult and positive affect as the point at which child directed attention from the adult occurs was shown across syndromes ($F(1.429, 25.726) = 4.046, p = .042$). No differences in strength of association were found between syndromes ($F(1, 18) = .001, p = .982$) and absence of an interaction indicated that increases were consistent across groups ($F(1.429, 25.726) = .166, p = .775$). When child directed attention from the adult occurred strength of association did not differ between syndromes ($t(18) = .004, p = .997$). After it occurred the association decreased ($F(2, 36) = 5.287, p = .01$) but no between syndrome differences were found ($F(1, 18) = .020, p = .890$) and no interaction was found ($F(2, 36) = .539, p = .588$).

Negative affect

The two syndromes showed similar overall patterns of association between child directed attention from the adult and negative affect, as illustrated in figure 4.7. Overlapping error bars suggest lack of difference between-groups in strength of association.

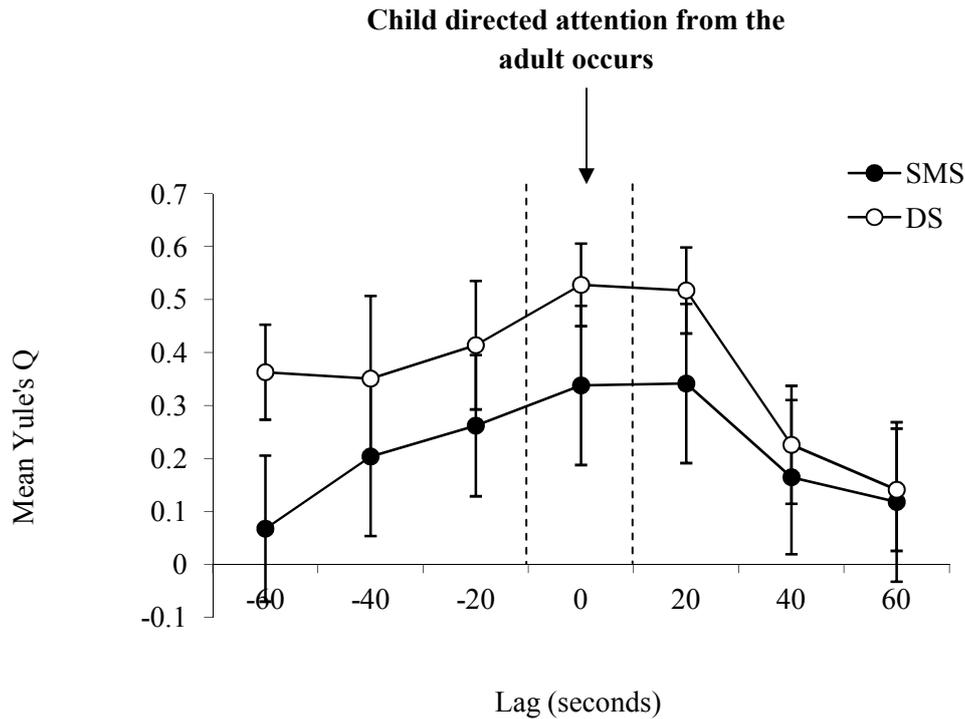


Figure 4.7 Association between child directed attention from the adult and child negative affect for the syndromes

Before child directed attention from the adult occurred there was no main effect of lag ($F(1, 18) = .996, p = .331$) or syndrome ($F(1, 18) = .036, p = .852$) on strength of association and no interaction between the two variables ($F(1, 18) = 1.001, p = .330$). Similarly when child directed attention from the adult occurred strength of association did not differ between-groups ($t(10.592) = -1.160, p = .267$ equal variances not assumed). After it occurred an overall decrease in association over time was found ($F(1.28, 23.127) = 13.911, p = .001$). Strength of association was the same for both groups ($F(1, 18) = .359, p = .556$) and absence of an interaction indicated patterns across times were the same for both syndromes ($F(1.28, 23.127) = 1.308, p = .276$).

Overall, these analyses suggest that for both positive and negative affect similar patterns of associations with child directed attention from the adult were shown by those with SMS and DS. The association became stronger leading up to the point attention was given and decreased after its occurrence.

4.4.3.5 Summary of sequential analyses

As expected, because variables were selected as they were anticipated to be related, for most analyses associations between criterion and target variables increased leading up to occurrence of the criterion variable and decreased after occurrence. Strength in association between child directed attention from the adult and adult directed attention from the child and vice versa were stronger in DS than SMS, both leading up when attention is given and after. This suggests adult and child behaviours were not as closely associated in SMS. However at the point attention is actually given no differences in association strength was found between syndromes. In contrast patterns of associations between child directed attention from the adult and affective responses did not differ across syndromes. Finally, initial decreases in association between adult directed looking from the child *after* child directed attention from the adult had occurred which were found in DS were not shown in SMS, suggesting prolonged looking in SMS.

4.5 Discussion

This is the first study to systematically observe social behaviour of children with SMS in schools, when interacting with both adults and peers and to contrast social behaviour directed towards these groups to evaluate preference. Use of a comparable contrast group, for whom mental age estimates were derived, suggests differences are unlikely to be artefacts of level of intellectual disability and enables evaluation of specificity of results to SMS. The study is also the first to examine sequences of behaviour in SMS to evaluate patterns of social initiation. Use of operationally defined, reliably coded behaviours and natural observation in schools, means that findings are likely to accurately reflect children's behaviour in their natural environment.

Reports that children with SMS have a strong preference for adult attention, over that of peers (see section 2.4.8.3) were supported in analyses of child directed attention and child directed looking. As hypothesised, children with SMS showed greater preference for directing attention to adults versus peers than children with DS and they also showed more preferential looking directed towards adults than DS (see section 4.4.2). This suggests strong preference for interactions with adults, evidenced by both looking at adults and giving them attention. This finding takes into account higher adult child ratio found in SMS classrooms, the result of the majority of children with SMS attending special schools, whereas most children with DS attended mainstream schools. This is unlikely to reflect difference in intellectual ability between groups, particularly as DS was a developmentally matched contrast group. It has been noted previously (Udwin *et al.*, 2001) that high rates of challenging behaviour shown in SMS may result in reduced adaptive behaviour which, together with social and emotional difficulties, can result in the requirement for special education (see section 2.3.2.3).

The practical importance of this preference for adult attention, particularly in an educational context, has been outlined previously by Haas-Givler (1994) and Haas-Givler & Finucane (1996) in the advice given to educators distributed by the American SMS support organisation Parents and Researchers Interested in Smith-Magenis Syndrome (PRISMS). It is noted that attention-seeking from adults shown by children with SMS can interfere with classroom activities (Haas-Givler, 1994). Furthermore challenging behaviour can arise when attention is unavailable (Taylor & Oliver, 2008). This is illustrated effectively by the following quote, “If I could provide constant, unwavering, one-on-one attention to this child throughout the day, she might never have another tantrum.” (Teacher of a child with SMS, cited by Haas-Givler, 1994, p. 36). It is notable in the only published direct observation study of behaviour in schools to date, by Taylor and Oliver (2008), all children received one-to-one adult support throughout the school day, yet despite this reductions in adult attention resulted in challenging behaviour. Clearly, maintaining constant attention is not achievable, either at school or home. Strategies for dealing with this elevated drive for adult attention may address challenging behaviour associated with reduced attention and the burden it places on those who care for and work with those with SMS.

The analysis took into account differences in classroom environment (greater number of adults and fewer children) in special needs schools, however there may be other qualitative differences in the classroom context and in adult interactions with children that cannot be controlled for statistically. Therefore, it is important to remain tentative when interpreting differences found in preference between children with SMS and DS. However, despite this limitation, this study provides initial empirical support for the preference for adult attention that has been suggested to be part of the behavioural phenotype since the earliest detailed

descriptions. Future research employing developmentally matched contrast groups also matched on schooling may address this potential confound.

In contrast to other syndromes associated with elevated drive for adult attention, increased positive affect was not found in SMS during social interaction. In AS increased smiling has been found when adult attention is available (see section 1.3.2). Oliver *et al.* (2007) described increased smiling in AS as an attention soliciting or maintaining behaviour. Whether smiling is considered to initiate interaction or as an index of enjoyment, it is clear that this behaviour was not elevated in SMS when children received social attention (i.e. in one-to-one and shared attention). It may be that increased preference to interact with adults may not be associated with increased enjoyment of their attention, a hypothesis explored in more detail subsequently.

Patterns of negative affect were noticeably similar across group, with comparable levels of negative affect shown in one-to-one attention and free-play and less in shared attention. This is contrary to the hypothesised increase in negative affect in situations with competition for attention (i.e. shared attention). Increased negative affect in one-to-one attention situations may be linked to increased demand from adults in these situations; children are most likely to experience one-to-one attention in school when an adult is working with them on academic work. Demands have been reliably found to be related to challenging behaviour, with a key function of challenging behaviour being escape from demand (Iwata *et al.*, 1994). It is possible that demands in one-to-one attention were aversive, resulting in increased negative affect. Negative affect shown in free-play may be attributed to responses to peers, such as challenges for access to tangible items during breaks (frequently noted informally by the

researchers during observations). Removal of preferred tangible items has also been associated with negative responses (Day, Rea, Schussler, Larsen & Johnson, 1988).

In addition to differences in overall levels of behaviour between the groups, differences in *sequences* of behaviour were found. Stronger associations between child directed attention from the adult and adult directed attention from the child and vice versa were found in DS compared to SMS, both prior to and after attention is given. This difference suggests behaviours of adults and children are more closely associated in DS, such that when child directed attention from the adult is occurring then adult directed attention from the child is also taking place and vice versa (i.e. there is greater reciprocity between adults and children in DS than SMS). During interaction no difference was found between-groups. Cues may become stronger immediately before and immediately after a person gives attention, prompting responses. Alternatively small sample size may have resulted in insufficient power to detect differences at this stage of interaction.

For adult directed attention from the child before and after and child directed attention from the adult occurred the weaker association between adult and child behaviours in SMS suggests that children were showing adult directed behaviours at times other than when child directed attention from the adult was occurring. Children with SMS may be less effective at responding the cues for initiating, maintaining and terminating interaction and they may be making overtures towards the adults at times when the adult is unavailable. Thus they may show adult directed behaviours at times that do not synchronize with adult behaviours towards them, explaining the reduced associations found. Physical constraints on communication and interaction may be an additional explanation, as those with SMS may be

more likely to fail to detect and reciprocate an adult interacting with them due to hearing impairment (Greenberg *et al.*, 1991; Greenberg *et al.*, 1996; Chen *et al.*, 1996). That the overall patterns of interactions were very similar across groups suggests the syndromes showed similar patterns of association between child directed attention from the adult and adult directed attention from the child across the sequence, failing to support the hypothesis that children with SMS would initiate interaction earlier and attempt to maintain it for longer than those with DS. This inconsistency is discussed subsequently in the context of additional findings regarding vigilance for adult attention.

It is somewhat surprising that adults also showed similar patterns of reduced association between child directed attention to the child before and after adult directed attention from the child. This suggests that adults respond less to cues that the child is initiating interaction, such that the adult makes initiations towards the child at times when the child does not respond. This may be linked to the previous explanation regarding children with SMS directing attention to adults at times when they cannot or do not respond, potentially reflecting deliberate strategies for dealing with attention-seeking behaviour (i.e. ignoring child initiations made at inappropriate times, an approach recommended by professionals working with those with SMS; Haas-Givler & Finucane, 1996).

No evidence was found supporting the hypothesis of hypervigilance before attention is given in SMS (in terms of earlier looking towards adults). There was some evidence suggesting children with SMS may show a less rapid decrease in looking after child directed attention from the adult ceases, than those with DS. Interestingly Mount, Oliver, Berg & Horsler (2011) also found children with AS did not try to establish eye contact with their mother more than a

stranger, but that once it was given they were more likely to try to maintain it with their mother than the unfamiliar adult. Therefore AS and SMS demonstrate similar patterns of maintaining, but not eliciting, eye contact with a preferred person (a familiar person in AS, an adult in SMS). It is unclear what the function of this eye contact is in either syndrome, whether it is an index of interest or functions to maintain interaction (for example after child directed attention from the adult has ceased in SMS). Alternatively in SMS specifically it may reflect lack of responsiveness to indicators of termination of attention from adults, such that children continue to look at them.

Overall findings relating to sequences of behaviour fail to support the hypothesis that children with SMS initiate interaction earlier than other children, or that they are more vigilant towards adult cues that they are going to provide attention, although they may maintain eye contact more than DS. This contrasts with suggestions that children with SMS *seek* more attention than other children (Dykens *et al.*, 1997, 1998; Feinstein & Singh, 2007; Haas-Givler, 1994), but does not directly contradict these. It suggests rather that any attention-seeking behaviours do not consistently start earlier in sequences of adult child interaction. Furthermore, findings that interactions between children with SMS and adults are less reciprocal suggest children make initiations at times when adult attention is unavailable, adults fail to respond to children's initiations or a combination of the two. This, combined with initial findings of greater preference for adults over peers, may support suggestions that children with SMS do seek attention from adults but possibly not always at appropriate times when attention is available.

Children with SMS also failed to show anticipated stronger association between child directed attention from the adult and positive affect at any stage of interaction. Increased association

before child directed attention from the adult occurred may have reflected positive affect functioning to solicit attention from adults, such as found in AS (see section 1.3.2). Lack of increased association at the point of child directed attention from the adult occurring suggests they did not derive greater enjoyment from adult attention than those with DS. Furthermore no difference was found between strength or patterns of association between child directed attention from the adult and negative affect in SMS and DS at any stage of interaction. This is inconsistent with expectations that children with SMS would find termination of attention more distressing than those with DS (whereby between group differences in association would be found *after* child directed attention from the adult was given). This was surprising as reduced attention has been associated with challenging behaviour in a diverse range of studies (see sections 2.4.8.2 and 2.4.8.3). Given this aversive nature of reduced attention it was expected to be associated with negative affect. Low power is particularly likely to have affected this result, however. Only eight children per group showed negative affect and there was relatively low incidence of negative affect overall, indicating this lack between group difference should be interpreted with caution.

As noted previously a key limitation of the current study is differences in schooling between the syndromes. While steps were taken to control for difference in numbers of adults and children in the classroom in analyses it is possible that other differences in schooling may have affected findings. Future research would also benefit from examination of peer behaviour, ethical constraints precluded direct examination of this in the current study (consent was not obtained from caregivers of all class members). Additionally, whilst the current study doubled the sample size of the only previous study to directly examine social behaviour in SMS, the sample size was still relatively small which may have reduced power

for some between syndrome contrasts. Future research would therefore benefit from a larger sample.

In summary, results indicated that in terms of directing their attention children with SMS show greater preference towards adults (compared to peers) than those with DS. Furthermore, children with SMS appear to show a weaker association between adult and child behaviours leading up to and after the point that attention is given than those with DS. This could indicate a less organised relationship between child and adult behaviours, possibly a result of children with SMS showing social behaviours that initiate social interaction at times when it is unavailable.

CHAPTER 5

Effect of adult familiarity and level of attention on social behaviours in Smith-Magenis syndrome

5.1 Preface

The study in chapter four used natural observations to examine social preferences and sequences of interactions in SMS to evaluate reports of unusual social drive characterised by seeking adult attention. Results indicated that children with SMS had a greater preference for interactions with adults (versus peers), supporting findings of unusual social preferences presented in chapter two. However, children did not appear to seek attention by initiating interactions at an earlier stage than a contrast group. The present study aims to extend these findings using experimental manipulations of social situations to examine social drive. Manipulations of adult familiarity will further delineate the social preferences identified in chapters two and three and manipulations of available attention will provide insight into children's response to reduced levels of adult attention.

5.2 Introduction

As noted previously (section 2.4.8.3) only one study to date has directly examined social behaviour in Smith-Magenis syndrome (SMS), using natural observations of behaviour in schools. In this study challenging behaviour was preceded by low levels of adult attention. The authors suggested this indicated an interaction in SMS between a genetically predisposed strong drive for adult contact and operant reinforcement of challenging behaviours by the presentation of social contact contingent on such behaviour (Taylor & Oliver, 2008). However, lack of experimental manipulation precluded examination of causal relationships. Experimental manipulation of environmental variables is crucial to examine factors purported to be related to unusual social behaviour in SMS. Quantification of behavioural responses to manipulations of these variables would enable evaluation of their effects, contrasting these responses to those shown by a different syndrome group would enable examination of specificity to SMS. This would address limitations noted previously that descriptions of social behaviour in SMS are based primarily on informant report measures and anecdotal accounts (see section 2.4.8.2).

As noted in the preface to chapter four, methodologies used with other genetic syndromes can inform approaches to examining social behaviour in SMS. In Angelman syndrome (AS) social behaviour has been studied using both natural observations of behaviour (as discussed in section 4.2) (e.g. Oliver *et al.*, 2007) and also experimental manipulations similar to the functional analytic methods devised by Carr and Durand (1985). Strachen *et al.* (2009) used this latter method, systematically altering the level of attention available in five minute episodes. Children's responses were coded using real time coding. Results showed increased aggression and evidence of positive affect in the high attention condition, indicating that aggression might both maintain and initiate social contact in AS.

Further examination of strong social drive in AS examined the familiarity of the adults with whom children are motivated to interact. Mount *et al.* (2011) also used structured social situations, manipulating both level of attention available and the familiarity of the person it was available from. Children were observed during social interactions with their mother or an unfamiliar adult, and the level of speech and eye contact from these adults was manipulated. While no effect of adult familiarity was found on child eye contact or smiling, they approached their mother more than an unfamiliar adult. The authors speculated increased approach behaviours towards mothers may serve to increase investment from caregivers, thus supporting the kinship theory of genomic imprinting in AS (see section 1.3.2).

Similar manipulations have been used to examine social drive in Williams syndrome (WS), where ‘hypersociability’ is reported. Jones *et al.* (2000) examined social behaviour in children with WS using the Parental Separation task from the LabTab (Goldsmith & Rothbart, 1992), in which children play with parents for a period of time, then the parent leaves, returning to the child after a short time. Affective responses were coded and results indicated children with WS showed less negative affect in response to parental separation and, importantly, in response to reunion (typically developing children showed initial negative affect at reunion). This suggests children with WS were more readily sociable on their parent’s return than chronological or developmental age matched typically developing children.

The studies described above demonstrate the utility of experimental methods for evaluating strong social drive in genetic syndromes. The need for robust methods of assessing behaviour in research investigating social behaviour in genetic syndromes has been emphasised (Oliver *et al.*, 2007). To advance understanding of social functioning in SMS, similar research, examining effects of manipulating key variables in controlled situations and with appropriate contrast groups is necessary. As social attention is an environmental variable associated with

challenging behaviour in SMS (and “attention-seeking” is frequently reported as problematic, see section 2.4.8) the need for increased understanding of factors affecting social functioning is evident.

The principal aim of the current study was to examine difference in social behaviours shown by individuals with SMS versus Down syndrome (DS) during social interactions with adults, to evaluate reports of uniquely elevated attention-seeking in SMS and specificity of this to familiar adults. The study aimed to examine the effect of adult familiarity by exposing children to social situations with an adult providing high levels of interaction, where this person was either their mother or an unfamiliar adult. In addition to this *interacting* adult, an *unresponsive* adult was present during interactions to introduce a competing potential source of attention which is consistently unavailable. It was anticipated this would elicit a greater range of behavioural responses (e.g. initiations towards the unresponsive adult when already receiving attention from the interacting adult, responses to denial of attention and attempts to interact with the unresponsive adult as an alternative source of attention when the interacting adult is unavailable). A further aim was to examine the influence of levels of available attention on behaviour by structuring observations to include conditions of high attention (interacting adult is in the same room as the child) and low attention (interacting leaves the room for a period of time).

Behaviours of interest were those independent of adult initiations and those shown in response to adult behaviours. Child initiated behaviours (independent of adult initiations) included social motivation (behaviours used to elicit social interaction) and affect (indicative of level of enjoyment of a situation). These behaviours were examined using a combination of real time coding of frequency and duration of occurrence and also rating scales which enable examination of more qualitative aspects of behaviour. Adult dependent behaviours, shown in

response to adult behaviours or close adult proximity, include avoidance of interaction, nature of eye contact and responsiveness to adult social overtures. These behaviours were examined using rating scales that capture the nature of interactions and interplay between adult and child behaviour, which real time coding may miss. Examination of communicative behaviours (e.g. verbalisations) is not presented for the current sample as there were more children with SMS than DS described by caregivers as non verbal (five in SMS and none in DS).²⁸ Furthermore communication may be considered an index of skills or ability to a greater extent than the behaviours associated with motivation and responsivity described above.

It was hypothesised that individuals with SMS and DS would demonstrate divergent profiles of social behaviour. Separate hypotheses were generated for effects of adult familiarity and available attention. Predictions were made about between syndrome differences in magnitude of within syndrome differences in behaviours shown at each level of the variables (familiarity, attention) to examine syndrome specificity of effects. Where significant differences are found post hoc analyses, with no formal hypotheses, will enable assessment of underlying patterns of differences in absolute levels of behaviour.

Effect of adult familiarity (in both high and low attention unless stated)

Child initiated behaviours

It was hypothesised that:

- i. Children with SMS would show greater motivation to access attention of familiar adults, demonstrated by more behaviours indicative of motivation to initiate interaction with their mother compared to an unfamiliar adult, than those with DS. It

²⁸ Because of this potential bias these behaviours are not discussed here, however language age equivalents on the VABS were comparable (see table 5.1) therefore results of exploratory analyses of these behaviours are presented in appendix N for reference.

was therefore predicted that the difference between these behaviours towards their mother and those towards an unfamiliar adult would be greater in SMS than DS, for both the interacting and unresponsive adult.²⁹

- ii. Children with SMS would show more behaviours indicative of positive affect in interactions with their mother than an unfamiliar adult, compared to children with DS. Thus, it was predicted that the difference in affect shown between interactions with their mother versus an unfamiliar adult would be larger in SMS than in DS.

Adult dependent behaviours

No hypotheses for behaviours dependent on adult behaviour, proximity or the availability of non-social stimuli (avoidance of social interaction, responsiveness, eye contact and focus of attention: adult versus object) were made. Reports of social behaviour in SMS clearly implicate motivation and affect as behaviours likely to be affected by familiarity, there is little to guide expectations of patterns of these other types of behaviour. Exploratory analyses therefore aimed to identify potential differences in these behaviours across levels of familiarity.³⁰

Effect of attention (with both mother and unfamiliar adult unless stated)

Child initiated behaviours

It was hypothesised that:

- i. Children with SMS would show greater motivation to access adult attention in low attention conditions than those with DS. It was therefore predicted that the difference

²⁹ For *ratings* this behaviour was only rated in low attention for the interacting adult (as in high attention their attention is not unavailable so the rating item which related to motivation to unavailable attention cannot be evaluated).

³⁰ Avoidance and responsiveness were only coded for the interacting adult (the unresponsive adult did not initiate interaction), thus effects of familiarity cannot be examined.

between motivation in low versus high attention would be greater in DS than in SMS (with high motivation in low attention in SMS reducing magnitude of difference between conditions).³¹

- ii. Children with SMS would be more sensitive in terms of affective responses to reduced attention, showing more positive affective responses when attention was available than when it was unavailable, than those with DS. It was therefore predicted that the difference between behaviours indicative of affect shown in high versus low attention would be greater in SMS than in DS.

Adult dependent behaviours

For reasons outlined regarding effect of adult familiarity, no hypotheses were generated for avoidance of social interaction, responsiveness, eye contact and focus of attention³²

³¹ For *ratings* of behaviour shown towards interacting adults predictions of effect of attention cannot be made as motivation was only rated in low attention.

³² For the interacting adult, eye contact, responsiveness and avoidance can only be shown in high attention and motivation can only be shown in low attention therefore the effect of attention cannot be assessed. Additionally, avoidance and responsiveness can only be shown towards the interacting adult as they require the adult to initiate interaction.

5.3 Methods

5.3.1 Recruitment

Participants were recruited from family support groups and an existing participant database. Family support groups were the main UK based support groups; the Smith-Magenis Foundation UK and the Down's Syndrome Association³³. The existing participant database consisted of families who had previously taken part in research with the Cerebra Centre for Neurodevelopmental Disorders based at the University of Birmingham, who expressed an interest in participating in future research projects. Opt in consent was gained from caregivers following processes outlined in appendix E. Inclusion criteria required children to have confirmed diagnosis of the genetic syndrome.

5.3.2 Participants

Table 5.1 describes the demographic characteristics of the sample. A total of 22 children with SMS and 21 children with DS were recruited. This final sample represents the total number of children (under 16 years at projected time of testing) with SMS for whom families returned consent forms (sent to them after their returning expressions of interest) within the recruitment timeframe of one year (following the procedure outlined in appendix E). Given the large recruitment timeframe and the inclusion criteria of being under 16 years reducing potential number of participants in a population of an already rare syndrome group, this was judged to be an adequate representation of the number of families willing to participate in the current research. Participants with DS were recruited until a comparable sample size was achieved. One child with SMS could not be assessed due to high levels of challenging behaviour, resulting in a final sample of 21 children with SMS. Twenty children with SMS

³³ Contact was made through affiliated local support groups.

were reported to have a deletion on chromosome 17p11.2, one had a mutation of gene RAI1. All children with DS were reported to have trisomy 21.

Participants were comparable in terms of chronological age, gender and estimates of adaptive behaviour (as a proxy measure of intellectual disability, obtained using the Wessex scale self help scores; Kushlick *et al.*, 1973) as indicated in table 5.1. Unsurprisingly, the SMS sample had a significantly higher mean score on the Autism Spectrum Disorder (ASD) screening measure (SCQ, Rutter *et al.*, 2003).

Table 5.1 Mean age (standard deviation) and range, gender (percent male), mean adaptive functioning scores (standard deviation), SCQ scores (standard deviation) in each syndrome group

		SMS	DS
N		21	20
Age (Months)	Mean	92.52	89.88
	(SD)	(56.37)	(35.59)
	Range	31-190	39-158
Gender	Number of males	12	10
	(%)	(57.14)	(52.38)
Adaptive functioning ^a	Mean	6.05	6.85
	(SD)	(1.80)	(1.14)
SCQ	Mean	17.16 (n = 14)	8.49 (n = 18)
	(SD)	(6.96)	(4.33)
VABS Expressive language age equivalent (Months)	Mean	33.5	32.20
	(SD)	(13.39)	(24.34)

^a Assessed using the self help subscale of the Wessex scale, as a proxy measure of intellectual disability (see section 3.3.2.2).

5.3.3 Measures

5.3.3.1 Demographic information

A demographic questionnaire (see appendix F1) was used to obtain details of participant characteristics (see section 3.3.2.1 for further details).

5.3.3.2 Measures of ability

The Wessex scale (Kushlick et al., 1973)

The Wessex scale (see appendix F2) is an informant report measure of level of adaptive behaviour, gathered as a proxy measure of intellectual disability, in children and adults with intellectual disability. A full description of this scale can be found in section 3.3.2.2.

Vineland Adaptive Behavior Scales – Interview edition, Survey form; VABS II -SF, Sparrow, Chicchetti & Balla (2005)

The Vineland Adaptive Behavior Scales consists of 261 items which form four domains (and sub domains noted in brackets) measuring adaptive behaviour; Communication (receptive, expressive and written), Daily-living skills (personal, domestic, community), Socialisation (interpersonal relationships, play and leisure time, coping skills) and Motor skills (fine and gross). The measure can be used to assess children with and without intellectual disabilities. It is administered as a semi structured interview with carers, asking open-ended questions to elicit information about the child. Scores represent what children habitually do, ranging from 0 (never) to 2 (usually). Standard and age equivalent scores can be derived for each domain and the composite score (age-equivalents are calculated for each sub-domain). The scales have high test-retest (.98-.99) and inter-rater reliability (.80-.98) and internal consistency for each domain is good (.83-.94) (Sparrow *et al.*, 1984).

5.3.3.3 Measure of ASD phenomenology

Social Communication Questionnaire (SCQ, Rutter et al., 2003)

The Social Communication Questionnaire (see appendix F3) is a screening tool for ASD. Full details of this measure are found in section 3.3.2.3.

5.3.3.4 Direct observation measures

Levels of attention were manipulated using a protocol based on the Parental Separation task from the LabTab (Goldsmith & Rothbart, 1992), a battery of tasks developed to assess temperament in children using realistic situations. In the original task mother and child play with toys, the mother then tells the child to stay and play and that she will be back soon. The mother then leaves, returning after 30 seconds.

For the current study this task was extended to include an episode of separation from an unfamiliar adult, to examine effect of adult familiarity on behaviour. A second adult was also introduced into the testing environment, in view of the child but instructed not to interact to expand potential behavioural responses of the child (see section 5.2). Thus each adult can either be an *interacting* or an *unresponsive* adult. To give the child opportunity to approach the unresponsive adult and to optimise likelihood of responses in older children, time left playing alone was extended.

Conditions were three minutes long, with six conditions in total, designed to run concurrently. Table 5.2 summarises the conditions. Testing was repeated three times, as recommended in the LabTab manual, to account for temporal variation in behaviour.

Table 5.2 Experimental conditions employed in observations

Condition	Interacting adult	Level of attention	Unresponsive adult	Adult behaviour
Mother plays	Mother	High	Unfamiliar adult	Mother engages the child in free play (unresponsive unfamiliar adult present in the room but unresponsive)
Mother leaves	Mother	Low	Unfamiliar adult	Mother leaves the room (unresponsive unfamiliar adult remains in the room)
Mother returns	Mother	High	Unfamiliar adult	Mother returns, reengaging the child in free play (unresponsive unfamiliar adult still present)
Unfamiliar adult plays	Unfamiliar adult	High	Mother	Unfamiliar adult engages the child in free play (Mother stops playing, is present in the room but unresponsive)
Unfamiliar adult leaves	Unfamiliar adult	Low	Mother	Unfamiliar adult leaves the child (unresponsive mother remains in the room not interacting with the child)
Unfamiliar adult returns	Unfamiliar adult	High	Mother	Unfamiliar adult returns, reengaging the child in free play (unresponsive mother still present)

If the child approached the interacting adult low attention conditions or the unresponsive adult in any condition the adult was instructed to verbally indicate they were busy, instructing the child to return to playing alone. To control for order effects, the order of which adult played with the child first was alternated and counterbalanced across participants.

5.3.3.5 Testing materials

The mother was asked to provide toys she felt would engage the child and encourage social interaction. Observations were recorded on a Sony TRV-48E handheld camera.

5.3.4 Procedure

5.3.4.1 Testing and ethical considerations

To maintain a consistent environment, participants were encouraged to remain in one room during testing. Procedures for dealing with children leaving the room or showing challenging behaviour in response to experimental manipulations are detailed in appendix I.

Ethical review was obtained from the University's ethics committee.

All but one of the participants were observed in their home environment (the remaining participant was observed in school). Testing episodes were filmed with the camera operator instructed to be inconspicuous but to provide prompts to adults.

5.3.4.2 Exclusion of off protocol episodes

Integrity of experimental manipulations was evaluated by examining adult and child behaviours indicative of divergence from the protocol or potential confounds. Low attention conditions where adult verbalising to the child exceeded a cut-off were excluded. Similarly, conditions where prolonged episodes of challenging behaviour or negative affect were shown which were determined to be unrelated to the experimental manipulation (e.g. response to denials related to accessing tangibles or leaving a particular room), or where challenging behaviour or negative affect was continued from a previous condition, were also excluded to avoid these off protocol events exerting an undue influence on coding/rating.

Appendix J (flowchart) details the decision making process for excluding off protocol episodes and the number of excluded conditions for each syndrome group.

5.3.4.3 Real time coding procedure

Behaviour was coded using ObsWin 32 software (Martin *et al.*, 2001), a real time coding software package that enables operationally defined behaviours to be recorded in terms of frequency and duration. Inter-rater reliability of behaviour definitions was calculated for 15%

of the total sample across groups. Kappa values for variables based on 5 second intervals ranged from 0.58-1 (mean = .83) indicating good inter-rater reliability (Fleiss, 1981). For operational definitions of all behaviours coded and associated Kappa coefficients see appendix K.

Several individual variables were combined, creating a composite variable labelled physical initiation (child approaching adult, touching adult, reaching to adult). Subsequently, two broad composite outcome variables were derived. Motivation (physical initiation, looking and the inverse of avoidance directed towards the adult) assessed behaviours indicative of desire to initiate and maintain social interaction. Affect (child positive affect and the inverse of negative affect) evaluated children's valenced affective responses to the current social situation.

5.3.4.4 Behavioural rating procedure

Rating scales were used to capture more qualitative aspects of social behaviour. Inclusion of additional variables similar in nature to real time behaviour codes enables examination of concurrent validity of the scales. Rating scales were based on The Child Sociability Rating Scale (CSRS, Moss *et al.*, in press), developed to assess behaviours and skills associated with social functioning in children with intellectual disability.

Four scale items referred to general behaviours (positive affect, negative affect, frequency and severity of challenging behaviour), eight referred to behaviour directed towards the interacting adult (frequency of spontaneous physical, spontaneous initiation of interaction, motivation for adult engagement, avoidance of social interaction, social responsiveness, focus

of attention, nature of eye contact and frequency of eye contact)³⁴ and four related to behaviour towards the unresponsive adult (motivation for adult engagement, focus of attention, nature and frequency of eye contact)³⁵. See appendix L for a copy of the full scales.

A number of individual items were combined to create composite variables; affect (positive affect and the inverse of negative affect) and motivation (spontaneous initiation of interaction and spontaneous initiation of physical contact). Remaining variables stayed as single items. The two eye contact items were rescaled to become one variable scored from 0-4 in line with other items, by multiplying the items together and rescaling (using the criteria of: 0=0; 1-4 =1; 5-8=2; 9-12=3; 13-14=4). Two items regarding frequency and severity of challenging behaviour were removed from analyses due to their low frequency (challenging behaviour including self injury, aggression and destruction were present in just .56% of SMS and .12% of DS conditions).

Inter-rater reliability of ratings was calculated for 20% of the total sample across groups using Spearman correlations between ratings for all original variables. Spearman's rho values ranged from .42-.85 (mean = .65) indicating moderate to strong correlations between ratings. Appendix M details reliability for each item. To assess concurrent validity between objective real time coding and the more subjective rating scales, Spearman's correlations were carried out between the measures. Moderate to strong associations, from .4 to .7, were found for relevant items on the rating scales and frequency of observable behaviours (mean = .55). Individual correlations are shown in appendix M.

³⁴ Items assessing responses to adult initiated interaction were not rated towards the responsive adult in interacting adult leaves condition. Motivation for adult engagement was only rated for the interacting adult in the adult leaves condition as it evaluated efforts to access unavailable attention.

³⁵ Behaviours directed towards the unresponsive adult were coded in all conditions, as they did not require adult initiations of interaction. Motivation was used as the sole item assessing initiation as it reflected efforts to access unavailable attention.

5.3.5 Data analysis

Ratings across the three repeats were averaged to produce a mean rating of variables for each child. For both coding and rating, these data were found to be highly non-normally distributed. Therefore non-parametric, Mann Whitney U tests were used throughout.

To assess effect of familiarity (mother versus unfamiliar adult) and level of attention difference scores were calculated by subtracting the percentage duration of behaviours in one level of the condition from the other. This enabled the magnitude of differences between conditions to be compared across groups, allowing non-parametric examination of effect of syndrome group on size of differences between conditions. As no differences were found in either rating or coding of behaviours in the mother plays/unfamiliar adult plays condition compared to those in the equivalent mother returns/unfamiliar adult returns conditions, these conditions were collapsed. The mean of the two conditions was calculated, resulting in a single 'mother present' and 'unfamiliar adult present condition' – reducing the number of potential comparisons required and potential for type one errors. Comparisons were carried out separately for interacting and unresponsive adults.

Where significant differences were found for these 'difference' scores, they were subjected to post hoc analyses (Wilcoxon comparisons for within groups comparisons and Mann Whitney for between groups analysis). Comparisons were made between and within-groups at each level of the variables. Alpha was set at ≤ 0.01 for these follow up analyses due to the number of comparisons conducted. One tailed analyses were used for analyses where a priori directional hypotheses were specified and thus anticipated direction of effects was already stated. Given the potential for low power when using non parametric analyses, the relatively small sample size and the clinical implications of the issues being examined it was felt this approach was appropriate for detecting these clinically significant behaviours.

The unfamiliar adult was found to give higher levels of attention than the mothers in the study, however as analyses primarily compared magnitude of differences between these two adults across syndromes this was not considered to be an issue for the analyses used here.

5.4 Results

5.4.1 Effect of adult familiarity

5.4.1.1 Child initiated behaviours

To test hypotheses that those with SMS would show greater motivation to access attention of, and greater enjoyment of interaction with familiar adults the magnitude of differences between these behaviours directed towards mothers and the unfamiliar adult were compared across groups. No significant between-syndrome differences were found when examining behaviours shown towards mothers compared to the unfamiliar adult, when they were the interacting adult³⁶.

However for the unresponsive adult, patterns of differences in motivation shown towards mothers compared to the unfamiliar adult differed significantly between syndrome groups. In high attention both coding and rating demonstrated significant between syndrome differences in patterns of motivation for the attention of the unresponsive adult when it was the child's mother compared to the unfamiliar adult. The similarity of the pattern of differences for both coding and rating outcome measures, characterised by relatively high motivation for the mother's attention in SMS when in high attention, is shown in figure 5.1.

³⁶ For either outcome measure; coding or rating.

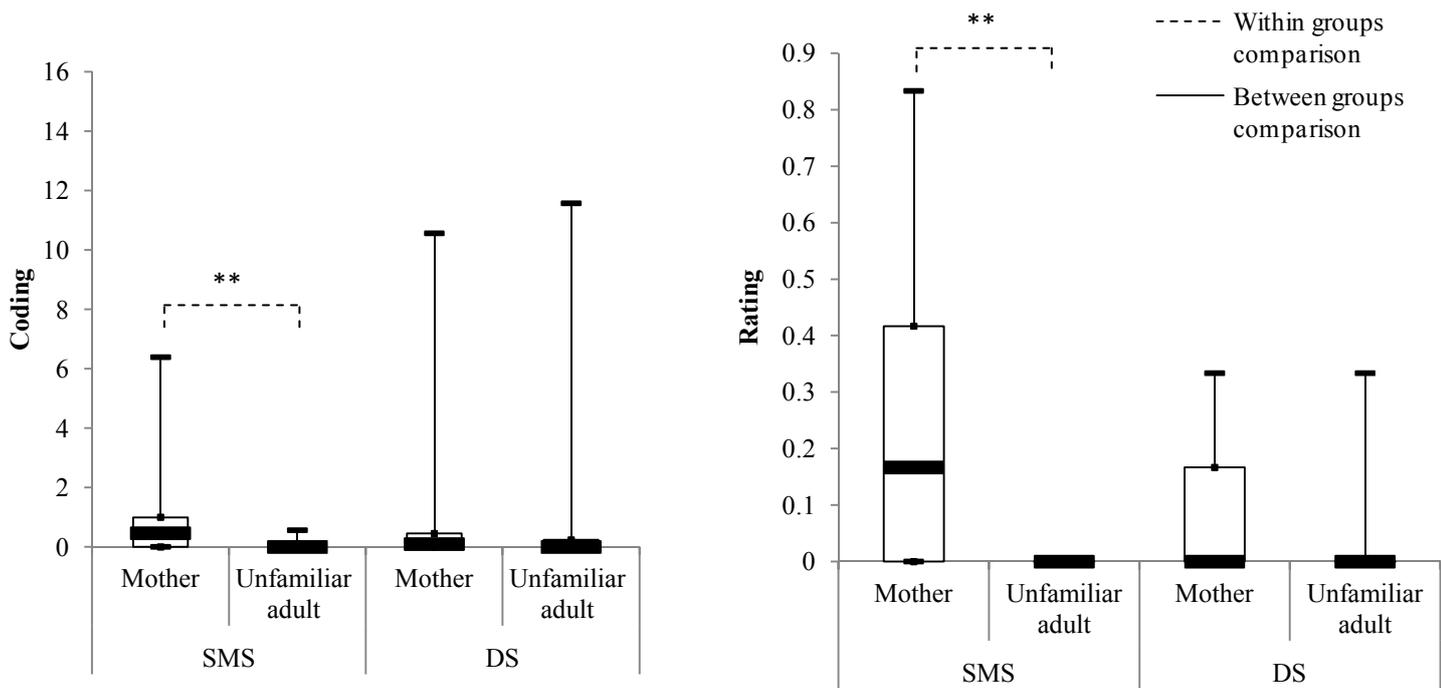


Figure 5.1 Coding and rating of motivation shown towards mothers and unfamiliar adults in high attention conditions by the syndrome groups (* $p \leq .01$, ** $p \leq .001$)

Those with SMS showed a greater difference between mothers and the unfamiliar adult than those with DS (coding $U = 121$, $p = .005$, one tailed, rating $U = 111$, $p = .001$, one tailed). Post hoc analyses indicated that SMS and DS did not differ in terms of motivation to access attention of either their mother (coding $U = 175.5$, $p = .351$, two tailed, rating $U = 126$, $p = .016$, two tailed) or the unfamiliar adult (coding $U = 177.5$, $p = .304$, two tailed, rating $U = 168$, $p = .048$, two tailed) when they were receiving high attention from another adult. However, while analyses of within syndrome differences found no difference between motivation for mothers' compared to unfamiliar adults' attention in DS (coding $z = -.105$, $p = .944$, rating $z = -.612$, $p = .279$, two tailed), SMS demonstrated less motivation when the unresponsive adult was the unfamiliar adult than when it was their mother (coding $z = -2.945$, $p = .001$, two tailed, rating $z = -3.193$, $p < .001$, two tailed).

These analyses therefore show that when receiving high levels of attention those with SMS showed greater motivation to interact with their unresponsive mother than an unresponsive unfamiliar adult, a preference not shown by those with DS.

Significant between-syndrome differences were also found in patterns of motivation for attention of the unresponsive adult when it was their mother compared to when it was the unfamiliar adult in *low attention* conditions. Both coding and rating outcome measures indicate similar patterns of findings, characterised in SMS by a relative lack of interest in the unfamiliar unresponsive adult in low attention as shown in figure 5.2 below.

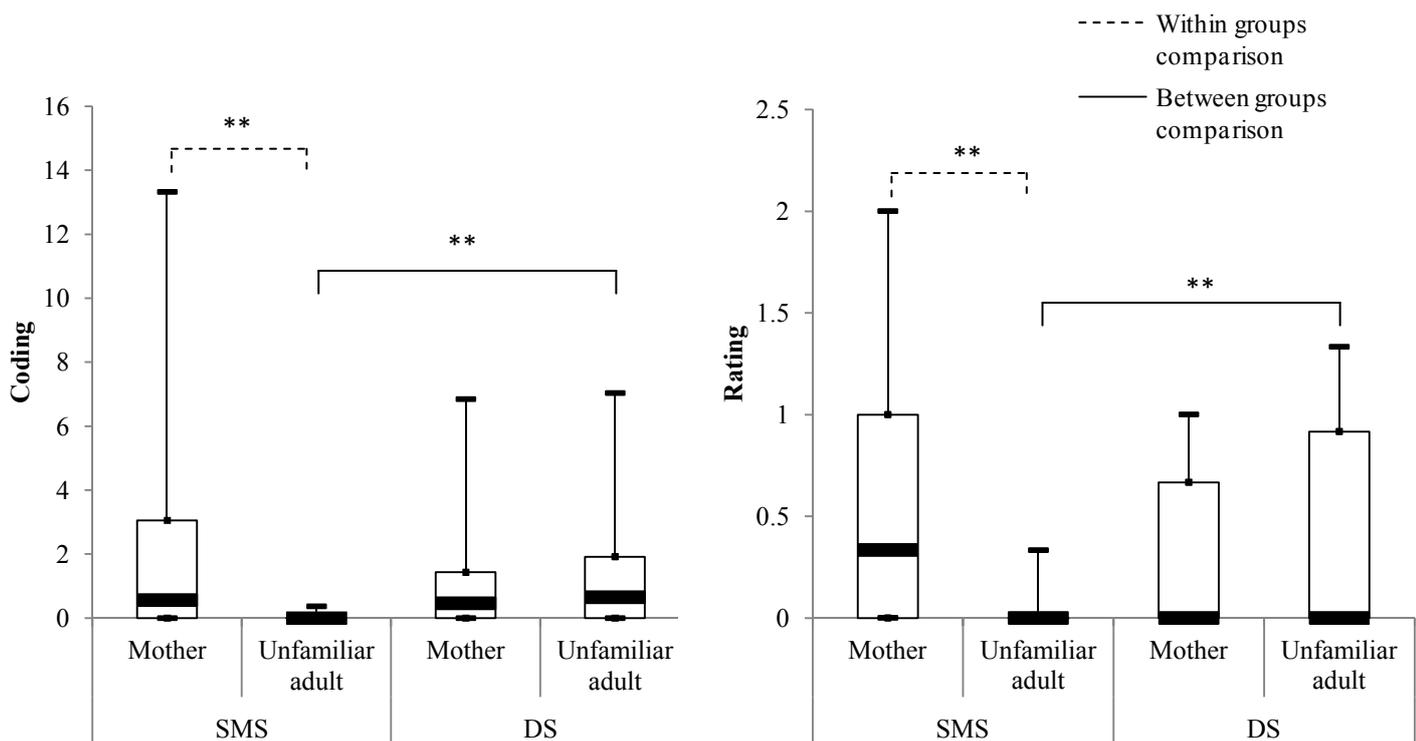


Figure 5.2 Coding and rating of motivation shown towards mothers and unfamiliar adults in low attention conditions by the syndrome groups (* $p \leq .01$, ** $p \leq .001$)

Those with SMS showed a greater difference between mothers and the unfamiliar adult than those with DS (coding $U = 108$, $p = .003$, one tailed, rating $U = 117.5$, $p = .005$ one tailed).

Post hoc analyses revealed that SMS and DS did not differ in terms of motivation to access their mothers' attention when the unfamiliar adult was absent from the room (coding $U = 196.5$, $p = .722$, two tailed, rating $U = 196.5$, $p = .711$, two tailed), however SMS had significantly lower motivation to access the unfamiliar adults attention when their mother was absent from the room than DS (coding $U = 89.5$, $p < .001$, two tailed, rating $U = 121.5$, $p = .001$, two tailed). In terms of within syndrome differences, no difference was found for DS between motivation towards their mother and the unfamiliar adult (coding $z = -.568$, $p = .590$, two tailed, rating $z = .000$, $p = .522$, two tailed). SMS, however, showed less motivation when the unresponsive adult was the unfamiliar adult than when it was their mother (coding $z = -2.982$, $p = .001$, two tailed, rating $z = -2.952$, $p = .001$, two tailed).

This analysis therefore indicates that when experiencing low levels of attention those with SMS showed more motivation to interact with their unresponsive mothers than the unresponsive unfamiliar adult and also that they showed less motivation to interact with the unresponsive unfamiliar adult than those with DS did.

No significant between-group differences in patterns of behaviour with mothers as the unresponsive adult compared to the unfamiliar adult were found for affect (for either coding or rating) in either high or low attention.

5.4.1.2 Adult dependent behaviours

To explore patterns of behaviours shown in response to adults, size of differences between these behaviours directed towards children's mothers and the unfamiliar adult was compared across groups. As with child initiated behaviours, no significant between-syndrome differences in patterns of differences were found between adult dependent behaviours shown towards children's mothers and the unfamiliar adult, when they were the interacting adult.

However, as with child initiated behaviour differences were found for adult dependent behaviours shown towards the unresponsive adult. While there were no differences in high attention, in low attention patterns of differences for both eye contact and focus of attention differed across syndrome groups. Figure 5.3 below shows patterns of results for these behaviours, characterised primarily by individuals with SMS demonstrating relatively low levels towards the unfamiliar adult.

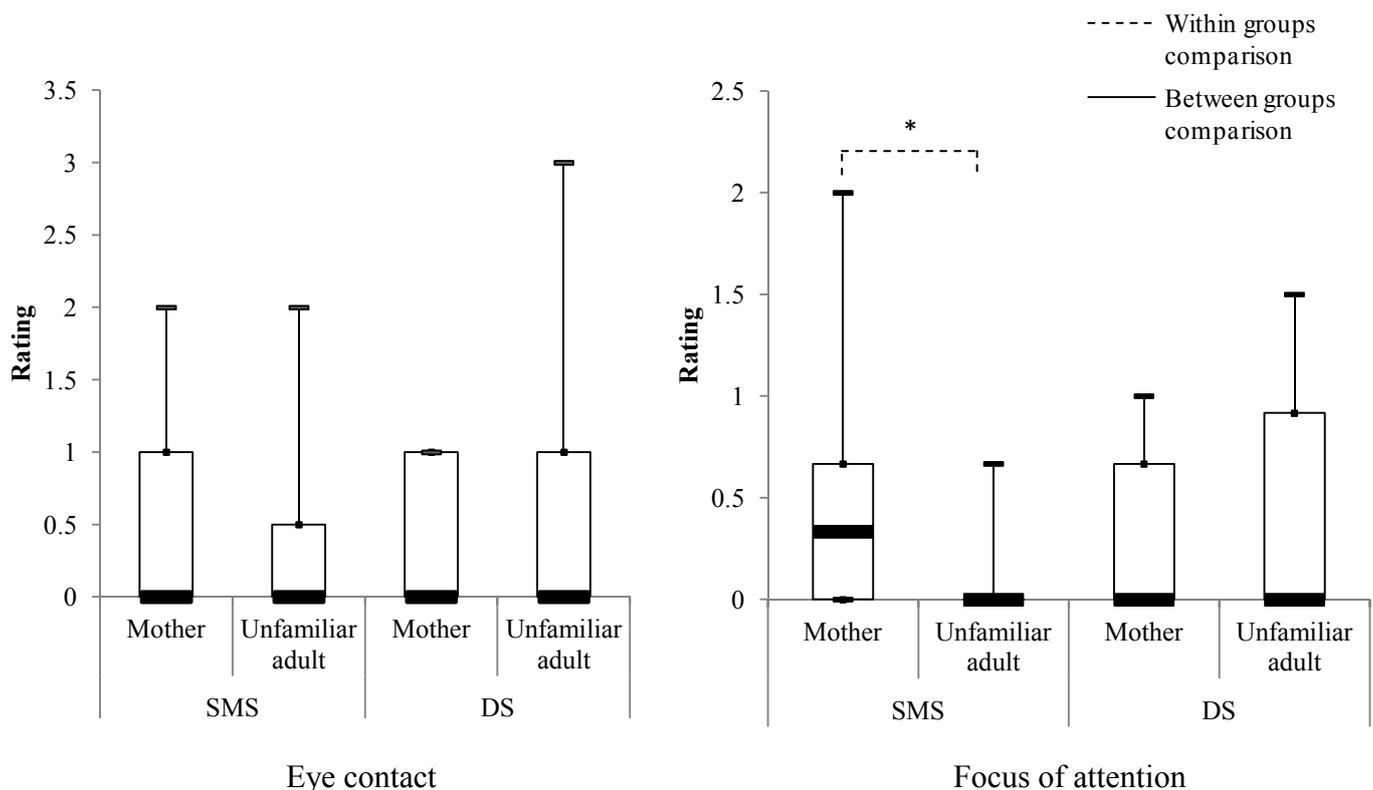


Figure 5.3 Ratings of eye contact and focus of attention shown towards mothers and unfamiliar adults in low attention conditions by the syndrome groups (* $p \leq .01$, ** $p \leq .001$)

Those with SMS showed greater differences in eye contact between mothers and the unfamiliar adult than those with DS ($U = 124$, $p = .01$, two tailed). Despite eye contact with the unfamiliar adult appearing reduced in SMS, post hoc analyses did not find any significant within or between syndrome differences. No between syndrome differences were found for eye contact with mothers ($U = 167$, $p = .246$, two tailed), nor with the unfamiliar adult ($U =$

172, $p = .235$, two tailed). No within syndrome differences were found between eye contact with mothers and eye contact with the unfamiliar adult, either in SMS ($z = -1.897$, $p = .109$, two tailed) or DS ($z = -1.897$, $p = .109$, two tailed).

This analysis suggests that the groups differed in terms of how much their eye contact with the unfamiliar adult changed from when it was with their unresponsive mothers to when it was with the unresponsive unfamiliar adult, but that the absolute ratings of eye contact did not differ either within or between groups.

Patterns of focus of attention with mothers and the unfamiliar adult were also found to differ between syndrome groups in low attention. Those with SMS showed a greater difference between mothers and the unfamiliar adult than those with DS ($U = 113$, $p = .008$ two tailed). Post hoc analyses found no differences between SMS and DS either when the unresponsive adult was the unfamiliar adult ($U = 148.5$, $p = .037$, two tailed) or when it was their mother ($U = 177.5$, $p = .372$, two tailed). Within syndrome analyses found no difference in focus of attention towards their mother compared to the unfamiliar adult in DS ($z = -.268$, $p = .811$, two tailed), however SMS showed less focus on the adult (compared to objects e.g. toys) when the unresponsive adult was the unfamiliar adult than when it was their mother ($z = -2.693$, $p = .005$, two tailed).

In summary this analysis shows that when children with SMS received low levels of attention, they focussed on the unresponsive adult less when it was the unfamiliar adult than when it was their mother, a difference not shown by those with DS.

No significant differences were found for differences in social responsiveness or avoidance of social interaction shown towards mothers compared to the unfamiliar adult, either in high or low attention.

5.4.2 Effect of attention

5.4.2.1 Child initiated behaviours

To test hypotheses that those with SMS would show greater motivation to access attention of adults and less positive affective responses in low attention conditions, magnitude of differences between high attention and low attention conditions were compared across groups. As with the effect of adult familiarity, no effects of attention were found for these behaviours directed towards the interacting adult.

Between syndrome patterns of motivation for unresponsive adult attention were found to differ significantly across levels of attention. This effect was only shown in ratings of behaviour directed towards the unfamiliar adult and is characterised by a smaller difference between high and low attention in SMS than DS. Figure 5.4 shows the medians and ranges of these ratings.

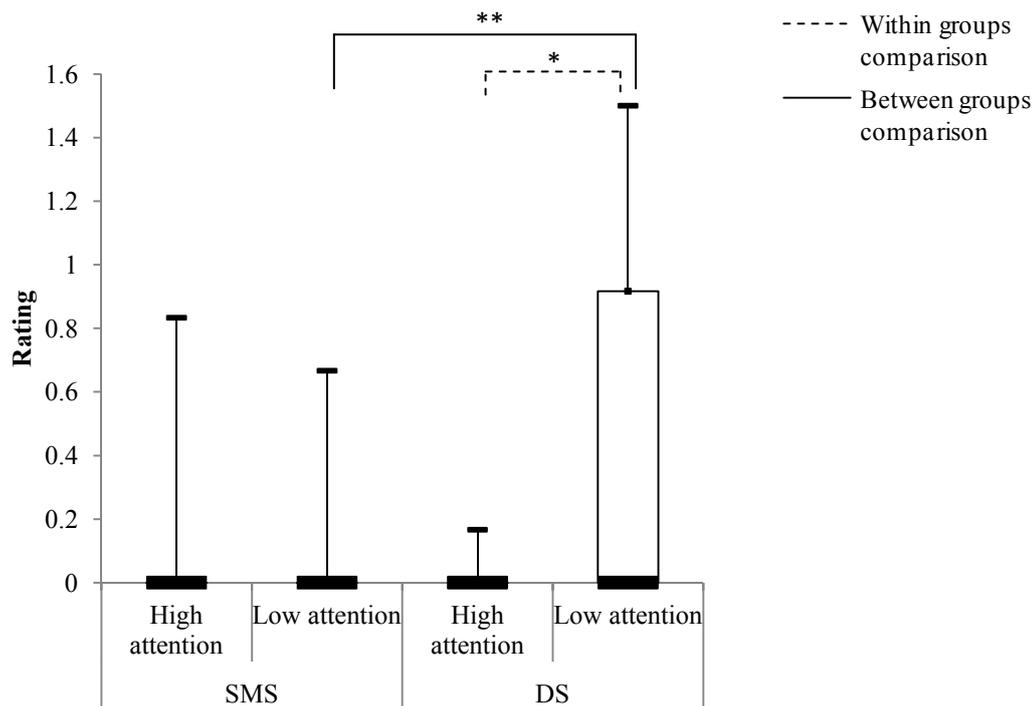


Figure 5.4 Rating of motivation shown in high and low attention conditions towards the unfamiliar adult by the syndrome groups (* $p \leq .01$, ** $p \leq .001$)

Children with DS showed greater difference between high and low attention than those with SMS ($U = 131.5$, $p = .002$ one tailed). Post hoc analyses found no significant differences in motivation to interact with the unresponsive adult between the groups in high attention (interacting adult present) ($U = 168$, $p = .048$, two tailed). However, in low attention when the interacting adult was absent DS showed greater motivation to access the unfamiliar adult's attention than SMS ($U = 121.5$, $p = .001$, two tailed). Within syndromes analyses found DS showed greater motivation to access the unfamiliar adult's attention in low attention than high ($z = -2.706$, $p = .004$, two tailed); however no difference was found between these two conditions with SMS ($z = -1.00$, $p = 1$, two tailed).

Therefore, this analysis shows that when the amount of attention available decreased, those with DS showed increased motivation to interact with the unresponsive unfamiliar adult,

however those with SMS did not. Furthermore when there were low levels of attention available those with SMS showed less motivation to interact with the unresponsive unfamiliar adult than those with DS did.

No significant differences were found for patterns of motivation for unresponsive mothers' attention in high and low attention.

5.4.2.2 Adult dependent behaviours

To explore effects of attention on adult dependent behaviours (assessed using ratings only), magnitude of differences between behaviours shown in high and low attention was compared across groups. No significant between syndrome differences were found in patterns of differences between adult dependent behaviours shown in high or low attention (either with the mother or the unfamiliar researcher) towards the interacting adult. However, differences were found for adult dependent behaviours shown towards the unresponsive adult.

While effects of attention were not found for eye contact, social responsiveness or social avoidance, an effect was found for focus of attention, shown towards the unfamiliar adult. Figure 5.5 shows how this is characterised by a smaller difference between high and low attention in SMS than DS.

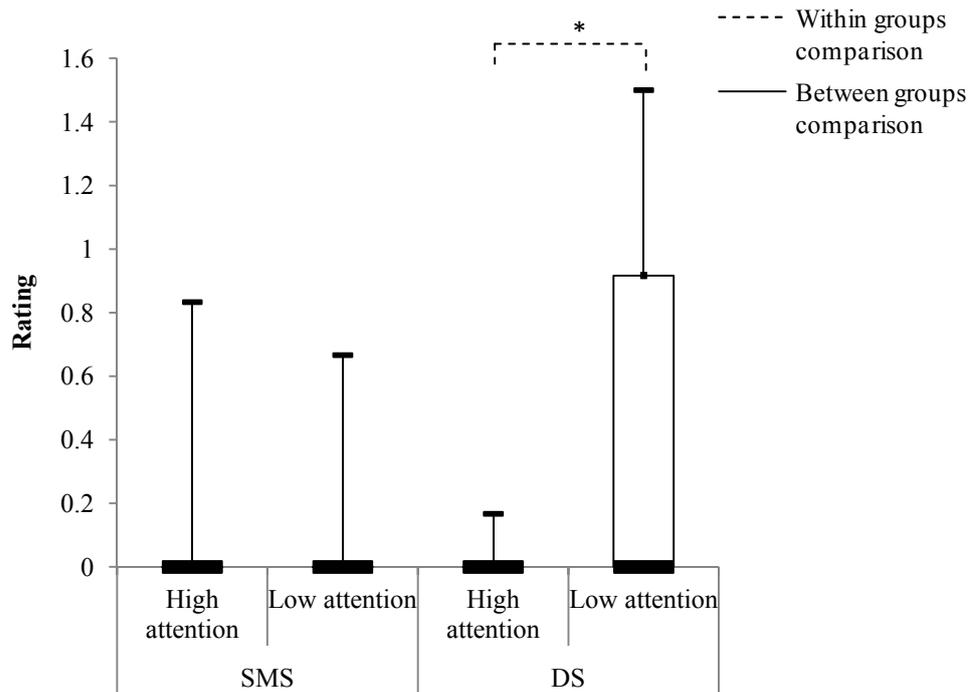


Figure 5.5 Focus of attention shown in high and low attention conditions towards the unfamiliar adult by the syndrome groups (* $p \leq .01$, ** $p \leq .001$)

Children with DS showed a significantly greater difference between high and low attention than those with SMS ($U = 122$, $p = .004$ two tailed). Post hoc analyses showed no significant differences in focus of attention with the unresponsive adult between groups either when the interacting adult is present (high attention) ($U = 207$, $p = .798$, two tailed) or when they are absent (low attention) ($U = 148.5$, $p = .037$, two tailed). Within syndromes differences indicated that DS showed more unresponsive adult (as opposed to object) focussed attention in low attention than high attention ($z = -2.527$, $p = .008$, two tailed); SMS showed no difference in focus of attention with the unresponsive adult depending on whether they were receiving high or low attention ($z = -.412$, $p = .813$, two tailed).

In summary, this analysis shows that when level of available attention decreased, those with DS increased the amount they focussed their attention towards the unresponsive unfamiliar adult, whereas those with SMS showed no difference.

No significant differences were found for patterns of focus of attention with the unresponsive adult attention in high and low attention when it was mothers.

5.4.3 Summary of results

Significant effects of familiarity were found only for behaviours directed towards the unresponsive adult. In contrast to DS, whilst receiving a high level of attention children with SMS showed relatively high motivation to interact with their unresponsive mother (compared to an unfamiliar adult) and whilst receiving a low level of attention they showed relatively low motivation to interact with the unfamiliar adult (compared to their mother). Similar effects were found for focus of attention when receiving low levels of attention, where the pattern of results was similar to that found for motivation, reflecting preferential focus of attention towards mothers rather than the unfamiliar adult in SMS.

Effects of attention were also only found for behaviours directed towards the unresponsive adult. When receiving low levels of attention, consistently low motivation to interact with the unfamiliar unresponsive adult in SMS was found, in contrast to elevated motivation in DS. Similar effects were found for focus of attention towards the unfamiliar adult when they were the unresponsive adult, where those with DS increased their attention towards the unresponsive unfamiliar adult when receiving low levels of attention, but those with SMS did not.

5.5 Discussion

Social behaviour in a group of children with SMS, in contrast to a comparable group with DS was examined in this study. Direct observations were conducted during structured social situations where both familiarity of the adults involved (mothers and unfamiliar adult) and level of available attention (high and low) were manipulated. This is the first study to undertake direct, controlled observations of social behaviour in children with SMS, employing a matched contrast group and manipulating environmental variables. Children's responses were evaluated using psychometrically robust methods to examine child initiated and adult dependent behaviours. Where coding and ratings assessed similar behaviours they demonstrated convergent results, supporting the validity of these behavioural measures. As predicted, analyses indicated those with SMS showed divergent profiles of social behaviour for a number of behaviours, broadly characterised by stronger motivation to access their mother's attention and reduced motivation to interact with an unfamiliar adult. The pattern of differences was dependent on the role of the adult in the social situation, i.e. whether they were interacting or unresponsive. Effects were found only for the unresponsive adult.

As predicted familiarity of adults with whom children were interacting was found to affect patterns of between syndrome differences in motivation to interact with that person. Findings indicated that even when children with SMS experienced high attention, if it was from an unfamiliar adult they showed more motivation to access the unavailable attention of their mother than those with DS did. When comparing motivation for interacting with each adult, as expected those with SMS showed consistently more motivation towards mothers than the unfamiliar adult, whereas those with DS showed no preference. Furthermore, it seems that when experiencing low levels of attention, unlike children with DS those with SMS did not turn to an unfamiliar (unresponsive) adult as an alternative source of attention. Overall, these findings indicate children with SMS showed unusually strong preference for interacting with

their mother and relatively little motivation to interact with the unfamiliar adult, a pattern of results not found in DS.

Indications of stronger preference in SMS for initiating interaction with a familiar adult (i.e. their mother), are consistent with findings from previous research. Attention-seeking is commonly reported in SMS (e.g. Dykens *et al.*, 1997, 1998) and a specific nature of this attention-seeking is implicated by anecdotal reports described in section 2.4.8.3 and findings presented in section 4.4.2.1 which suggest individuals with SMS have unusual preference for interacting with adults. It is likely that attention-seeking from adults in SMS is directed towards familiar adults, as generalised hypersociability, such as seen in WS (Jones *et al.*, 2000) is not reported in SMS and was not evident in the preliminary study of caregiver reports of sociability in SMS (see section 3.4.1). The current finding gives further insight into the nature of this preference for adult attention, supporting suggestions that it is directed specifically towards familiar adults.

Results of the current study suggest that the ‘attachment’ to particular people found in SMS (see section 3.4.2) may be to highly familiar adults, with strong motivation shown in this instance toward primary caregivers (although it cannot be inferred this is exclusively so as no other familiar adults were included). These results may implicate a role of attachment as defined by Bowlby (1969) and Ainsworth *et al.* (1978) (see section 2.4.8.4), however the current results can only indicate preference for a familiar adult over a stranger, not specificity to primary caregivers required to make assertions about attachment.

Effects of adult familiarity on social motivation in genetic syndromes have been found previously in AS and linked specifically to accessing attention of caregivers. Mount *et al.* (2011) found children with AS showed more behaviours indicative of social motivation

(approach behaviours) towards their mother than unfamiliar adults. This finding was interpreted as supporting theories that these approach behaviours functioned to access maternal resources (attention), in line with existing theories that elevated sociability in AS increases access specifically to maternal resources - a function linked to the underlying genetic mechanism (see section 1.3.2). The authors further interpret this as evidence for an interaction between genetic characteristics and the environment in AS. As noted previously (in section 3.5) it is unclear whether there is any such genetic link to drive for attention from specific people in SMS, although it cannot be related to imprinting as SMS is not caused by an imprinted gene.

That these results were found for the unresponsive adult only is unexpected. This appears initially to conflict with reports of attention-seeking (e.g. Dykens *et al.*, 1997, 1998), which seems likely to be evoked by reductions in desired attention when a highly familiar adult leaves the room for five minutes. However, this may suggest sensitivity to more prolonged withheld attention, particularly of someone within view. It may be a case of 'out of sight out of mind' for absent adults but adults being in sight and consistently unavailable may be less tolerable for children with SMS. It is also possible that five minutes absence was an insufficient manipulation of attention to evoke attention-seeking behaviour, whereas 15 minutes of consistent unavailability resulted in a state of sufficient deprivation of attention. Future replications may consider extending the period of absence.

Contrary to predictions, no differences were found for affect shown when interacting with either their mother or the unfamiliar adult, suggesting familiarity of adults with whom the child interacts does not affect their enjoyment of the interaction. This is interesting considered in the context of previous results suggesting children with SMS have stronger *motivation* to interact with their mother, suggesting that although there may be strong desire to interact with

their unavailable mother, when she is available and providing high levels of attention children with SMS do not seem to enjoy her attention more than they enjoy that of an unfamiliar adult. The disparity between motivation to initiate interaction and behaviour when interaction takes place contrasts with behaviour in other genetic syndromes associated with strong social motivation.

In AS, children have been described as showing high levels of socially motivated behaviour, (see section 1.3.2) however, this syndrome is associated with increased positive affect during interactions, indicating enjoyment of the social episode (Horsler & Oliver, 2006; Oliver *et al.*, 2002) which was not found in SMS. This also contrasts with anecdotal reports that children with SMS enjoy adult attention (Haas-Givler, 1994). This finding does however add further context to findings that SMS was not found to be more sociable than DS (see section 3.4.1), as it appears drive to interact demonstrated in this study was not accompanied by elevated levels of ‘typically’ sociable behaviours e.g. positive affect, when attention was provided. It is unclear why children with SMS would be more motivated to access attention from a particular adult but then not show greater enjoyment of their attention. It is possible that while children with SMS try to initiate more interaction their actual social interaction skills do not match this motivation, thus the interaction may potentially not be as rewarding. At this stage this remains a tentative suggestion which would benefit from further direct investigation.

For aspects of behaviour dependent on adult interaction effects of familiarity were only found for eye contact and focus of attention. Similar patterns were found as for motivation, indicating preferential eye contact and focus of attention towards mothers (in low attention conditions). Similarity of these findings to those of motivation suggests that the behaviours were linked to, and may be further indices of, motivation. Increased focus of attention toward their mother (suggesting they are monitoring that adult more than their play items) and greater

eye contact both indicate attentional bias towards the mother (versus the unfamiliar adult). Lack of findings for behaviours such as responsiveness, which rely on interaction between the adult and child, may relate to previous points regarding potentially impaired social skills shown during social interactions.

In terms of effects of attention, while reduced attention increased motivation of children with DS to interact with the unresponsive unfamiliar adult, those with SMS showed little difference between high and low attention conditions. That those with SMS showed less difference between high and low attention than DS is in line with predictions. However, follow up analyses indicate that this was for a different reason than anticipated. Where it was expected that SMS would have high motivation in both low and high attention, results indicated SMS had very low motivation to interact with the unfamiliar adult in both conditions.

That children with SMS did not access an alternative source of attention (the unfamiliar adult) when their mother left the room, leaving them experiencing low levels of attention, is a key finding of the current study. This may add to perceptions of attention-seeking in SMS as it suggests high specificity of increased motivation towards this familiar adult, such that those with SMS do not utilise other sources of attention. If children are motivated to access attention from only one source and do not use other possible sources of attention this may increase perception of burden felt by the person who is the focus of this attention-seeking.

In AS where high levels of attention-seeking is directed specifically toward the familiar adults (Mount *et al.*, 2011; Oliver *et al.*, 2007) caregivers have higher rates of stress and anxiety than caregivers of those with autism, Cornelia de Lange syndrome and Cri du Chat syndrome and mothers were found to have higher rates than fathers (Griffith *et al.*, 2011). Isles (2011)

speculates that this reflects higher rates of social motivation aimed specifically towards primary caregivers in AS, relating this to kinship theory (see section 1.3.2). It is possible therefore that attention-seeking directed towards one person specifically is particularly demanding. Similarly, although not found in the current study (where levels of challenging behaviour could not be examined due to low incidence in assessed footage), the challenging behaviours reported anecdotally (Haas-Givler, 1994) and in empirical research (Taylor & Oliver, 2008) to result from reduced attention are likely to make the impact of attention-seeking greater.

As with familiarity, no effect of attention was found on levels of affect shown by the groups, failing to support predictions that those with SMS would show more positive affective responses to high levels of attention and less positive responses to low attention. Findings that higher attention did not result in more positive affective responses suggest that children with SMS may not be necessarily enjoy attention once it have been given by an adult (regardless of their familiarity) any more than children with DS. This further supports previous discussions relating to the role of familiarity, that high drive to interact may not be associated with greater enjoyment (reflected by increased positive affect) when interaction is available. This contrasts with increased positive affect when attention is available found in AS (Horsler & Oliver, 2006; Oliver *et al.*, 2002).

Findings for ratings of other aspects of behaviour which are dependent on adult interaction or proximity indicated effects of attention for focus of attention only. Children with SMS did not appear to increase their attention towards the unfamiliar adult when the interacting familiar adult leaves the room. The pattern of this effect was similar to that that found for motivation, further supporting suggestions that focus of attention may be an index of motivation, where

children who were more motivated to access the attention of a particular adult are more likely to focus their attention on them (as opposed to an object in their environment).

As noted previously in section 1.4.2 use of a single genetic syndrome as a contrast group presents inherent difficulties when interpreting findings of this type of study. It is possible that children with DS demonstrated an unusual pattern of behaviour themselves, for example unusually high interest in the unfamiliar adult which would have made the SMS group seem relatively uninterested when in fact they were behaving in a typical way. However, within-groups analyses of SMS demonstrated a lack of interest in the unfamiliar adult in conditions of low attention which even without comparison to DS indicates unusual behaviour, as does their elevated efforts to interact with their mother when they are already receiving high levels of attention from another source. Use of multiple contrast groups would go some way to addressing this concern, although the issue regarding behavioural phenotypes for specific syndromes remains if other genetic syndromes are used therefore a heterogeneous intellectual disability contrast group could be used.

A further potential limitation is the analysis used in the current study; follow up analyses of actual levels of behaviour were performed only where initial analyses of differences between behaviours at each level of variables of interest indicated they had a differential effect on how individuals with SMS and DS behaved. A key aim of the current study was to evaluate effects of variables purported to be specifically influential on social behaviours in SMS, which required contrasting effects in SMS to an appropriate group. Therefore evaluating whether SMS showed objectively higher levels of behaviour than DS was only of interest if it was indicated this resulted from manipulation of the experimental variables. Addressing this would require comparison of each group's behaviour at each level of the independent variables, introducing a very large and not inherently informative set of comparisons.

To extend the findings of the current study the role of the identity of the familiar adult warrants further examination. In mainstream child development literature strong motivation to interact specifically with primary caregivers is typically considered to reflect attachment processes; however the current findings cannot be interpreted in relation specifically to primary caregivers, only familiar adults. Given this framework for understanding social interactions between children and caregivers it would be interesting to examine this further using the standard Strange situation paradigm (Ainsworth & Wittig, 1969) with children with SMS to explore whether their behaviour can be understood within this theoretical framework.

In summary, the current study provides further evidence for an unusual social drive in SMS and provides novel evidence suggesting that that it appears to be directed towards familiar adults rather than strangers and is further characterised by a relative lack of interest in unfamiliar adults as a source of attention. This pattern of behaviour was found to be specific to those with SMS and provides additional support for suggestions that there may be an interaction in SMS between their genetic characteristics and the environment such that there is an inherently strong drive to access adult attention which interacts with environmental variables such as adult attention. However, negative consequences of unavailable attention such as challenging behaviour and negative affect were not found in this study and when interaction is established children with SMS syndrome did not appear to find the interaction more rewarding in terms of enjoyment.

CHAPTER 6

Inhibition and impulsivity in children with Smith-Magenis syndrome

6.1 Preface

The studies in chapters three to five examined social functioning in Smith-Magenis syndrome (SMS), an aspect of the behavioural phenotype which was identified in the overview of the literature presented in chapter two as requiring further delineation. More specific examination of key aspects of the behavioural phenotype of SMS enables consideration of how behaviours may be understood within a model of pathways from genetic characteristics of the syndrome to behavioural outcomes as delineated in chapter two. Within this context, impulsivity was identified as a second relatively under researched aspect of behaviour in SMS. High rates of impulsivity in SMS have been associated with challenging behaviour, but underlying causes of this behaviour are unclear. Therefore, this chapter aims to examine the underpinnings of impulsivity in SMS using a combination of direct cognitive testing and survey methodologies to identify associations between impulsive behaviour and underlying cognitive and related functions.

6.2 Introduction

Evidence is mounting that impulsivity is a key feature of the behavioural phenotype of SMS (2.4.7.1). As well as being highly prevalent it is also reported to be a difficult behaviour to manage and may be a risk-marker or risk factor for other challenging behaviours such as aggression (Arron *et al.*, 2011, Sloneem *et al.*, 2011). Furthermore, it has been suggested that high levels of impulsive behaviour may account, in part, for disproportionately low daily-living skills (compared to cognitive abilities), which result in individuals with SMS being more dependent on caregivers than expected (Udwin *et al.*, 2001). To address the potential role of impulsive behaviour in some negative outcomes associated with SMS, direct investigation of the nature and aetiology of impulsive behaviour in SMS is needed. Understanding what drives this impulsive behaviour may suggest targets for intervention and behaviour management strategies.

To investigate impulsivity directly it is important to establish what the term impulsivity represents, with regard to behaviours shown and potential underlying processes. Barratt's definition emphasises that impulsivity is a multidimensional concept incorporating failure of response inhibition, rapid processing of information, novelty seeking, and inability to delay gratification (Barratt 1985, 1994). There are many other definitions of impulsivity (see Evenden, 1999 for a review), but definitions generally involve four basic elements (Vitaro, Arseneault & Tremblay, 1999): desire for immediate reinforcement, impetuous responding with inability to foresee consequences, lack of sensitivity to punishment and deficits in inhibitory control (Barratt & Patton, 1983; Buss & Plomin, 1975; Carlton *et al.*, 1987; Eysenck & Eysenck, 1977; Gray, Owen, Davis & Tsaltas, 1983; White *et al.*, 1994). Such definitions implicate two key processes that may underlie impulsive behaviour: inhibitory control and ability to delay gratification.

One approach to understanding impulsivity defines it primarily as a failure of inhibition, where impulsive individuals cannot control their behaviour (e.g. Schachar & Logan, 1990; Schachar & Wachsmuth, 1991). Inhibition has been described as the deliberate, controlled suppression of prepotent responses (Miyake, Friedman, Emerson, Witzki & Howerter, 2000). Deficits in inhibition, specifically in *response* inhibition (the cognitive process required to cancel an intended movement, Aron, Robbins & Poldrack, 2004), have been found in several other conditions associated with impulsivity, including trichotillomania, obsessive-compulsive disorder and chronic substance abuse (Chamberlain & Sahakian, 2007).

While there is good evidence suggesting inhibition deficits may be associated with impulsive behaviour, an additional ‘motivational’ pathway to impulsive behaviour has also been proposed. In Sonuga-Barke’s (2003) model of behaviour in ADHD (a syndrome in which impulsivity is a key feature, DSM-IV-TR) it is suggested that impulsivity can also reflect motivation to avoid delay of gratification, which is aversive to those with ADHD due to biological differences in reward mechanisms (Sonuga-Barke, 2002). The dual pathways to impulsive behaviour included in Sonuga-Barke’s model suggest that the two accounts, neurocognitive and motivational, do not necessarily conflict in terms of explaining impulsivity (Sonuga-Barke, 2003) but may be separable but interacting pathways to the outcomes in ADHD, including impulsive behaviour. Examining processes underlying impulsivity potentially enables further understanding of the paths from genetic difference to behaviour, via cognition, and importantly suggests potential opportunities for intervention. For example, if an underlying cognitive deficit is identified then interventions such as cognitive training may improve this function and consequently related behaviour outcomes.

As noted in the previous review of the behavioural phenotype of SMS (section 2.4.7), deficits in inhibition in SMS seem likely given findings of possible structural frontal lobe abnormalities and elevated repetitive behaviours (hypothesised to be linked to impaired inhibition). It may be hypothesised therefore that such inhibition deficits may also account for elevated impulsivity found in the syndrome. Specific consideration of inhibition and how it can be measured is therefore warranted.

Inhibition is one of the multiple abilities that make up executive function, the higher order functions that enable individuals to monitor and control their behaviour (Carlson, 2005), including abilities such as working memory and cognitive flexibility (Griffith, Pennington, Wehner & Rogers, 1999). The development of executive functions is believed to progress from birth, through preschool and into the school years (Garon, Bryson & Smith, 2008; Haith, Hazan & Goodman, 1988; Carlson, 2005). Behaviours indicating the ability to inhibit dominant responses have been demonstrated in infants as young as seven months (Willats, 1999). Despite this early development, most batteries that have been developed to test executive functioning primarily assess typically developing populations of older children and adults. Henry and Bettenay (2010) reviewed tests available for assessing executive function in children. Of the batteries examined, only five included assessments of inhibition³⁷. Recent research has attempted to address this paucity, developing executive function assessments suitable for use with younger children, which do not rely on complex motor or verbal responses (e.g. Carlson, 2005).

³⁷ The Cambridge Neuropsychological Test Automated Battery (Cambridge Cognition Ltd, 2006), the Delis-Kaplan Executive Function System (Delis, Kaplan, & Kramer, 2001), the NEPSY II (Korkman, Kirk & Kemp 2007), the Animal Stroop task (Wright, Waterman, Prestcott & Murdoch-Eaton, 2003) and the Test of Everyday Attention for Children (Manly, Robertson, Anderson & Nimmo-Smith, 1999).

Carlson (2005) compiled the results of 24 different tests of executive function requiring inhibition of a prepotent response, designed to be developmentally sensitive measures of executive function in young (preschool) children. Results enabled scaling of these tests in terms of developmental ages needed to pass for each task. In terms of the current study this has particular utility in development of a battery of tests tapping inhibition in a sample likely to have wide ranging of ability and developmental delay. Scaling of tasks would enable participants to progress through the battery until they reach the ceiling for their level of ability, maximising sample sizes and providing multiple converging measures of inhibition.

In addition to direct tests, informant report measures of executive function have also been developed. For example the Behavior Rating Inventory of Executive Function (BRIEF, Gioia, Isquith, Guy, & Kenworthy, 2000) asks parents and teachers to rate individuals' behaviour on various aspects of executive functioning, including inhibition. The Behavior Rating Inventory of Executive Function: Preschool (BRIEF – P, Gioia, Espy, Isquith, 2003) is a version of this assessment which is suitable for use with preschool children and, by implication, may also be suitable for individuals with intellectual disability. The BRIEF – p measures five different aspects of executive function; 'inhibition', 'shifting', 'emotional control', 'working memory' and 'plan/organise'. This method of assessing executive function in those with a lower developmental level has been found to be both reliable and valid (Gioia *et al.*, 2003) and enables assessment of behaviour in ecologically valid contexts.

In summary, research has identified significant difficulties with impulsive behaviour in SMS and suggests these difficulties may cause problems for both individuals with the syndrome and their caregivers. Together with links between impulsivity and challenging behaviour, these findings implicate a need for further understanding of this behaviour. Studies examining

impulsivity have primarily used parent report methodologies with limited research undertaking direct investigation. Direct tests of cognitive functions associated with impulsivity, which draw on the mainstream literature, may enable identification of cognitive underpinnings of impulsivity in SMS. Use of developmentally scaled tasks which tap inhibition, identified as a candidate cognitive process underpinning impulsivity, could assess whether there are deficits in this process. Use of standardised, ecologically valid behavioural measures, would enable assessment of children's impulsive behaviour in everyday contexts and evaluation of its relation to cognitive assessments of inhibition.

The current study therefore aimed to investigate impulsive and disinhibited behaviour in children with SMS using both behavioural descriptions and cognitive assessments. To examine everyday behaviour of children with SMS, caregiver reports were compared to a mental age matched contrast group of children with similar level and profile of intellectual disability to identify whether children with SMS are reported to show greater difficulties with impulsivity, inhibition and emotional control. Down Syndrome (DS) was selected as the contrast group as it has been found previously to have a similar expressive language delay and range of IQ to SMS (see section 3.5). Cognitive tasks were used to examine response inhibition, a potential cognitive process underpinning impulsive behaviour. Performance of children with SMS on a battery of three developmentally scaled tasks testing response inhibition (taken from the mainstream executive function literature) was compared to performance of two contrast groups, the DS sample and a normative sample of typically developing children matched on estimates of mental age (using chronological age as a proxy for mental age).

In addition to these primary aims, the study also aimed to investigate relationships between ecologically valid measures of behaviour and cognitive function, i.e. whether performance on the inhibition battery correlated with informant report measures of behavioural difficulties related to impulsivity, inhibition and emotional control (Gioia *et al.*, 2000 link inhibition and emotional control in their measure of executive functioning, with analyses of underlying factors suggesting they form a factor labelled ‘inhibitory self control’). A further aim was to explore whether informant report measures of behaviour correlated with one another, indicating relationships between behavioural difficulties described, particularly whether inhibition and emotional control correlate with informant reports of impulsive behaviour.

Based on the literature presented suggesting significant problems with impulsive behaviour and the range of behavioural difficulties described suggesting a potential deficit in response inhibition, the following hypotheses were developed:

- i) Caregiver ratings of impulsivity and difficulties with inhibition and emotional control would be higher in SMS than ratings of a similar group of children with DS.
- ii) Individuals with SMS would perform less well on a battery of cognitive tests of this ability than both the mental age matched contrast groups (the DS group and the normative contrast group of typically developing children).

As examination of relationships between informant report measures of behaviour and these measures and task performance was exploratory, no directional hypotheses are proposed.

6.3 Methods

6.3.1 Recruitment

6.3.1.1 Syndrome groups

Participants with SMS and DS were recruited as part of a larger study examining aspects of the behavioural phenotype of SMS. Full details of the recruitment process for this study are explained in section 5.3.1 and appendix E.

6.3.1.2 Normative sample

Normative data, gathered as part of a previous study examining executive function, was collected from typically developing children attending schools and nurseries in the West Midlands area. Children were included in this sample if they had no diagnosis of an intellectual disability and had English as a first language. Opt out consent was gained for typically developing children.

6.3.2 Participants

6.3.2.1 Initial sample

Syndrome groups

Sample characteristics of the initial SMS and DS groups are described in section 5.3.2. For the purposes of the current study an additional participant with SMS was excluded from comparison because mental age could not be assessed due to participant fatigue. Therefore the total sample size of children with SMS was 20 and DS was 21.

Normative sample

A total of 262 typically developing children were recruited into the original normative sample. Their ages ranged from 36 to 89 months.

6.3.2.2 Final sample

The final sample of children with SMS consisted of those children from the initial sample who were able to be successfully tested in line with criteria outlined in appendix O (i.e. could be engaged in an initial warm up activity and were able to pass the rule understanding checks in the warm up stages of each experimental task). Different children were able to complete different tasks, therefore samples differed depending on the task.³⁸

To ensure optimal matching, participants from the contrast groups were selected for inclusion in final samples based on best mental age matches for each task's SMS sample (full details of matching process are described in appendix O). This resulted in different contrast group samples for each task and for each type of comparison (SMS-DS, SMS-Normative, DS-Normative). Demographic details of the final samples for each task and group comparison are described table 6.1. Groups were found to be well matched, with no differences between mental age for any matched groups. Additionally SMS and DS groups did not differ on chronological age: both syndrome groups were significantly older than the normative contrast group.

³⁸ No differences in parent ratings of key behaviours (see section 6.3.3.3) was found between those children in the final sample and those who were excluded, suggesting final sample can be considered to be representative of the larger initial group of children with SMS).

6.3.2.3 Questionnaire sample

As the normative sample was collected as part of a previous, unrelated study, only individuals with SMS and DS from the current study completed informant report measures of behaviour. To negate the need for repeated analyses of questionnaire data depending on which task was completed (potentially inflating type one error), results of participants from the final sample of individuals with SMS and DS who completed *any* task were included for analysis.

6.3.3 Measures

6.3.3.1 Inhibition battery

A battery of three tasks which measure ability to inhibit dominant behavioural responses was constructed. Tasks which do not require a verbal response were selected due to expressive language deficits in both SMS and DS. The battery consisted of a Reverse categorisation task (based on Perner & Lang, 2002), the Bear/dragon task (from Reed, Pien and Rothbart, 1984) and the Black and white Stroop (Simpson & Riggs, 2005). These tasks have been used successfully with typically developing children aged 2-3 years (Carlson, Mandell & Williams, 2004; Cuskelly, Zhang & Hayes, 2003) and children with intellectual disabilities (Waite, 2011). The measures have also been found to discriminate effectively developmental stages in typically developing children (Heald, 2010). All tasks included practice trials to check understanding and rule reminders midway through. Tasks and scoring are summarised briefly below and described in full in appendix P.

Bear dragon

Participants are instructed to do what a ‘nice’ bear puppet tells them, but to not do what a ‘naughty’ dragon puppet tells them to do. There are 16 commands in total (eight bear, eight dragon). Performance of the commanded action receives a score of 1 if given by the bear, 0 if from the dragon. No movement is scored as 0 for the bear command and 1 for the dragon. Total scores, out of 16, are calculated by summing the bear and dragon scores.

Reverse categorisation

Participants are required to reverse colour sort a set of 12 blue and red balls, such that blue balls are put in a red bucket and red balls are put in a blue bucket. Scores, of a maximum 12, reflect the number of correctly sorted balls. Where children change their response on a trial their first response is recorded.

Black white Stroop

Participants are required to point to a black coloured square when the researcher says ‘white’ and a white coloured square when the researcher say ‘black’. There are eight ‘white’ commands and eight ‘black’ commands. A correctly reversed response scores 1 and an incorrect response (no reversal) scores 0, scores are summed to derive a total score out of 16. Where children change their response on a trial their first response was recorded.

6.3.3.2 Demographic information

Demographic Questionnaire

The demographic questionnaire gathers information about participant characteristics. A full description of this measure is provided in section 3.3.2.1 (see appendix F1 for copy of the measure).

6.3.3.3 Measures of impulsivity, inhibition and emotional control

Activity Questionnaire; TAQ (Burbidge et al., 2010)

The Activity Questionnaire (see appendix F4) is an 18 item informant based questionnaire designed to obtain information about children and adults with intellectual disabilities. Informants rate behaviour on a 5 point scale from 0 (Never/almost never) to 4 (Always/almost all the time). The questionnaire can be used with both verbal and non-verbal individuals. Both inter-rater and test-retest reliability have been found to be robust (Burbidge *et al.*, 2010). The measure contains three subscales, overactivity, impulsivity and impulsive speech. For the purposes of the current study only the impulsivity subscale was analysed.

Behaviour Rating Inventory of Executive Function—Preschool; BRIEF-P (Gioia et al., 2003)

The Behaviour Rating Inventory of Executive Function—Preschool Version (BRIEF-P) is a 63 item informant report measure (see appendix F6). Items measure children's executive functions in an ecologically valid context (home and school) and form five scales; Inhibit (ability to inhibit responses), Shift (ability to shift attention), Emotional Control, Working Memory, and Plan/Organize. Three broader indexes can be derived from the scales (Inhibitory Self-Control, Flexibility, and Emergent Metacognition) and a single composite score can also

been calculated (Global Executive Composite). For the purpose of the current study only the inhibition and emotional control subscales were analysed. Internal consistency, reliability and test-retest reliability have all been found to be good and convergent and discriminant validity are robust (Gioia, *et al.*, 2000).

6.3.3.4 Assessments of ability

Wechsler Abbreviated Scale of Intelligence; WASI (Wechsler, 1999)

The Wechsler Abbreviated Scale of Intelligence comprises four subtests: Vocabulary, Similarities, Block Design, and Matrix Reasoning. It can be administered as a four or two subtest form. The four subtest form provides a Verbal IQ score (derived from the Vocabulary and Similarities subtests), Performance IQ score (derived from Block Design and Matrix Reasoning subtests) and Full Scale IQ score. The two subtest form results in only a Full Scale IQ score (derived from Vocabulary and Matrix Reasoning subtests). Both four and two subtest versions of the scale have good test-retest (FSIQ-4 0.98, FSIQ-2 0.96) and inter-rater reliability (0.98 Vocabulary, 0.99 Similarities). The measure is suitable for use from 6 - 89 years (typically developing individuals) and has been used previously with individuals with intellectual disability. During test development validation was carried out with individuals with intellectual disability (including those with DS).

Mullen Scales of Early Learning (Mullen, 1995)

The Mullen Scales of Early Learning assess infants and children on five areas of development; Gross motor, Fine motor, Visual Reception, Expressive Language and Receptive Language. It is suitable for use with typically developing children from 3 - 68 months and has been used effectively in past research with individuals with intellectual

disability (e.g. Hartley, Sikora & McCoy, 2008). The scales can be used to compute Scale scores, an Early Learning Composite, percentile ranks and age equivalents. The test has been found to have robust reliability and validity.

6.3.4 Procedure

6.3.4.1 Cognitive testing

Inhibition

Where possible tasks were completed seated at a table with the researcher sat opposite the participant. Where children would not sit at a table, tasks were administered with researcher and child seated on the floor. Tasks were administered in a set order. The Bear/dragon task was presented first as the initial copying activity enabled assessment of children's ability to follow requests (see appendix O) and was considered to be the most socially engaging task to create rapport between the participant and researcher. Tasks were presented in order of level of difficulty (Bear dragon, Reverse categorisation, Black white Stroop) to ensure children were not faced initially with tasks beyond their level of ability (thus affecting engagement and motivation in this and subsequent tasks).

General ability

Where possible these assessments were carried out as a tabletop task as described above. Cognitive assessments were carried out at suitable time point in the day, determined by children's level of engagement with the researcher. If a child refused to participate in the testing, this was revisited at a later point in the day.

6.3.4.2 Questionnaire measures

Questionnaire packs were distributed to caregivers of participants with SMS and DS on the day of the data collection visit. Carers returned completed questionnaires and consent forms either on the day or shortly after using a provided prepaid envelope.

6.3.4.3 Testing and ethical considerations

Ethical review was obtained from the University's ethics committee. All but one testing sessions were carried out in participants' home (the remaining participant was tested in school). Tasks were recorded by a second researcher using a handheld camcorder for subsequent coding.

Table 6.1 Gender (percent male), mean age (standard deviation) and range, mean mental age (standard deviation) and range for each group

Comparisons	SMS -DS						SMS – Normative						DS - Normative					
	Reverse categorisation		Bear dragon		Black white Stroop		Reverse categorisation		Bear dragon		Black white Stroop		Reverse categorisation		Bear dragon		Black white Stroop	
Tasks	SMS	DS	SMS	DS	SMS	DS	SMS	Norm	SMS	Norm	SMS	Norm	DS	Norm	DS	Norm	DS	Norm
Syndrome	SMS	DS	SMS	DS	SMS	DS	SMS	Norm	SMS	Norm	SMS	Norm	DS	Norm	DS	Norm	DS	Norm
N	13	13	13	13	12	12	13	13	13	13	12	12	13	13	13	13	12	12
Gender (n male)	5	6	6	7	4	6	5		6		4		6		7		6	
Chronological age (Months) Mean	122.62	102.54	122.92	102.85	129.75	109.33	122.62	51.62	122.92	51.62	129.75	52.75	102.54	53.15	102.85	53.15	109.33	54.83
(SD)	(48.65)	(35.28)	(48.32)	(34.91)	(43.12)	(31.52)	(48.65)	(15.60)	(48.32)	(15.60)	(43.12)	(15.72)	(35.28)	(15.23)	(34.91)	(15.23)	(31.52)	(15.47)
Range	37-190	49-158	37-190	49-158	56-190	61-158	37-190	36-77	37-190	36-77	56-190	36-77	49-158	36-77	49-158	36-77	61-158	36-77
Mental age (Months) Mean	54.54	51.60	53.40	50.78	56.63	54.61	54.54	51.62	53.40	51.62	56.63	52.75	51.60	53.15	50.78	53.15	54.61	54.83
(SD)	(27.76)	(18.43)	(28.77)	(19.36)	(27.91)	(17.15)	(27.76)	(15.60)	(28.77)	(15.60)	(27.91)	(15.72)	(18.43)	(15.23)	(19.36)	(15.23)	(17.15)	(15.47)
Range	24-123	24-82	23.-123	24-82	24-123	30-82	24-123	36-77	24-123	36-77	24-123	36-77	24.25-82	36-77	24-82	36-77	30-82	36-77

6.3.5 Data analysis

Using Kolmogorov-Smirnov tests for normality, data were found to be highly non-normally distributed ($p < .05$), therefore non-parametric techniques were used throughout. Alpha was set at .05. One tailed analyses were used for comparisons for which directional a priori hypotheses had previously been stated. As in stated in section 5.3.5, one tailed analyses can be used where the direction of anticipated effects has been previously specified. Because of onstraints relating to smaller sample size, reduced power of non parametric analyses and clinical significance of issues relating to impulsive and disinhibited behaviour it was felt this type of analysis would optimise the ability to detect clinically significant effects.

Questionnaire data assessing behavioural profiles relating to impulsivity and inhibition were only available for SMS and DS participants, therefore only data for these two groups is presented. To assess these differences, behavioural rating of individuals with SMS and DS were compared on subscales assessing impulsivity, inhibition and emotional control.

To explore how these behaviours relate to one another and examine possible associations between behaviours, correlations between each of the questionnaire scales were performed, separately for each syndrome group. Correlations between questionnaire measures of behaviour and task performance (separately for each task) were carried out to identify relationships between behaviour and cognitive performance on inhibition tasks.

To identify differences in task performance on the inhibition battery, scores were compared between each pair of matched comparison groups. These are presented separately for each of the three comparisons made (SMS-DS, SMS-Normative, DS-Normative).

6.4 Results

6.4.1 Caregiver behavioural descriptions

Caregiver ratings of behaviours reflecting impulsivity, inhibition and emotional control for individuals with SMS and DS were compared using one tailed Mann-Whitney analyses. Figure 6.1 below shows the average and spread of scores for these comparisons, illustrating the elevated averages for SMS on each measure.

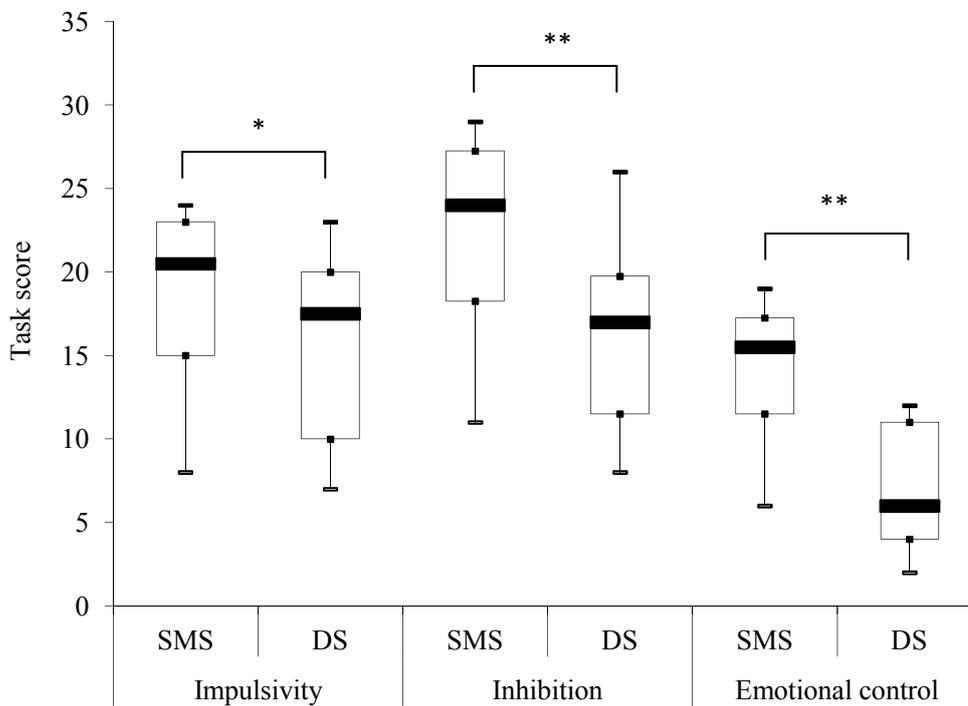


Figure 6.1 Median, maximum, minimum and inter-quartile range of caregiver ratings of impulsivity, inhibition and emotional control for SMS and DS (* $p \leq .05$, ** $p \leq .005$)

Results demonstrated that the groups differed significantly on all three behaviours, with those with SMS rated as showing higher levels of impulsivity ($U = 70.5, p = .043$) and more difficulties with inhibition and emotional control ($U = 49.5, p = .004$ and $U = 23, p < .001$).

6.4.2 Cognitive assessments of inhibition

Performance on the battery of cognitive inhibition assessments was compared between each of the pairs of matched comparison groups.

Median SMS and DS scores for the reverse categorisation, bear dragon and black white Stroop were compared. Figure 6.2 below demonstrates the overall similarities of syndrome group averages for the three tasks.

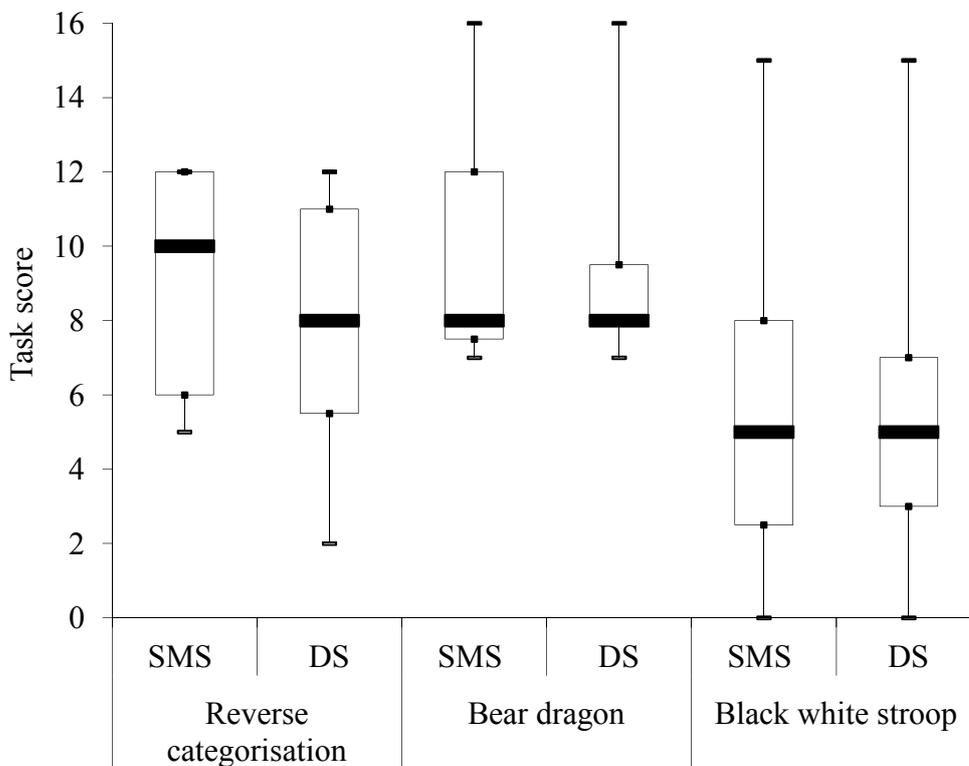


Figure 6.2 Median, maximum, minimum and inter-quartile range of inhibition tasks in Smith-Magenis syndrome and Down syndrome (* $p \leq .05$, ** $p \leq .005$)

Using Mann-Whitney analyses no significant difference was found between the performance of individuals with SMS and DS on any of the tasks from the inhibition battery (Bear dragon;

$U = 83.5, p = .491$, Reverse categorisation; $U = 67.5, p = .196$, Black white Stroop; $U = 66.5, p = .383$.

The SMS sample and the normative sample (typically developing children) were also compared across each of the three inhibition tasks. Figure 6.3 below shows the differences between the two groups on task scores, with SMS having lower average scores on all tasks.

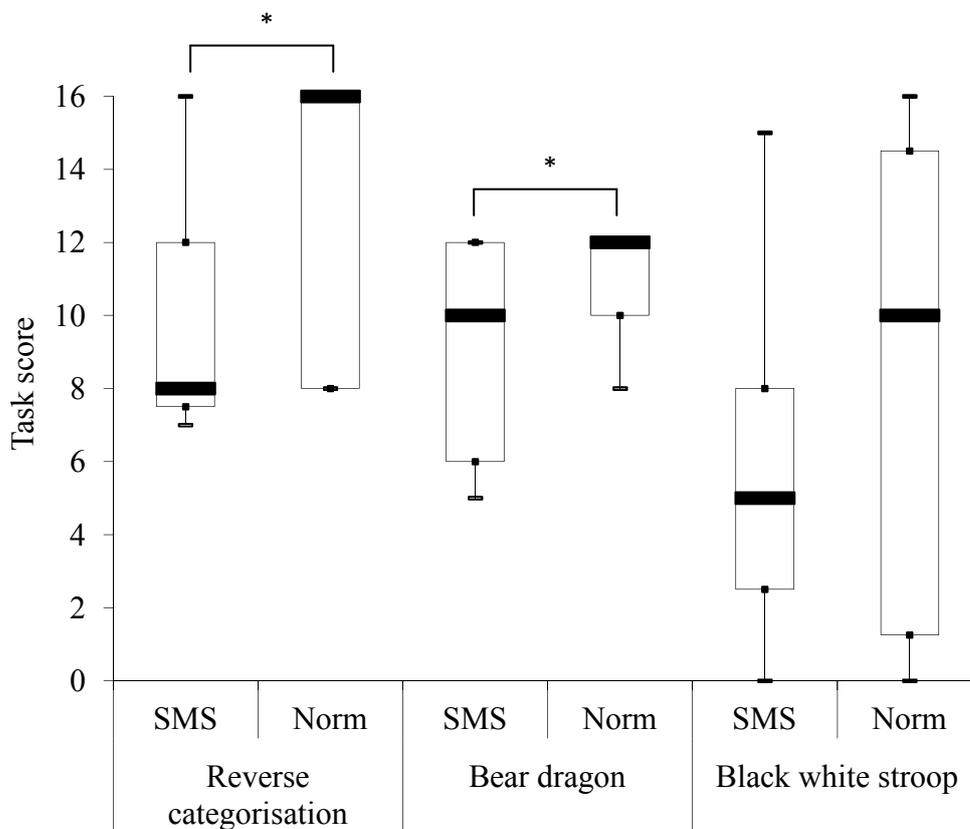


Figure 6.3 Median, maximum, minimum and inter-quartile range of inhibition tasks scores for Smith-Magenis syndrome and typically developing (normative sample) participants (* $p \leq .05$, ** $p \leq .005$)

Mann-Whitney comparisons highlighted significant differences between the SMS group and the normative contrast group on two of the three inhibition tasks. Individuals with SMS

performed significantly less well than the typically developing sample on the Reverse categorisation ($U = 52, p = .038$) and Bear dragon tasks ($U = 41, p = .01$). No difference was found between the SMS group and the normative contrast group for the Black white Stroop task ($U = 49, p = .095$).

Finally the DS and normative samples (typically developing children) were compared. A similar pattern of results to those identified for the SMS-Normative sample comparison was found for comparisons between the DS and Normative sample groups, with these similarities illustrated in comparison between figure 6.4 below and figure 6.3 above.

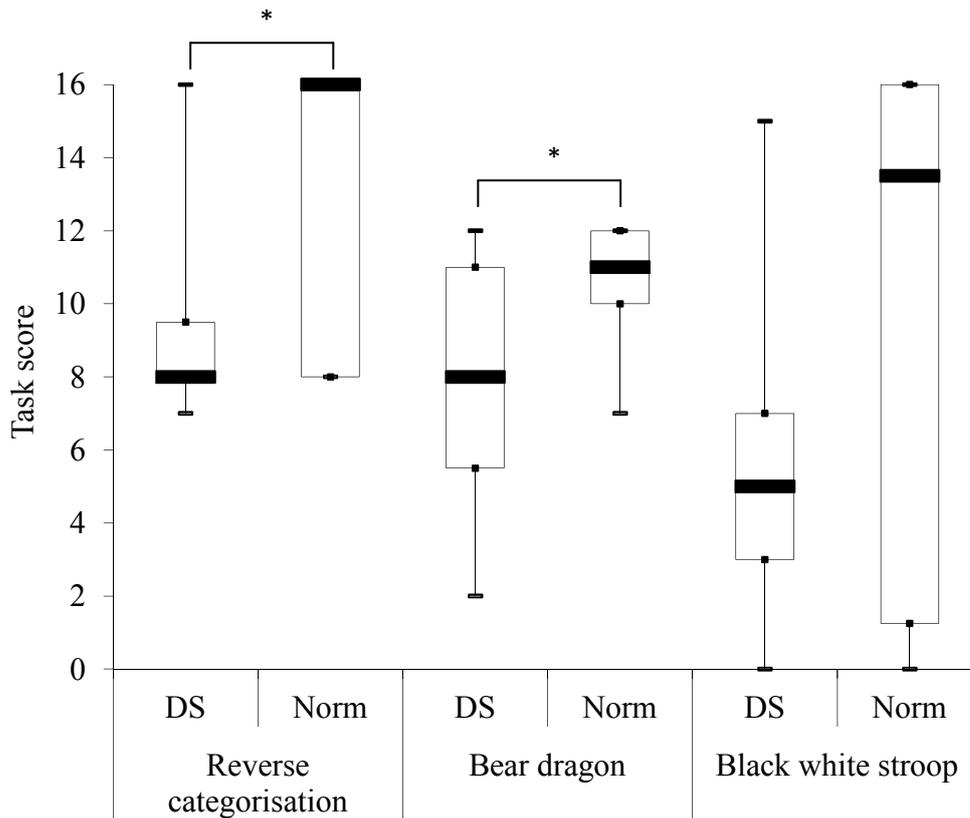


Figure 6.4 Median, maximum, minimum and inter-quartile range of inhibition tasks scores for Down syndrome and typically developing (normative sample) participants (* $p \leq .05$, ** $p \leq .005$)

Mann-Whitney comparisons identified that the DS group performed less well on both the reverse categorisation and bear dragon task ($U = 39.5$, $p = .009$ and $U = 48$, $p = .025$ respectively). Performance on the Black white Stroop however, did not differ between the two groups ($U = 50.5$, $p = .110$).

6.4.3 Correlations between behavioural descriptions and task performance

Performance on each inhibition task was correlated with scores on questionnaire measures using Spearman’s correlations, separately for each syndrome. These correlations are shown in table 6.2 below, which shows significant relationships only for the Bear dragon task.

Table 6.2 Spearman correlations between caregiver ratings of impulsivity, inhibition and emotional control and task performance for the syndrome groups (* $p < .05$, ** $p < .005$)

	SMS			DS		
	Impulsivity	Inhibition	Emotional control	Impulsivity	Inhibition	Emotional control
Bear dragon	-.49*	-.61*	-.63*	-.53*	.001	.15
Reverse categorisation	.03	.28	.14	-.38	-.14	-.26
Black white Stroop	-.49	-.43	-.44	-.19	-.04	-.10

For each significant relationship identified performance on the Bear dragon task was negatively related to behaviour problems reported by caregivers, such that increased difficulties were associated with poorer performance. In SMS every problem behaviour was correlated with task performance, whereas in DS only impulsivity was.

6.4.4 Associations between behavioural descriptions

To identify correlations between behavioural descriptions, caregiver ratings of each behaviour (impulsivity, inhibition and emotional control) were correlated. Table 6.3 shows the correlations between caregiver ratings of behaviour and the inconsistencies between SMS and DS patterns of significant associations.

Table 6.3 Spearman correlations between caregiver ratings of impulsivity, inhibition and emotional control for the syndrome groups (* $p < .05$, ** $p < .005$)

	SMS		DS	
	Impulsivity	Inhibition	Impulsivity	Inhibition
Inhibition	.45		.52*	
Emotional control	.92**	.62*	.39	.32

In SMS no correlation was found between measures of impulsivity and inhibition. However, significant positive correlations were found between impulsivity and emotional control difficulties (increased emotional control problems being related to increased impulsivity) and also inhibition difficulties and emotional control difficulties (increased emotional control problems being related to increased difficulties with inhibition). For the DS sample the reverse pattern of results was found; significant positive correlations were only found between ratings of impulsivity and inhibition (increased inhibition problems being related to increased impulsivity) and no correlation was found between impulsivity and emotional control or inhibition and emotional control.

6.5 Discussion

Behavioural reports of impulsivity and potentially associated behaviours were examined in a group of children with SMS and a comparable DS contrast group. Additional direct testing of response inhibition was carried out, where each group was separately matched with a typically developing contrast group, to examine the role of response inhibition as a potential cognitive substrate of impulsivity. This study is the first to directly examine the potential cognitive endophenotype of impulsivity in SMS, employing contrast groups from both typically developing and intellectual disability samples, against which the findings for SMS can be anchored. Contrast groups were selected using methods to optimise comparability in terms of cognitive ability (see section 6.3.2.2 and appendix O). Additional use of informant report measures of behaviour enables ecologically valid assessment of behaviour, which aims to reflect children's everyday level of functioning and enables associations to be made between these behaviours and cognitive assessments.

Results showed individuals with SMS were reported to have more difficulties than those with DS with impulsivity, inhibition and emotional control. In contrast, and unexpectedly, no difference was found between performance of children with SMS and DS on any tasks assessing response inhibition (both syndrome groups were impaired compared to mental age matched typically developing children). For relationships between behaviours examined in informant reports, impulsivity was only correlated with inhibition in DS, whereas in SMS it was only correlated with emotional control. Finally, task performance was only correlated with informant reports of behaviour for one task (the Bear dragon task) and patterns of correlations were inconsistent across syndrome groups.

Suggestions in the literature that individuals with SMS have elevated and problematic impulsivity (see section 2.4.7) are supported by caregiver reports of behaviour in the current study, with findings indicating that children with SMS have more problems across a range of related areas of behaviour (impulsivity, inhibition and emotional control). This cluster of behaviour indicates that those with SMS have difficulties across a range of behaviours that are likely to be related and relate to dysregulation of control systems. Elevated impulsivity has implications for the well being of those with SMS and those who care for them. As noted in section 2.4.5.3, impulsivity is not only considered to be a difficult behaviour in itself (Clarke & Boer, 1998) but it has also been linked to other challenging behaviours such as aggression (Arron *et al.*, 2011; Sloneem, Arron, Hall & Oliver, 2009; Sloneem *et al.*, 2011). Challenging behaviours, such as self-injury, pose potential risks to physical health and also negatively impacts on quality of life including community inclusion, home placements and access to services (Borthwick-Duffy, 1994; McGill, Papachristoforou, & Cooper, 2006; Rusch, Hall, & Griffin, 1986) and is a significant source of stress, impacting negatively on the mental health of caregivers (Hastings, 2002). Identifying SMS as a genetic disorder associated with particularly high levels of impulsivity has implications for early intervention and behavioural management strategies. Furthermore, examination of the underpinnings of impulsivity in SMS carried out in the current research, may suggest specific targets for intervention strategies.

It is important to note here that the finding of significant deficits in impulsivity in comparison to DS were the result of a one tailed analysis. As the one tailed probability level of the SMS-DS comparison was .043, had this been a two tailed analysis the difference would not have been significant. Use of a one tailed analysis was justified in section 6.3.5 and is the result of consistent application of principles relating to use of a priori directional hypotheses for comparisons where a known effect is expected to be replicated. Furthermore if a one tailed analysis had been carried out this finding would still represent a trend of clinical interest and relevance, particularly in the context of the existing literature discussed in section 2.4.7

reflecting high levels of carer reports difficulties with impulsive behaviour. It is however interesting that the difference found between SMS and DS in emotional control was associated with a notably smaller probability level. Whilst this is not a direct indication of the size of the effect it does suggest emotional control may be an important factor in the cluster of behaviours investigated here.

In the context of likely difficulties with impulsive and more generally dysregulated behaviours indicated in both the current findings and the literature on behaviour in SMS, the finding that children with SMS were reported by caregivers to have more difficulties with inhibition is interesting, as inhibition was identified as a strong candidate cognitive process underpinning impulsive behaviour (see section 2.4.7.3 and Barratt 1985, 1994). The measure of inhibition in the current study is purported to be an ecologically valid measure (Isquith, Gioia & Espy, 2004), indicating that children with SMS may demonstrate behaviours in their every day environments that indicate difficulties in inhibiting responses. However, the extent to which this suggests that *cognitive* inhibition is actually impaired and thus might be an explanatory mechanism for impulsive behaviour in SMS is questionable. ‘Inhibition’ measured by this type of scale is not synonymous with inhibition as a cognitive process (i.e. response inhibition) and the two may not refer to the same concept. Many measures that aim to assess executive dysfunction in an ecologically valid context do not correlate well with cognitive task performance on executive function tasks (Anderson, Anderson, Northam, Jacobs & Mikiewicz, 2002; Vriezen & Pigott, 2002). This is supported by lack of differences in inhibition as assessed using direct cognitive assessments, discussed in detail below.

Greater difficulties with emotional control reported in SMS are of note given the authors of the informant report measure of inhibition and emotional control identified these two aspects

of executive function as forming an underlying factor of Inhibitory Self Control (Isquith *et al.*, 2004). Having deficits in both inhibition and emotional control, children with SMS may therefore be described as having a broader deficit in inhibitory self control. Deficits in both inhibition and emotional control are particularly interesting considered in the context of Barratt's multidimensional definition of impulsivity, which includes inability to delay gratification in addition to failure of response inhibition (Barratt, 1985, 1994). Difficulties with emotional control are likely to impair ability to delay gratification, as delay is conceptualised as emotionally aversive (Sonuga-Barke, 2003). Relationships *between* caregiver ratings of impulsivity, inhibition and emotional control, reflected a divergent pattern of relationships between the two syndrome groups that again implicates a specific role of emotional control in impulsive behaviour in SMS. However, it is important to note that emotional control and inhibition are unlikely to operate independently (indeed in SMS emotional control was also correlated with inhibition, despite inhibition not being correlated with impulsivity). Furthermore caution must be exercised at this level of interpretation as causality cannot be inferred from these measures or the analyses used in the current study.

While emotional control difficulties have not been specifically investigated in SMS, reports of behaviour in the syndrome such as explosive temper outbursts with subsequent contrition (Haas-Givler, 1994) implicate such difficulties, suggesting these behaviours are out of the control of those showing them. It is possible therefore that individuals with SMS may have difficulties controlling their emotional responses as well as with inhibition and that these difficulties, either separately or in conjunction, result in impulsive behaviour. There is converging evidence therefore for difficulties with emotional control in SMS, which in the context of literature regarding pathways to impulsive behaviour implicate potential deficits in

ability to delay gratification in SMS. Consideration of this as a specific deficit in SMS therefore seems warranted.

As noted above, findings that those with SMS were reported to show more behavioural difficulties associated with impulsivity and dysregulated behaviour than those with DS, contrast with lack of anticipated impairments in performance on cognitive tasks assessing response inhibition (a potential cognitive function underpinning impulsivity) in comparison with this group. This key finding is contrary to the hypothesis that deficits in response inhibition would be found in SMS. If deficits in response inhibition underpin impulsive behaviour, a group that is significantly less impulsive than SMS may also be expected to show fewer difficulties in response inhibition. Lack of response inhibition deficits in SMS compared to DS, who were reported to have significantly fewer difficulties with impulsive behaviour, therefore suggest that it may not be specific inhibition deficits in SMS which underpin the impulsive behaviour. Findings described above relating to emotional control implicate this as a novel candidate function which may account of the elevated impulsivity in SMS.

Both groups did however show response inhibition deficits compared to typically developing children. Explanations for this latter difference may be linked to the role of language in enabling children to manage their own behaviour. Children with DS and SMS both have expressive language delays that are separate from and greater than their cognitive delay (Chen *et al.*, 1996; Gunn & Crombie, 1996). It has been suggested previously that this may explain, in part, difficulty in inhibiting behaviour (Cuskelly *et al.*, 2001)³⁹. Thus differences in

³⁹ in relation to DS specifically

expressive language may also account in part for differences between the syndrome groups and typically developing mental age matched children.

Low correlations between performance on response inhibition tasks and informant report measures are unsurprising. As noted previously lack of relationships between informant report measures and cognitive tests is common (Anderson *et al.*, 2002; Vriezen & Pigott, 2002). Performance-based tests tap individual components of executive function over a short time window rather than the more complex and multidimensional decision-making required in real-world situations (Goldberg & Podell, 2000; Shallice & Burgess, 1991). Thus, the two measures may not be strongly associated. The measure of inhibition used in the current study (BRIEF-P) was designed specifically to capture real-world behavioural manifestations of executive dysfunction and it seems likely that even when executive function performance in everyday contexts is narrowed to individual components such as inhibition, there are more influences on behaviour in this context than in response inhibition tasks.

Relationships were found for performance on the Bear dragon task, which was associated with all behavioural measures in SMS and to impulsivity in DS. Level of social interaction involved in the task (children are required to actively engage with both researcher and puppets) may account for this, with additional social and emotional components increasing similarity of this task to those in everyday life. In SMS, correlations were found between emotional control and performance on this task, possibly because children with this syndrome find it harder to control the impulse to respond to requests in a socially and emotionally motivating context. Specificity of these findings to SMS again implicates a syndrome specific role of emotional control. Findings that inhibition was also linked with task performance in

SMS again suggest emotional control is unlikely to operate independently from ability to inhibit responses more generally.

Emotional control has been discussed in relation to broad conceptualisations of impulsivity and also deficits in the current sample of children with SMS and possible links with the impulsivity identified. It has also been considered more generally in the mainstream executive functioning literature. Recent conceptualisations of executive function take into account the affective components of tasks that involve executive functions. This approach makes a distinction between ‘hot’ executive function and ‘cool’ executive function. Hot executive function involves control over reward systems and is linked to motivation and emotion and to emotional and social responses (and associated limbic brain regions) (Hongwanishkul, Happaney, Lee, & Zelazo, 2005).

In contrast, cool executive function has been described as governing more abstract tasks with no emotional component. Everyday decision making and behaviour (for example impulsive acts) is unlikely to be performed in the absence of emotional and motivational influences, thus the importance of considering these factors is evident. While hot and cool executive functions are potentially distinct in terms of behaviour and underlying brain structures, theorists emphasise that they are still considered to interact together as a part of a single coordinated system (see Hongwanishkul *et al.*, 2005; Zelazo & Müller, 2002). Thus, when evaluating the processes underpinning impulsive behaviour in SMS, it is important not to put too much emphasis on this distinction.

While response inhibition and delay of gratification, (and related hot and cool executive functions) are not considered to operate independently, understanding potential contributions of each to behavioural outcomes such as impulsivity is important, particularly for potential interventions. For impulsivity related primarily to deficits in response inhibition, cognitive training may improve this ability. Training of executive functions has been shown to be effective for children with ADHD (specifically working memory, but working memory training was found to have a positive effect on inhibition) (Klingberg *et al.*, 2002; Klingberg *et al.*, 2005). However, if emotional control rather than inhibition is a primary deficit then this should be the target of intervention. Training to improve children's control of their desire for a reward, (i.e. delay their gratification) has been successfully carried out with children with DS, suggesting that emotional responses may be amenable to change (Schweitzer & Sulzer-Azaroff, 1988).

A number of limitations should be considered when interpreting the results of the current study. The use of DS as a control group has been identified previously as a potentially problematic issue in behavioural phenotype research, as they have their own characteristic behaviour phenotype (see sections 1.4.2 and 5.5). Individuals with DS have been found to be more impulsive than typically developing children (e.g. Coe, Matson, Russell, Slifer, Capone, Baglio & Stallings, 1999; Pueschel, Bernier & Pezzullo, 1991) and direct testing has found that young children with DS were less able to inhibit responses (wait to touch a tempting stimulus) than a group of typically developing children matched on developmental age (Kopp, 1990). DS is itself may therefore be associated with elevated impulsivity which, despite being less than those with SMS (as evidenced in behavioural reports), is driven by deficits in inhibition and thus similar inhibition deficits are found in the two syndromes. This may account in part for the finding that had a two tailed test been employed a significant difference

would not have been found between the groups. However, given striking differences in caregiver reports of impulsivity between the groups in the broader literature and the fact that differences were still found in the current study, if inhibition were the primary driver of the behaviour in SMS differences in this may still be expected to be found.

Given the potential role of expressive language in inhibiting behaviour (Cuskelly, Einam & Jobling, 2001), ensuring groups are comparable on this key cognitive characteristic was particularly important when selecting a contrast group for the current study. This ensures that the ‘same but different’ criteria for selection of contrast groups is considered. More general arguments for the utility of DS as a contrast group when examining behaviour in SMS are covered in the discussion of studies of social behaviour in sections 3.5, 4.5 and 5.5. Together, evaluation of the use of DS as a contrast group suggests that it is a valid choice given overall similarities with SMS in ability and difference on key variables of interest and despite potentially elevated impulsivity, clear differences between this in DS and SMS suggest valid contrast can still be made. Use of an additional contrast group of typically developing children may address some of the issues caused by the use of a contrast group with an intellectual disability (for example that disinhibited behaviour may be associated with developmental delay).

An additional limitation is that the sample sizes were quite small, thus it is possible the study was underpowered. Use of individual mental age matching to ensure samples were comparable, robust and developmentally sensitive tests of inhibition and carefully selected contrast groups may go some way to addressing this. Direct testing of children with SMS presents unique challenges; high levels of challenging behaviour, short attention span and high levels of impulsivity associated with the syndrome (Dykens *et al.*, 1997; Greenberg *et*

al., 1996; Smith *et al.*, 1986) can result in sample attrition. Given the rarity of the syndrome, recruitment of sufficient numbers of participants able to complete testing poses a further challenge. These types of difficulties are inherent in behavioural phenotype research with rare disorders and should be addressed by using effective matching and strong experimental paradigms.

Participants with SMS able to undertake the direct assessments of response inhibition were a subset of a larger sample, as were the DS group. As such it is possible children with SMS may not have differed from those with DS on inhibition tasks because those with the greatest difficulties with inhibition and impulsive behaviour may have been unable to complete the direct tests. However, as noted in section 6.3.2.2 (footnote), analysis of those with SMS who were unable to complete tasks does not support this. No differences were found on measures of impulsivity, inhibition, emotional control between the children who did and did not complete each task. This suggests the sample of children who were assessed form a representative sample of the larger initial group of children with SMS in terms of key behavioural characteristics.

In summary the current study failed to support the hypothesis that there would be specific response inhibition deficits in SMS compared to DS, commensurate with deficits in impulsive behaviour, which was posited as a potential explanatory mechanism for high levels of impulsivity reported in the syndrome. Elevated levels of impulsive behaviour were however found to be reported in SMS (using a one tailed significance test) and these were associated with deficits in emotional control, an association not found in DS, implicating a possible role of emotional control in impulsive behaviour in SMS.

These novel findings regarding the potential role of emotional control in impulsive and dysregulated behaviour in SMS could be extended using direct tests which assess ability to delay gratification. Tasks such as the Tea task where children are instructed not to touch a tempting food item while the mother is distracted or the Gift task where children are required to not touch a tempting, wrapped gift have been used previously with children with intellectual disability (Cuskelly *et al.*, 2003). Using this assessment may clarify whether children with SMS do have specific difficulties in this area. To further explore the role of emotional control neuroimaging studies could be undertaken, examining brain structures associated with performance on tasks considered to involve 'hot' executive functions, which involve emotionally salient aspects, compared to those involving 'cool' executive functions, which are more abstract. Examination of patterns brain activation while completing these tasks would enable exploration of underlying neuroanatomy.

CHAPTER 7

General discussion

7.1 Preface

The study in chapter six identified a potential association between impulsivity and emotional control in SMS. In the context of findings in chapters three, four and five indicating a profile of atypical social functioning in the syndrome, social-emotional deficits appear to be emerging as a potential endophenotype of the syndrome. Aspects of the behavioural phenotype of SMS such as attention-seeking and impulsivity may be associated with such deficits. This chapter will briefly summarise the results of all studies in the context of the literature presented in chapters one and two. The hypothesised model of behaviour in SMS presented in chapter two will then be re-evaluated and extended to integrate the findings of the studies.

7.2 Introduction

The introductory chapters to this thesis presented an overview of behavioural phenotype research (chapter one) and research to date examining the behavioural phenotype of SMS (chapter two). In sections 1.3 and 1.4, trends in behavioural phenotype research, differing methodological approaches and issues in behavioural phenotype research were discussed. Key issues such as need for theoretically driven choices of contrast groups, use of measures of behaviour likely to be sensitive to between group differences and consideration of how genetic difference can lead to specific behavioural outcomes were identified.

The behavioural phenotype of SMS was then described. The behavioural phenotype is characterised primarily by developmental delay, a range of difficult behaviours and sleep disturbance (see sections 2.4.2, 2.4.3 and 2.4.10). In addition to the very commonly reported behaviours associated with SMS, other features such as Autism Spectrum Disorder (ASD), impulsivity, ‘unique’ behaviours and ‘attention seeking’ are also purported to form part of the behavioural phenotype (see sections 2.4.9, 2.4.7, 2.4.6 and 2.4.8). Based on the SMS behavioural phenotype literature, a hypothetical model of pathways from genetic characteristics to behaviour in this syndrome was made explicit (see section 2.5, figure 2.1). The model incorporated key behaviours outlined above and highlighted their potential interrelations. The model also identified environmental influences on behaviour, enabling conceptualisation of interactions between genetic difference and the environment. In addition to relatively well researched features of SMS represented in the model (e.g. challenging behaviour), the review of the SMS behavioural phenotype identified two aspects of behaviour which have received very little examination to date: attention-seeking and impulsivity.

Attention-seeking is commonly reported as part of the behavioural phenotype of SMS, (see section 2.4.8.2), however, its specific nature and the behaviours it incorporates were unclear. Need for direct examination of attention-seeking in SMS was determined. Empirical description of social behaviours and subsequent identification of environmental influences that might influence these were identified as next steps needed in future research. Approaches used to investigate social motivation in other genetic syndromes, including natural observations and experimental manipulations of social variables, were reviewed guiding this novel area of research in SMS (see sections 4.2 and 5.2).

Impulsivity was a second commonly reported aspect of the behavioural phenotype of SMS that to date has been investigated primarily using informant report measures. The need for a greater understanding of impulsivity was reinforced by strong associations found between impulsivity and aggression in SMS (see section 2.4.5.3). Examination of existing impulsivity literature identified deficits in behavioural inhibition as a cognitive impairment thought to underpin impulsive behaviour (see sections 2.4.7.3 and 6.2). Approaches to investigating both impulsivity and inhibition, including informant report measures and direct testing, were discussed and their utility for assessing these aspects of behaviour in SMS was evaluated (see section 6.2).

The paucity of focussed research of these aspects of the SMS behavioural phenotype requires attention as both are associated with a range of negative outcomes for those with SMS and their caregivers (see sections 2.4.7 and 2.4.8). The two main aims of this thesis were therefore to evaluate reports of unusual social behaviour in SMS characterised by attention-seeking and preference for adult attention and to examine impaired inhibition as a potential explanatory

mechanism of elevated impulsivity in SMS, building on approaches used successfully in the past with other relevant populations.

7.3 Summary and discussion of results

Each of the studies designed to address the first aim of evaluating reports of an unusual profile of social behaviour, characterised by what is labelled attention-seeking and preference for adult attention, will be considered in turn.

7.3.1 Refining the description of atypical social behaviour in Smith-Magenis syndrome

An initial questionnaire study (chapter three) aimed to describe a number of key aspects of social functioning in the syndrome, using caregiver report measures that specifically assess social behaviour. Sociability, targeted social drive (found previously to be elevated in SMS, Moss *et al.*, 2009) and ASD phenomenology were evaluated. Behaviour in SMS was contrasted to a developmentally matched group with Down syndrome (DS) and a group with ASD. Questionnaire methodologies built on previous approaches using informant report measures, extending beyond a single item relating to attention-seeking by using multiple, broader social measures and employing multiple contrast groups. This enabled more detailed understanding of diverse aspects of social functioning in SMS and enabled contrasts to be made both within groups for these different aspect of social functioning and across groups to explore specificity of behaviours to SMS.

Caregiver reports of social behaviour in SMS broadly supported past research (reviewed in section 2.4.8) suggesting an unusual profile of social behaviour. Findings provided insight into both the nature of attention-seeking and social preference in SMS. ‘Attachment’ to particular people, characterised by continually asking to see, speak to or contact a particular person, was elevated in SMS. This is consistent with previous research in which this behaviour was also found to be elevated in SMS compared to a number of other genetic

syndromes (Moss *et al.*, 2009) and suggests these behaviours may be a definitive property of attention-seeking in SMS. However these behaviours were not accompanied by generally increased ratings of sociability, compared to DS (contrasting with hypersociability described in Williams syndrome, WS, Jones *et al.*, 2000), suggesting increased social drive to interact with specific people is not characterised by behaviours generally considered to indicate sociability (e.g. heightened smiling reported in Angelman syndrome, AS, Oliver *et al.*, 2007). Rather it may be characterised by difficult behaviours (e.g. negative affect, challenging behaviour) which may then be labelled ‘attention-seeking’ by caregivers (e.g. Dykens *et al.*, 1997, 1998). This is credible given high rates of challenging behaviours in SMS (see section 2.4.3 for a review) and findings presented in chapters four and five indicating that positive affect was not elevated in SMS during social interactions (see sections 4.4.2.2, 4.4.3.4 and 5.4.2.1).

Despite overall similarities in sociability in DS and SMS, those with SMS did not differ in sociability with familiar peers from those with ASD (who showed generally decreased sociability) and sociability with familiar peers did not differ in SMS from sociability with unfamiliar individuals. This represents relatively low sociability with peers, which has been noted previously within the school environment (Haas-Givler, 1994). Lack of interest in peers may increase perceptions that those with SMS seek attention from adults as they may not turn to peers as alternative sources of social interaction. In this context the focus of the ‘attachment’ to people described previously seems more likely to be an adult than a peer further increasing perceptions of attention-seeking by adults.

In summary, the first study found support for an unusual social drive in SMS and provided insight into the nature of the attention-seeking behaviours and social preferences reported to characterise this. Two further studies employed direct observation of social behaviour in SMS, guided by the findings of this informant report study and past research. This direct observation of behaviour enabled systematic, reliable and objective assessment of social behaviour. In both studies behaviour was contrasted to that of a developmentally comparable group of children with DS.

7.3.2 The nature of social preference and interactions in Smith-Magenis syndrome.

A natural observation study was conducted, observing children with SMS throughout the school day, thus assessing behaviour in an ecologically valid context (see chapter four). Findings of the initial questionnaire study (section 3.4) implicated preference to be a key feature of unusual social behaviour in SMS, therefore this study examined social preferences specifically. Children's social behaviour and key environmental variables were assessed. Behaviour in different settings (one-to-one attention, shared attention and during free-play when there was no direct attention available) and with different people (adults and peers) was contrasted, evaluating effects of attention and social preference. Additionally, sequences of behaviour were examined to explore the reciprocal nature of interaction between children and adults.

Findings further supported the characterisation of relatively strong preference for adult attention and provided new insights into structure and content of the interactions between children with SMS and adults in their environment by fine grained examination of sequences

of behaviour. Compared to the contrast group a consistently higher preference for interacting with adults over peers was found across all conditions in which children were observed (one-to-one attention, shared attention and free-play). This preference was demonstrated both in terms of the attention children with SMS gave to adults and how much they looked at adults. This validates accounts of attention-seeking towards teachers, and reduced interest in peers, (Haas-Givler, 1994; Haas-Givler & Finucane, 1996) which to date has only been reported anecdotally. In contrast to a clear preference for initiating interaction with adults, greater positive affect was not evident when interacting with adults, and negative affect did not increase when available adult attention reduced. This is inconsistent with other syndromes associated with strong social motivation where increased positive affect has been associated with high levels of attention suggesting enjoyment of the interaction (e.g. AS, Oliver *et al.*, 2007).

Examination of sequences of behaviour failed to support hypotheses that attention-seeking in SMS would be characterised by earlier initiation of interaction with adults compared to the contrast group. Similarly there was no evidence that children with SMS were hypervigilant for adult attention. However, there were indications that children with SMS maintained eye contact for longer after the interaction, which has also been suggested to occur in AS (Mount *et al.*, 2011). The function of this is unclear and warrants further investigation. Reduced reciprocity of social behaviour between adults and children with SMS was found, suggesting that turn taking is compromised in SMS, a finding interpreted as reflecting possible initiations from children with SMS at times when adult attention was not freely available. Given the potentially inappropriate nature of initiations in SMS they may be considered to be more problematic, thus being reported as attention-seeking.

Together key findings from this study provide further empirical support for reports of unusual social behaviour in SMS, more specifically the suggestion that children with SMS have a preference for adult attention over that of peers. Novel findings suggested atypicalities in the reciprocal nature of interaction between children with SMS and adults in their environment and that preference for adult attention may not be reflected in increased reciprocity, earlier initiation of interaction or increased enjoyment during interactions with adults.

7.3.3 Effect of adult familiarity and level of attention on social behaviours in Smith-Magenis syndrome

A final study of social behaviour experimentally manipulated environmental variables during structured social situations to evaluate the effect of differing levels of attention and preference for familiar adults (see chapter five). This enabled causal inferences about determinants of social behaviour in SMS and further delineation of social preferences outlined in the first two studies. Children were engaged in play by an interacting adult (high attention) who then left the room (low attention). Children's mothers and an unfamiliar adult alternated in this role. An unresponsive adult was also present in the room but instructed to provide no attention, potentially evoking a wider range of behaviours. Real time coding and rating scales were used to assess children's behaviour, including motivation and affective responses.

Results (section 5.4) portray a complex pattern of behaviours in response to experimental manipulations of social variables, depending on the role of the adult in the scenario.⁴⁰ The primary findings were i) children with SMS had a preference for the attention of a familiar

⁴⁰ Neither level of available attention nor adult familiarity had a differential effect across the syndromes on behaviours directed towards the main interacting adult.

adult (their mother) and ii) children failed to turn to an unfamiliar adult as an alternative source of attention when their mother had left the room. This implicates a role of familiarity whereby preference for adults (and seeking of attention from them) may be restricted to familiar adults rather than a generalised drive for adult attention (supporting suggestions presented in section 3.5). This finding was discussed in the context of perceived burden (Isles, 2011) for this target of the child's attention. Reliance on one particular person for attention may increase perceptions (and thus reports) of attention-seeking. As with natural observations (section 4.4.2.2) affective responses during social interactions did not differ between groups as a function of level of available attention or adult familiarity, suggesting again that elevated attention-seeking shown by children with SMS is not characterised by a similar level of enjoyment during interactions.

Findings of this controlled study of social behaviour in SMS therefore provide both insight into the nature of attention-seeking (characterised by approach behaviours rather than positive affective responses) and further objective and reliable descriptions of social preferences (found to be specifically towards familiar adults) reported to be shown by those with the syndrome. These findings are novel and significantly extend understanding of the potential manifestation of atypical social behaviour in SMS.

7.3.4 Overall summary of studies of social behaviour

Reports of unusual social behaviour have been supported by three studies using diverse methodologies to evaluate social behaviour.

Taken together, findings suggest that children with SMS:

- 1) Show elevated attention-seeking behaviour toward familiar adults but not a generalised increase in sociability.
- 2) Demonstrate reduced accessing of alternative sources of attention, such as peers and unfamiliar adults.
- 3) Do not appear to enjoy or actively reciprocate in interactions with preferred adults more, despite increased initiation of interaction.

7.3.5 Impulsivity and inhibition

A fourth study examined impulsivity in line with the second aim of the study of evaluating impaired inhibition as an explanatory mechanism of elevated impulsivity in SMS (see chapter six). This study experimentally assessed the ability to inhibit dominant behavioural responses in order to evaluate whether compromised inhibition underpins elevated impulsivity. Performance on inhibition tasks was related to caregiver reports of impulsivity and everyday difficulties with behavioural inhibition.

Findings challenged the role of inhibition as an explanatory mechanism for impulsivity in SMS, and provided a potential alternative underlying mechanism. Impulsive behaviour (assessed by caregiver report) was supported as a difficult aspect of behaviour in SMS. Unexpectedly inhibition deficits (measured using cognitive assessments) relative to those with DS were not found, despite significant deficits relating to impulsive and dysregulated behaviour in comparison to this group. It is important here to note the caveat outlined in

detail in section 6.5 regarding the use of a one tailed analysis, whereby the significant difference between SMS and DS on caregiver reports of impulsive behaviour would not be found in a two tailed analysis. However, a difference was found given the a priori analysis strategy employed and in the context of the existing literature reporting impulsivity problems in SMS this difference (or the trend that would be found with a two tailed analysis) remains clinically significant. That inhibition deficits were not found given the impulsive and dysregulated behaviours found in the current study and past research challenges the explanatory power of inhibition deficits for impulsive and dysregulated behaviour in SMS. Furthermore reports of inhibition deficits were not related to reports of impulsive behaviour in SMS but emotional control, a prominent deficit in SMS, was. This relationship (not found for the contrast group) suggests that deficits in emotional control may account at least in part for impulsive behaviour in SMS. A role of emotional control in impulsivity is supported by the dual pathway model of ADHD (Sonuga-Barke, 2003, see section 2.4.7.3) where one pathway describes impulsive behaviour as resulting from an inability to delay gratification (whereby delay is emotionally aversive). While inhibition and emotional control are not believed to function independently, thus the influence of inhibition in SMS should not be discounted, consideration of a role of emotional control in impulsivity in SMS seems appropriate in this context. Emotional dysregulation and self control as a difficulty in and of itself in SMS is an issue that requires attention both in research but also in clinical practice, in terms of intervention to increase ability to control emotional responses.

In summary, rather than expected deficits in inhibition, deficits in emotional control were related to impulsive behaviour in SMS in the current study. The finding is in line with conceptualisations of the causes of impulsivity which include deficits in delay of gratification (where delay causes an aversive emotional response).

7.4 **Updating the model of the behavioural phenotype of SMS**

Findings can now be considered in the context of the hypothetical model of behaviour in SMS, outlined in section 2.5.

Key features of the model are:

- Genetic characteristics of SMS which affect development of the brain, central nervous system, endocrine system and structural physiological features.
- Biological differences then affect behaviour through
 - direct pathways.
 - indirect pathways (e.g. biological atypicalities affect either cognitive *or* physiological states which then affect behaviour, biological atypicalities affect cognition which then affects physiological responses which subsequently influence behaviour).
- Environmental influences on behaviour which represent phenotype-environment interactions.
- Reciprocal effects of child characteristics on environmental factors.
- Links *between* behaviours (e.g. impulsivity and aggression) at the behavioural level.

The updated model is presented in figure 7.1, with additions highlighted in a darker colour.

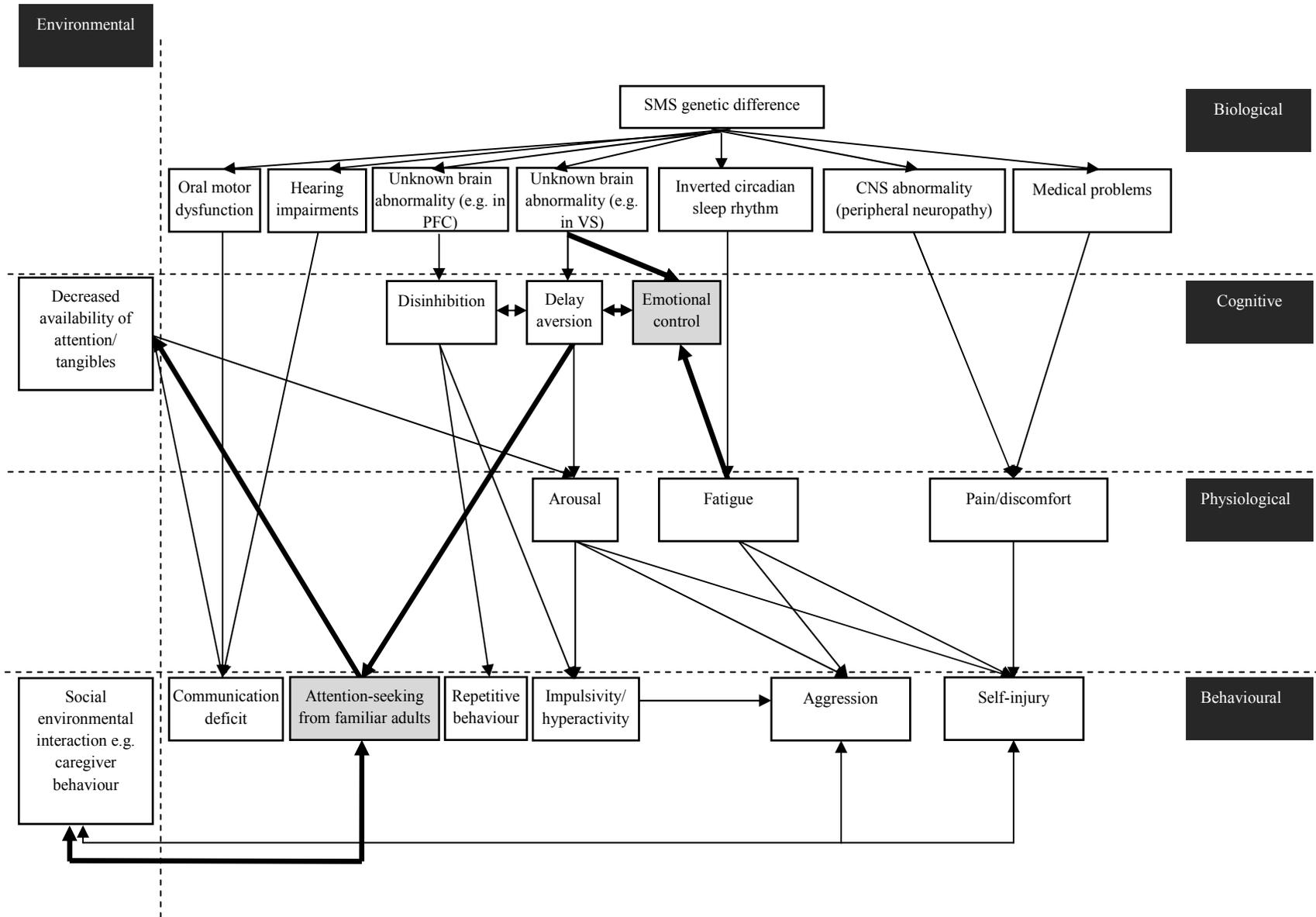


Figure 7.1 Updated model of pathways from genetic difference to behaviour in Smith-Magenis syndrome

7.4.1 Pathways to behaviour in the updated model

While inhibition was unrelated to impulsive behaviour in SMS, it was still compromised compared to typically developing children. Furthermore, it was emphasised in section 6.5 that emotional control and ‘hot’ executive function are unlikely to operate independently of ‘cool’ executive functions proposed to underpin inhibition (Hongwanishkul *et al.*, 2005; Zelazo & Müller, 2002). Furthermore elevated repetitive behaviours in SMS are hypothesised to be linked to inhibition deficits (Turner, 1997, see section 2.4.6.1), therefore inhibition deficits are retained in the model.

Deficits in ability to delay gratification become central to the model, together with the addition of associated difficulties with emotional control. Emotional control was found to be strongly associated with impulsive behaviour in SMS, suggesting that deficits in this are likely to underpin at least some aspects of impulsive behaviour in the syndrome. Delay of gratification has been identified as a function that may be upstream of impulsive behaviour (Sonuga-Barke & Taylor, 1992; Sonuga-Barke *et al.*, 1992). This aversion to delay can be conceptualised as an emotional response to waiting (resulting in physiological arousal), thus the two aspects of delay of gratification and emotional control are presented in the model as interconnected.

Attention-seeking toward familiar adults has also been added to the model at the behavioural level as evidence, both from the existing literature (section 2.4.8) and presented in chapters three, four and five, points to this being specifically associated with SMS. The operant model of challenging behaviour states behaviours are learnt through positive reinforcement (where presentation of a stimulus increases challenging behaviour) or negative reinforcement (where

removal of a stimulus increases challenging behaviour). Extending the operant model to include specific characteristics of individuals with a given genetic syndrome, as proposed by Oliver, Murphy, Crayton & Corbett (1993) and Taylor & Oliver (2008), enables consideration of how person characteristics may interact in the model to increase the likelihood of a particular behavioural outcome. Identifying how familiar adults specifically may be particularly reinforcing for individuals with SMS, by examining how they differ from peers and unfamiliar adults in terms of reinforcing properties, may enable understanding of this unusual social behaviour within this well established theoretical framework.

7.4.1.1 Reinforcing properties of familiar adults

In the context of reinforcing approach behaviours, familiar adults can be considered to differ from peers and unfamiliar adults in two main ways: their capacity to respond favourably to the approach and their willingness to do so. The expressive communication deficits in SMS (e.g. Greenberg *et al.*, 1996, see section 2.4.2.2) may make approaches of individuals with the syndrome less easy to understand. As adults have greater cognitive abilities and more developed social skills than children, they are more likely to be able to understand approaches of individuals with SMS. They are thus more likely to respond appropriately (e.g. by engaging or providing a requested item), reinforcing the approach behaviour. Furthermore, familiar adults are likely to be better able than strangers to understand those with SMS, being familiar with their communication style, preferences and habits.

Therefore, those with SMS, who are impaired in effectively communicating requests, are likely have to ‘work’ least hard to get a reward with familiar adults demonstrating how the characteristics of the syndrome can interact with the operant model of learnt behaviour. This

can be understood in terms of response efficiency (how efficient a behaviour is at eliciting reinforcement). Response efficiency is determined by the effort needed to perform the behaviour, the schedule of reinforcement (how often the response is reinforced) and how long it takes between when a discriminative stimulus⁴¹ (e.g. an adult) is presented for a target response (e.g. social initiation) and delivery of the reinforcer for that response (e.g. provision of attention or tangible reward) (Horner, Sprague, O'Brien, & Heathfield, 1990).

Familiar adults may also be more likely to respond quickly and consistently to individuals with SMS. Thus, delay between presentation of the discriminative stimulus (adult) and delivery of the reinforcer (attention) would be shorter, increasing response efficiency of approaching a familiar adult over an unfamiliar adult or peer. Familiar adults in the environment of someone with SMS are likely to be in a position of responsibility for that person and expected to respond to approaches and requests as part of their role. In contrast, peers and strangers will not respond as reliably as it is not part of their role. This quick and consistent responding would therefore result in greater, faster and more reliable reward (i.e. a richer schedule) for an individual with SMS who approaches familiar adults than peers or strangers.

In summary, it seems probable familiar adults are most likely to consistently understand and respond to approaches of children with SMS, making them particularly reinforcing to children with SMS. Presence of familiar adults may come to represent availability of a desired reward (attention or a tangible object). These reinforcing properties of adult attention may then

⁴¹ Discriminative stimuli are stimuli 'in the presence of which a particular response will be reinforced' (Malott, 2007, p. 202), thus familiar adults may come to signal that a response, such as initiation, will be reinforced e.g. by provision of attention or a tangible reward.

become part of a cycle of reinforcement ultimately resulting in strong preference for interacting with familiar adults.

7.4.1.2 Role of delay aversion

In addition to communication deficits in SMS, hypothesised delay aversion and difficulties in emotional control may also make attention-seeking from familiar adults more likely. Difficulties with delaying gratification may result in children with SMS being less able to wait for the response that they desire and associated difficulties with emotional control may make deprivation of social attention particularly difficult given the strong emotional component of social interactions. For reasons outlined previously familiar adults are likely to be better able to respond quickly, thus avoiding the challenge of delay of gratification. Social behaviour in SMS may therefore initially involve ‘normal’ levels of attention-seeking, reflecting a typical social drive. However, children may rapidly learn that familiar adults are more predictably able to respond quickly and in the way that is more reinforcing and thus develop a preference for interacting with them.

In terms of links to challenging behaviours reported to be shown when attention is unavailable (Haas-Givler, 1994; Sarimski, 2004), this can be considered within existing models of difficult behaviours shown by those with genetic syndromes. Woodcock and colleagues (2009b) suggested that when individuals with Prader Willi syndrome (PWS) are exposed to tasks in which their task switching capacity is exceeded, this results in an aversive physiological state leading to challenging behaviour. When attention is unavailable or is delayed, individuals with SMS may become physiologically aroused, creating an aversive state resulting in challenging behaviour. Difficulties with controlling emotion described

previously may exacerbate this process. SMS specific setting events (factors which change the ongoing stimulus response relationship, Wahler & Fox, 1981) such as fatigue (due to sleep disturbance) may also alter the qualities of a stimulus/event (e.g. having to wait), making it more aversive. Caregivers may then respond to the difficult behaviours, providing positive reinforcement for the child in the form of attention. If this then results in a reduction in aversive difficult behaviours this may in turn be reinforcing for caregivers resulting in a mutual reinforcement cycle (Oliver, 1995).

Given postulated links between ability to delay gratification and inhibition (see section 2.4.7.3 and 6.5) it is notable that existing research has also identified links between inhibition and social functioning. Inhibition deficits have been theorised to account for inappropriate social approach both in patients with frontal lobe damage (Green & Phillips, 2004) and in WS and DS (Porter, Coltheart & Langdon, 2007). Some evidence supports this in WS and DS, where impairments on tasks assessing response inhibition were found, together with lack of deficits on a social approach task. This was interpreted as indicating that these individuals ‘know’ not to approach strangers but in real-world situations inhibition deficits results in indiscriminate approach. This interpretation is limited by lack of direct comparisons to typically developing controls and lack of replication, therefore the updated model does not include direct pathways from inhibition to inappropriate social approach (‘attention-seeking’ in the model).

7.4.2 Alternative explanations

The hypothetical model focuses on operant explanations of attention-seeking behaviour seen in SMS. While this is a well established framework for understanding behaviour in individuals with ID, it contrasts with conceptualisations of the strong social motivation in AS

as a biologically determined drive (see section 1.3.2 for review). That the strong drive to interact with familiar adults in SMS may be a simple drive for maternal resources (as in AS) is still tenable at this stage; no evidence exists which contradicts this possibility. Furthermore, Crespi *et al.*, (2009) have suggested that the genetic characteristics of SMS may underpin strong social drive. They suggest that duplications and deletions of the same chromosome region can have a similar effect to diametric changes in imprinted genes, resulting in contrasting behavioural phenotypes (Crespi *et al.*, 2009). They refer to Potocki Lupski syndrome (PTLS), the reciprocal of SMS (see section 1.2.2) and contrast the social phenotypes of the syndromes, suggesting SMS is characterised by strong social motivation compared to high rates of behaviours associated with ASD (including reports of eye contact avoidance) in PLTS. However, no direct comparison of these groups has evaluated the extent to which they are actually diametric phenotypes. As SMS is frequently associated with behaviours related to ASD (see section 2.4.9 for a summary) such contrasts require further support before they can be considered as evidence for a genetic basis for sociability in SMS. Given lack of empirical evidence for a specific genetic basis for social drive in SMS, the pathways hypothesised in the model present the most parsimonious framework for understanding strong preference for interacting with familiar adults based on evidence from SMS literature, broader theories of learnt behaviour and findings of the current studies. However, an alternative explanation, related more directly to genetic difference in SMS, (similar to imprinting theory in AS) cannot be ruled out.

A second alternative hypothesis regarding attention-seeking towards familiar adults relates to attachment. Attachment, the emotional bond between an infant to primary caregiver, has been conceptualised to protect the child, offering security (Bowlby, 1969). There is some overlap between these proximity seeking behaviours and the attention-seeking from familiar adults in

SMS, where attention-seeking may serve to keep an attachment figure in close proximity. However, there is no evidence as yet that social preference is restricted only to primary caregivers, just familiar adults.

In addition to this lack of evidence that the targeted social behaviours are directed preferentially to the primary caregiver above other familiar adults, two further issues suggest that attachment theory may not be able to account fully for the targeted social drive evidenced in SMS. The first issue relates to the variable nature of the targeted figure. Anecdotally the targeted social drive reported in SMS has been described as transferring between individuals from one context to another and the targets of this social drive can include those who are not in a clear caregiving role. For example one child's parent described how she would continually ask to contact the school bus driver – the basis of such a targeted drive within the attachment theory framework outlined above is not clear. Other anecdotal examples include siblings and teaching assistants. While it is accepted that children can have more than one attachment and attachments to figures other than mothers, such as fathers, Ainsworth (1979) unambiguously states that “No infant has been observed to have *many* attachment figures” and furthermore states that preference in attachment are generally for the mother figure.

The second issue which challenges the ability of attachment theory to account for the targeted social drive observed in SMS is that the mechanism by which an attachment similar to that found in typically developing infants would persist into later childhood in this syndrome is unclear. Although it is recognised that the attachment of a child to an attachment figure does not cease once children become older (Bowlby, 1973), it is clear that the attachment behaviours that are related to this attachment figure do change. For example proximity seeking behaviours as shown by infants are replaced by more sophisticated behaviours.

Ainsworth (date) states that children's development 'profoundly changes' the behaviours that mediate attachment. For example Bowlby (1969) theorised that before the age of two typically developing children begin to develop working models of their relationship with their attachment figure and the ability to plan which results in more complex relationships and different attachment behaviours in typically developing children as they develop. It is unlikely that early attachment behaviours would persist in children with SMS due to a general plateauing of development or profound developmental delay. Measures of both cognitive ability and adaptive behaviour in SMS clearly indicate that individuals with SMS do progress in their development, although at a delayed rate to a developmental age above that at which attachment behaviours such as proximity seeking are strong indicators of attachment (see section 2.4.2 for discussion of cognitive ability and adaptive behaviour in SMS). Again, therefore, the hypothetical model outlined above more clearly reflects the literature and current findings.

7.4.3 Summary of model updates

The original model, (section 2.5), was extended, adding attention-seeking toward familiar adults and deficits in emotional control. Integration of attention-seeking from familiar adults to the model reflects transition from tentative evidence based on anecdotal accounts and informant reports towards empirical evidence for this behaviour being a specific feature of SMS. Deficits in emotional control are a second novel construct in the model, reflecting findings of the study presented in chapter six, they are proposed to affect ability to delay gratification. The role of deficits in ability to delay gratification in influencing behaviour is reinforced in the revised model, as are causal links with the impulsive behaviour shown in the syndrome. Pathways from this deficit in ability to delay gratification to attention-seeking behaviour were elucidated, reflecting influence of delay aversion on increased likelihood of

seeking attention from familiar adults due to their reinforcing properties of increased likelihood of responding⁴². Reciprocal pathways between attention-seeking from familiar adults and social environmental influences were also illustrated. Alternative causal pathways specifically to the attention-seeking behaviour were considered. While they remain viable the current model was considered to be most clearly supported by the available literature and current findings.

⁴² Due to their capacity as caregiver and ability to understand requests for attention/tangible objects.

7.5 Limitations of the research

Limitations specific to particular studies are covered in detail in the discussion sections of each empirical chapter (sections 3.5, 4.5, 5.5 and 6.5). Limitations which are broadly applicable across studies will be discussed here (except the use of DS as a contrast group which although a broadly applicable limitation is discussed in detail in relation to each study).

7.5.1 Recruitment

Participants were primarily recruited from parent support groups, potentially introducing bias into samples used in this research. It has been hypothesised that those who choose to become involved in parent support groups may differ from those with no involvement. For example Hyman, Oliver & Hall, (2002) suggest families of those with challenging behaviour are more likely to be part of a syndrome support group. Results of these studies may therefore not generalise to the broader SMS population. However, as SMS and DS groups were recruited in the same manner, bias resulting from this recruitment strategy should be consistent across syndromes. Furthermore, the focus of the current research is not challenging behaviour, therefore concerns about challenging behaviours driving support group membership may be attenuated.

7.5.2 Sample size

As SMS is a rare genetic syndrome, recruitment of large samples presents a common challenge. In addition to rarity, compliance with testing is an issue which further reduces sample sizes. SMS is associated with one of the highest rates of challenging behaviour of the genetic syndromes (e.g. Arron *et al.*, 2011) and also challenging behaviour associated with escape from demands (Sloneem *et al.*, 2011), thus direct testing is likely to result in increases

in difficult behaviours which preclude testing. Few studies of SMS have carried out batteries of cognitive tests, as such the study presented in chapter six can be considered as a preliminary investigation not only of impulsivity and inhibition but also the utility of methods to assess these constructs in SMS. Low sample size and significant within-syndrome variation are likely to result in decreased power and potential type two errors. This threat may have been mitigated somewhat by the highly comparable nature of the groups recruited, such that those with SMS did not differ significantly from the DS sample.⁴³

It is possible sample sizes in chapter six could have been increased by creating a battery with more tests covering a wider range of abilities, particularly lowering the floor of the tasks so that those with lower ability could be tested. However, at present there are relatively few tasks shown to effectively measure inhibition in younger children (Henry & Bettenay, 2010, see section 6.2), restricting choice. As literature on inhibition develops, interest in developing tasks suitable for assessing younger samples may result in more appropriate tasks - future research should re-evaluate available tests.

7.5.3 Static representations of behaviour

Taking an approach that considers developmental trajectories is a technique advocated by leading researchers in the field of behavioural phenotypes (Thomas *et al.*, 2009) (see section 1.3.3). The current research adopted a cross sectional group design approach, using groups shown to be comparable. While only children were used in this study, limiting to an extent the range of development included in the study, ages ranged from two to fifteen years,

⁴³ No significant differences were found in key variables of either mental or chronological ages between the two syndrome groups.

encompassing a wide range of development. Using groups containing varying ages may have masked some effects if they were highly dependent on (developmental) age. However, effects were found for many key variables and were typically in the direction expected, suggesting this is unlikely to have fundamentally compromised the aims of the study. However it is possible more subtle age dependent differences may have been masked.

Group designs are very commonly used in behavioural phenotype research due to small group sizes. Such group design studies have provided insight into important aspects of behaviour in genetic syndromes, including pathways from genetic characteristics to behaviour, through examination of repetitive questioning in PWS and fragile X syndrome (Woodcock *et al.*, 2009 a, b) and social cognition through examination of face processing in ASD and WS (Riby & Hancock, 2008, 2009). As these initial studies were successful in establishing potential characteristics of behavioural phenotypes, further research can then build on these findings and assess how phenotypic characteristics manifest at different points in the lifespan. In the current research, group designs provided novel empirical evidence suggesting those with SMS had an unusual preference for familiar adults but did not enable insight into the developmental path of this behaviour. It is unclear at what age this behaviour manifests or how the course of this behaviour relates to that of those without the syndrome.⁴⁴ Employing a developmental trajectory approach would enable insight into this issue for this behaviour in SMS. Approaches for addressing these limitations are considered in more detail in section 7.6.1.

⁴⁴ It may be the case that all children show this type of preference at an early developmental stage but while their preferences may reduce with development this may be delayed in SMS, analogous to the delayed onset described by Thomas *et al.* (2009). Alternatively reduction in preference may never occur, as with the premature asymptote from Thomas *et al.*'s account.

7.6 Future research directions

7.6.1 Developmental trajectories

Social behaviour is likely to be highly susceptible to developmental changes (for example changes in attachment behaviour from infancy to childhood, changes with experience of schooling) and manifestation of social motivation may also change with age. It is important therefore to build on findings of group designs used in studies described here to evaluate unusual preference for attention from familiar adults in a developmental framework. Use of developmental trajectories (Thomas *et al.*, 2009) to understand preference for adult attention would involve evaluating preference for familiar adults in individuals with SMS (potentially using a similar experimental paradigm to that employed in the study described in chapter five) as a function of age, and comparing the derived function to a typically developing contrast group. Identification of differences and comparison of group intercepts and gradients would enable insight into how this behaviour develops in SMS and how this development relates to that of typically developing individuals.

7.6.2 Self control evaluation and intervention

Ability to delay gratification has been hypothesised in this thesis to be a deficit in SMS potentially underpinning not only impulsive and dysregulated behaviour but also attention-seeking behaviour. To test this hypothesis ability to delay gratification in children with SMS should be evaluated against that of typically developing children and appropriate contrast groups of individuals with intellectual disability. Using tasks specifically designed to evaluate self control (ability needed to delay gratification) it could be determined whether individuals with SMS have a specific impairment in this ability. These tasks include the Tea task and Gift task (Cuskelly *et al.*, 2003) which require individuals to wait to access a rewarding stimulus

(section 6.5). This type of impulsive behaviour could then be related to other measures of real world impulsive behaviour and emotional control, gathered through informant reports (e.g. BRIEF-P, Gioia *et al.*, 2003, TAQ, Burbidge *et al.*, 2010) to evaluate whether associations exist as hypothesised in the model.

If ability to delay gratification is impaired in SMS, training in self control may improve this ability. As noted in section 6.5, this has been carried out successfully with individuals with intellectual disability and difficulties with impulsive behaviour (Schweitzer & Sulzer-Azaroff, 1988). In this study children with DS were trained to choose larger, delayed reinforcers (tangible rewards) above smaller immediate rewards (one reward immediately or three after a delay). Length of delay was gradually increased over the training sessions. After training the majority of participants showed significantly more self control. In older or more able individuals, training developed to address impulsive decision making in individuals with ID may also be beneficial. Fisher, Bailey and Willner (2012) demonstrated use of a visual calculator (where participants manipulate green and red bars of varying lengths, representing good and bad respectively to derive a single evaluative outcome) resulted in improved (less impulsive) performance on temporal discounting tasks (choosing between a small immediate reward or a larger delayed reward).

Research could either replicate methods described, using tangible rewards or could be extended to include the provision of attention as a reward. As attention-seeking is considered to be a significant problem (as supported in this thesis), this may suggest whether this difficult behaviour can be targeted for intervention. Previous interventions suggest that attention-seeking behaviours are amenable to change. For example cues can be used to teach both for typically developing children and those with ID to discriminate between times of adult

availability and unavailability (Grow, LeBlanc, & Carr, 2010; Tiger & Hanley, 2004). Baseline measures of impulsive behaviour prior to the intervention and measures of impulsive behaviour post intervention would evaluate the extent to which this training may generalise to children's everyday behaviour.

7.7 **Implications for practice**

The findings of the current research have a number of specific clinical and educational implications. Difficult behaviours such as attention-seeking and impulsivity have a detrimental effect on the well-being both of those with SMS and their caregivers (see section 2.4.3). This is particularly pertinent given links between these behaviours and challenging behaviour (see sections 2.4.7 & 2.4.8), whereby they also present possible reliable antecedents to challenging behaviour (reduced attention, waiting). Impaired expressive language skills may affect ability to communicate effectively with those in their environment, resulting in reduced access to resources such as attention or tangible objects. This may result in frustration, challenging behaviour and possibly reliance on familiar people able to understand or predict their requests. Enhancing communication, using functional communication training (Carr & Durand, 1985) or early referral to speech and language therapy, may therefore be beneficial.

It may also be beneficial to encourage caregivers not to be the sole responder and encourage others in the child's environment to respond to their requests, thus avoiding preference becoming established. Preventing behaviours becoming established has been suggested as an intervention for other difficult phenotypic behaviours. For example, Woodcock *et al.* (2009a) report anecdotal evidence from caregivers of individuals with PWS that deliberately varying children's routine from when they were young resulted in routines not becoming established. A more formal version of this may form the basis of an intervention in SMS.

As findings also support anecdotal accounts of preference for adult attention in schools, they have implications for behaviour management in this context. Haas-Givler & Finucane (1996)

outlined strategies to manage difficult classroom behaviour, including attention-seeking from adults. Given this preference now has empirical support, wider dissemination of these guidelines to educational professionals working with individuals with SMS may be appropriate. Guidelines include maintaining neutral tone to reduce perceived reward for attention-seeking behaviours, ensuring negative responses to behaviour are monitored to avoid them becoming reinforcing and using visual prompts so teachers can reduce the need to respond with rewarding attention to repeated questioning.

7.8 Conclusion

“SMS is an ongoing "onion" that has so many complex layers that continually unravel. When one behavior settles down, another one emerges, and you never know what is coming next. There are still so many unknowns with this disorder, and many uncertainties apply.” (Parent of a child with SMS, cited in Foster, Kozachek, Stern & Elsea, 2010, p. 196).

The above quote highlights the importance of knowledge about SMS to caregivers of those with the syndrome. Understanding likely outcomes in SMS may reduce the uncertainties described, enabling caregivers and professionals to plan for what is coming next. The goal of fully understanding a complex, multisystem disorder such as SMS remains some way off. However, research into aspects of the syndrome that are of clinical significance, including difficult behaviours, can make inroads into developing the understanding sought by caregivers.

This work has evaluated attention-seeking and impulsivity, two aspects of difficult behaviour thought to be part of the behavioural phenotype of SMS which have thus far received little empirical investigation. Given links between these behaviours and challenging behaviour in SMS and also potential direct effects on wellbeing of caregivers and those with the syndrome, these more subtle features of the SMS behavioural phenotype clearly require focussed research. This thesis therefore sought to extend current understanding of the phenomenology and potential aetiology of attention-seeking and impulsivity, using diverse, reliable and valid methodologies. This resulted in novel findings regarding the highly specific nature of social preferences in SMS and the potential role of emotional control in impulsivity, which were then placed within a hypothetical model of the SMS behavioural phenotype.

In addition to further delineating the behavioural phenotype of this syndrome, hypotheses regarding pathways from genetic characteristics to behaviour suggested areas for targeted interventions, which should be a priority in SMS given high levels of clinically concerning behaviours. Understanding causes of difficult behaviours, and the interplay between genetic, cognitive, physiological and environmental factors associated with SMS represents the first steps in identifying strategies for managing behaviour so that individuals with this syndrome can achieve the potential they evidently possess.

The final quote in this thesis, from a father of a child with SMS (below), illustrates both this potential of individuals with SMS to be a very positive aspect of family life but also the concerns that accompany having a child with this syndrome.

“My daughter means the world too (sic) me, and I worry about the future, what it holds for her. SMS children are most loving and wonderful. As a father of a beautiful little girl with SMS, I have experienced the highs and lows of this rare disorder.”

(Parent of a child with SMS, cited in Foster *et al.*, 2010, p. 196).

Ensuring that research continues to focus on understanding behaviours shown in SMS and moves towards developing targeted intervention strategies, may go some way to addressing the concerns of such caregivers.

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Appendices

APPENDIX A

Letter confirming ethical approval



UNIVERSITY OF
BIRMINGHAM

Research and Commercial Services

Dr J H Wilkie
BSc(Hons) PhD MBA CEng MIMMM

Lucy Wilde
School of Psychology
University of Birmingham

10th March 2010

Dear Lucy

**Re: Typical and atypical social behaviour
Application for Ethical Review ERN_09-945**

I am writing to confirm that the above project was conditionally approved by the Life and Health Sciences Ethical Review Committee on the 15th December 2009, and that these conditions were met on the 22nd January 2010.

Best wishes.

A handwritten signature in black ink, appearing to read 'Susan Cottam', written over a horizontal line.

**Susan Cottam
Research Ethics Officer
Research and Commercial Services**

cc Chris Oliver



APPENDIX B

Expression of interest forms, initial letters and information sheets



UNIVERSITY OF
BIRMINGHAM

lvw894@bham.ac.uk

0121 414 2855

EXPRESSION OF INTEREST IN 'TYPICAL AND ATYPICAL SOCIAL DEVELOPMENT'

I would like to receive further information about the 'Typical and atypical social development' study
(please tick box)

Name

Address

.....

.....

.....

Telephone number.....

Please return this slip using the stamped addressed envelope supplied. Alternatively you can contact us by email (lvw894@bham.ac.uk) or telephone (0121 414 2855) to request a further information pack.



Appendices

**UNIVERSITY OF
BIRMINGHAM**

lvw894@bham.ac.uk

0121 414 2855

Dear X,

We are writing to inform you of a new research project that is being conducted at the University of Birmingham.

The research will examine social behaviour in children with genetic syndromes and typically developing children. Specifically we aim to further our understanding of behaviour in the genetic disorder Smith Magenis syndrome by comparing social behaviour of children with this syndrome to behaviour of children with Down syndrome and typically developing children. We hope to explore the factors that influence social behaviour and potential links between social functioning and challenging behaviour in these groups of children. This is an important area of study but has rarely been attended to in previous research.

We have selected individuals from our database of families who have these syndromes and who have expressed an interest in taking part in further research studies carried out at the Cerebra Centre for Neurodevelopmental Disorders. Including children with Down syndrome in the study will enable insights into how social behaviour differs across different genetic neurodevelopmental syndromes. Down syndrome has been chosen as a comparison group as individuals with this syndrome are understood to have relative strengths in social functioning and to have a similar level of intellectual disability to those with Smith Magenis syndrome. It is hoped that, in addition to increasing our understanding of the rare disorder Smith Magenis syndrome, the findings from this research can add to the understanding of social behaviour in children with Down syndrome.

We would like to invite you to consider taking part in this study. There is an information sheet enclosed that gives you some more detailed information about why the research is being carried out and what it will involve. If you feel it is appropriate you may wish to discuss the research with your child/the person that you care for.

Please take the time to read the enclosed information sheet. If after reading this information you decide that you would be interested in taking part in this study, please return the expression of interest slip in the free post envelope provided, or contact Lucy Wilde by email or phone using the details above. If you are unclear about any aspect of the study or have any queries then please contact Professor Chris Oliver by telephone: 0121 414 4909, email: c.oliver@bham.ac.uk or at the below address.

Thank you for your time and continued support for our research at the University of Birmingham.

Yours sincerely,



Professor Chris Oliver (Project Director)

Lucy Wilde (Project Investigator)



UNIVERSITY OF
BIRMINGHAM

lvw894@bham.ac.uk

0121 414 2855

Dear X,

We are writing to inform you of a new research project that is being conducted at the University of Birmingham.

The research will examine social behaviour in children with genetic syndromes and typically developing children. Specifically we aim to further our understanding of behaviour in the genetic disorder Smith Magenis syndrome by comparing social behaviour of children with this syndrome to behaviour of children with Down syndrome and typically developing children. We hope to explore the factors that influence social behaviour and potential links between social functioning and challenging behaviour in these groups of children. This is an important area of study but has rarely been attended to in previous research.

We have selected individuals from our database of families who have these syndromes and who have expressed an interest in taking part in further research studies carried out at the Cerebra Centre for Neurodevelopmental Disorders/You have expressed an interest in taking part in research being carried out at the Cerebra Centre for Neurodevelopmental Disorders. High rates of challenging behaviour have been associated with Smith Magenis syndrome and links have been made between challenging behaviour and social factors. It is hoped that furthering our understanding of these factors may enable the development of better intervention and behaviour management strategies for individuals with Smith Magenis syndrome who show challenging behaviour and improve the health and well-being of individuals and their families.

We would (therefore) like to invite you to consider taking part in this study. There is an information sheet enclosed that gives you some more detailed information about why the research is being carried out and what it will involve. If you feel it is appropriate you may wish to discuss the research with the person that you care for.

Please take the time to read the enclosed information sheet. If you are unclear about any aspect of the study or have any queries then please contact Professor Chris Oliver by telephone: 0121 414 4909, email: c.oliver@bham.ac.uk or at the below address.

Thank you for your time and continued support for our research at the University of Birmingham.

Yours sincerely,

A handwritten signature in black ink, appearing to be 'C. Oliver', written in a cursive style.

Professor Chris Oliver (Project Director)

Lucy Wilde (Project Investigator)

Centre Director: Prof. Chris Oliver
The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.bham.ac.uk **E-mail:** cndd-enquiries@contacts.bham.ac.uk



INFORMATION SHEET FOR PARENTS AND CARERS

Introduction to the research and invitation to take part:

We have identified you and your child/the person you care for as potential participants in a new study being conducted at the University of Birmingham.

The study aims to improve our understanding of the role of social factors in influencing behaviour in children with Smith Magenis syndrome by comparing their behaviour to that of children with Down syndrome and typically developing children. We will examine social behaviour in each of these groups, including the factors that influence social behaviour and potential links between social functioning and challenging behaviour (e.g. attention seeking). We hope that greater understanding of social behaviour will help to develop better intervention and behaviour management strategies for individuals with challenging behaviour and improve the health and well-being of individuals and their families.

What does it involve?

Participation in the research project will involve the following:

- Because of the requirements of the research, parents/carers are required to have English language abilities at native speaker level.
- You will be asked to complete a brief questionnaire which will provide us with general information about your child/the person you care for and their abilities. It will also ask questions regarding your child's/the person you care for's behaviour, communication and health.
- We will conduct a day of activities and assessments with your child/the person you care for, either in your own home, at school or at the University of Birmingham, which ever is your preferred location. During this time, we will carry out short observations of your child/the person you care for in different situations and during a series of games and activities. We will need the child's main caregiver to be present for some of these activities. We may also carry out a brief, non intrusive, eye tracking task. Additionally, assessments of your child's/the person you care for's

general ability level will also be conducted. These different assessments and activities will be presented to your child/the person you care for by two members of the research team.

An example of the timetable for collecting the above information from you, and your child/the person you care for is shown below.

- Stage One: You receive the further information pack and return enclosed consent form.
- Stage Two: Two research workers will visit you and your child/the person you care for at home/school or you and your child/the person you care for will travel to the University of Birmingham for a day of activities and assessments (duration: a day's testing including rest breaks).
- Stage Three: You will receive a detailed individual feedback report about your child's/the person you care for's assessments.

How will behaviours be observed and recorded?

- When we see your child/the person you care for we will carry out short observations with them in different situations and during a series of games and activities. Video recordings of your child/the person you care for during these situations and activities will be made. This allows us to return to the video recordings for detailed analysis of information and means that we can check the accuracy of our observations.
- The privacy and dignity of your child/the person you care for will be respected at all times and video recordings will not take place if there is evidence that the observations are causing distress.
- You may ask to see a copy of the video recordings of your child/the person you care for.
- When video recordings are not in use they will be stored in a locked filing cabinet.
- Video recordings may only be viewed by legal guardians or individuals providing a service to your child/the person you care for and members of the research team working on this project.
- Information identifying your child/the person you care for will not be stored on or with the tape.

Consent:

After reading this information and the subsequent detailed further information that we will send out if you contact us expressing an interest in participating, if you decide to become involved in the project then you will be required to complete a consent form and return this us.

Withdrawal:

Should you or 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 reason. You can decide to withdraw your child/the person you care for from part or all of the study at any time if he or she becomes distressed. Even after the assessments have been completed, 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 information collected will be kept on a confidential database that is only accessible to those working on the project. 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/the person they care for. A summary of the project's findings will be circulated to anyone involved who wishes to see a copy. 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.

Any concerns or queries?

If you are unclear about any aspect of the study or have any questions, please do not hesitate to contact Professor Chris Oliver by telephone: 0121 414 4909, by email: c.oliver@bham.ac.uk or at the address below.

Thank you very much for taking the time to read this information

Centre Director: Prof. Chris Oliver
The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.bham.ac.uk **E-mail:** cndd-enquiries@contacts.bham.ac.uk

APPENDIX C

Confirmatory letters and information sheets



UNIVERSITY OF
BIRMINGHAM

lvw894@bham.ac.uk

0121 414 2855

Dear X,

Further to your expression of interest in participating in our research, I write to formally invite you and your child/the person you care for to participate in the University of Birmingham research project investigating typical and atypical social development. If you agree to take part in the study please complete the enclosed consent forms and return them to us in the envelope provided.

We enclose a detailed information sheet further explaining the project and what it will entail. If you have any further questions, please do not hesitate to get in touch with Lucy Wilde, using the contact details above, or Prof. Chris Oliver, using the contact details below.

Many thanks for your support

Yours Sincerely,

Lucy Wilde
(Project Investigator)

Professor Chris Oliver
(Project Director)

Centre Director: Prof. Chris Oliver
The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.bham.ac.uk E-mail: cndd-enquiries@contacts.bham.ac.uk



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INFORMATION SHEET FOR TYPICAL AND ATYPICAL SOCIAL DEVELOPMENT

You and your child/the person you care for are being asked to take part in a research study. Before you decide if you wish to take part it is important that you understand why we are doing the research and what it will involve. Please take time to read the following information carefully and if it is appropriate, explain and discuss it with your child/the person you care for. If there is anything that is unclear, or if you have any medical/other problems which make it difficult for you to read this information, please contact Lucy Wilde for a verbal explanation of the research.

When you are happy that you have all of the information you need to be able to decide whether or not you and your child/the person you care for would like to take part in the study, please complete the enclosed consent forms and return them to us in the prepaid envelope provided.

What is the research and what is the purpose?

This study is being conducted at the University of Birmingham. The study aims to further our understanding of behaviour in the genetic disorder Smith Magenis syndrome by comparing social behaviour of children with this syndrome to behaviour of children with Down syndrome and typically developing children. We will compare social behaviour across these groups of children in order to explore the factors that influence social behaviour and potential links between social functioning and challenging behaviour.

We hope that greater understanding of the role of social factors in influencing behaviour will help to develop better intervention and behaviour management strategies and improve the health and well-being of individuals and their families.

Do we have to take part?

It is up to you and your child/the person you care for whether or not you decide to take part, the decision you come to will not affect any services you receive. If you and your child/the person you care for do decide to take part you will be asked to sign a consent form.

Will I be able to withdraw from the research?

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. You can decide to withdraw your child/the person you care for from part or all of the study at any time if he or she becomes distressed. Even after the assessments have been completed, 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.

Will our information be confidential?

All information collected will be kept on a confidential database that is only accessible to those working on the project. If published, information will be presented without reference to any identifying information.

What does it involve?

Participation in the research project will involve the following:

- Because of the requirements of the research parents/carers are required to have English language abilities at native speaker level.
- You will be asked to complete a questionnaire pack for this study. The questionnaire pack will contain several questionnaires which ask you to describe various aspects of your child's/the person you care for's behaviour. You will be asked for some background information, including about your child's/the person you care for's diagnosis, you will then be asked about their communication, their activity levels, how sociable they are and how much they try to interact with different people. You will also be asked about any challenging behaviour they show (e.g. self injury/aggression), how impulsive they are, any repetitive behaviours that they show and about their levels of self control.
- We will complete a day of activities and assessments with your child/the person you care for either at your home, at school or at the University of Birmingham depending on which location you prefer. During this time, we will carry out short observations of your child/the person you care for in different situations and during a series of games and activities. We will need the child's main caregiver to be present for one of these activities. Video recordings of the observation sessions will be made, as it is necessary for another psychologist at the University of Birmingham to check the accuracy of the observations (additional information on videoing is provided further on in this information sheet). The

different situations and activities will be presented to your child/the person you care for by two members of the research team.

- The research is expected to take a day of testing to complete, including breaks between testing sessions. The questionnaire pack should take around 45 minutes to complete, the parental separation task is approximately 20 minutes of duration and will be repeated three times (total 60 minutes) and the social image processing tasks are typically completed within 10 minutes. The 6 impulsivity tasks should take a maximum of 5 minutes each and will be interspersed between the other testing episodes.
- For one of the activities we are interested in observing your child/the person you care for with different types of toys. We would like to include a toy that we can be confident would appeal to them and so we will ask you to make their favourite toy available on the day of testing.
- We are also interested in how your child/the person you care for views particular social images and would like to show them photos of different people, including their mother (or primary female caregiver) and another familiar female adult. Ideally the familiar female adult would be someone that your child/the person you care for knows well but not a member of their immediate family e.g. a family friend. If your child/the person you care for is visually impaired it may not be possible to complete this task with them and so we will contact you once we receive your consent form to assess the suitability of this task for them. If the task is appropriate we will ask you to provide us with 2 photographic images prior to the day of the visit; one of your child's/the person you care for's primary female caregiver and one of a familiar female adult.
- During our time with your child/the person you care for we will also carry out some observations to help understand how they behave when they are interacting with different types of people in different situations. For half of these observations a researcher will be interacting with the child and for half we will ask you to interact with them. The situations will be very natural and we will not ask you to create any situation that is not usually experienced by your child/the person you care for in the home. The situations will involve short (5 minute) periods of high attention, low attention and absence. For high and low attention periods we will simply ask you to think of a time in your daily routine where this situation may occur (e.g. high attention may occur when you play a game at a certain point in the day), we will then ask you to run through this situation so we can observe the effects that it has on your child's/the person you care for's behaviour. For absence we will ask you to move out of sight of your child/the person you care for (but into a location where you can still observe them). It is possible that these situations will cause an increase or decrease in

particular behaviours. If your child/the person you care for becomes extremely distressed or is at excessive risk of injuring themselves we will immediately stop the session.

How will video recordings be made?

- Observations and video recordings will only take place during previously specified times that have been agreed by parents/ legal guardians and/or teachers.
- The privacy and dignity of your child/the person you care for will be respected and video recordings will not take place if children are in a state of undress or when there is evidence that the observations are causing distress.
- When video recordings are not in use they will be stored in a locked cabinet in the School of Psychology, University of Birmingham and will only be viewed by research workers from the University of Birmingham. Information identifying your child/the person you care for will not be stored on or with the recordings.
- The video recordings may only be viewed by parents/legal guardians, individuals providing a service to the person, Professor Chris Oliver and research staff at the University of Birmingham. Any data that are derived from the recordings will remain anonymous.
- Video recordings will not be shown for the purpose of teaching without your permission.

At the end of the study

Each parent/ legal guardian will receive a personalised feedback report on their child/the person they care for. A summary of the overall project's findings will be circulated to anyone involved who wishes to see a copy. 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.

Who has reviewed the study?

The University of Birmingham Research Ethics Committee has reviewed and approved the study. If you have any problems with the conduct of the study, you can contact the Research Ethics Officer of the Ethics Committee who has considered this application, on 0121 4148825.

Consent

After having read all of the information and having received appropriate responses to any questions that you may have about the study you will be asked to give your consent to participate in the study if you

decide that you do wish to participate. The section below on 'Giving consent' will explain this process. We need to receive consent from/on behalf of potential participants before we can arrange for them to participate.

Giving consent

Now it is up to you whether you decide that you and your child/the person you care for would like to participate. The decision about whether or not to take part in the study must be 'informed'. This means that anyone making the decision must understand exactly what is involved in the study, what will be required from participants and why.

If you feel that your child/the person you care for would be able to communicate informed consent but that they are not able to read and fully understand the information that is presented in this sheet on their own, we encourage you to discuss this with them order to give them the information they need to decide whether they would like to participate or not.

There are three different ways that consent can be gained from your child/the person you care for, depending on which of the below statements apply – please identify which statement applies to your child/the person you care for and complete the appropriate consent form:

1) I am a child with Down syndrome and I understand what is involved in the study and what will be required from me if I participate:

If you have read and understood enough information to make an 'informed' decision about whether you would like to participate and you have decided that you would like to participate, then please complete the enclosed consent form A and return it to us in the prepaid envelope provided. As you are under 16 years old please also ask a parent/ legal guardian to sign the consent form A to say that they are willing to give their 'informed' consent for you to participate.



PLEASE COMPLETE CONSENT FORM A (THE YELLOW FORM)

2) The person I care for understands what is involved in the study and what will be required from them if they participate and has communicated their decision to me:

If you are reading this information on behalf of someone who you care for, you need to decide whether that person is able to understand enough about the study to make an 'informed' decision about whether or not they would like to participate *and* to communicate this decision to you. If you would like the research team to assist you with explaining the research to someone else in a more accessible way, please contact us. If the person *is* able to make an 'informed' decision and they decide that they would

like to participate then please ensure that they complete the enclosed consent form B or that you complete it on their behalf. Please return the consent form to us in the prepaid envelope provided.



PLEASE COMPLETE CONSENT FORM **B** (THE **BLUE** FORM)

3) The person I care for cannot understand what is involved in the study or cannot communicate their decision to me:

If you are reading this information on behalf of someone you care for and you decide that the person *is not* able to make an ‘informed’ decision about whether or not they would like to participate, then we would like to invite you to act as a ‘personal consultee’ or a ‘nominated consultee’ for that person. Please read either the enclosed ‘Personal Consultee Information Sheet’ (if you are an UNPAID carer) or ‘Nominated Consultee Information Sheet’ (if you are a PAID carer). Once you have finished reading the sheet please decide whether or not you feel able to act as a personal/nominated consultee for your child/the person you care for.

If you feel able to act as a personal or nominated consultee for your child/the person you care for please think about whether the person would decide to participate if they were able to make an ‘informed’ decision themselves about whether or not to participate. If you decide that the person would decide to participate, please complete the enclosed consent form C and return it to us in the prepaid envelope provided.



PLEASE COMPLETE CONSENT FORM **C** (THE **PURPLE** FORM)

Any concerns or queries?

If you are unclear about any aspect of the study or have any questions, please do not hesitate to contact Lucy Wilde using the contact details provided previously or Professor Chris Oliver by telephone: 0121 414 4909, by email: c.oliver@bham.ac.uk or at the address below.

Thank you very much for taking the time to read this information – please keep this information sheet for future reference.

Centre Director: Prof. Chris Oliver
The Cerebra Centre for Neurodevelopmental Disorders,
School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Website: www.cndd.bham.ac.uk **E-mail:** cndd-enquiries@contacts.bham.ac.uk

APPENDIX D

Consent forms and personal/nominated consultee forms



**UNIVERSITY OF
BIRMINGHAM**

lvw894@bham.ac.uk

0121 414 2855

CONSENT FORM A FOR TYPICAL AND ATYPICAL SOCIAL DEVELOPMENT: For those under 16 year olds with Smith Magenis syndrome who can provide informed consent

Section 1: Please read the following statements and tick EACH ONE to show that you agree.

I am under 16 years old and I have read and understood the typical and atypical social development information sheet. I understand what the study is trying to find out and why, and what I would have to do if I take part. I have enough information to decide whether or not I want to take part.	
I understand that it is up to me whether or not I take part in the study	
I understand that even after consent has been given, I can withdraw from the study at any time simply by telling the researchers of my decision or by asking someone else to tell the researchers for me	
I understand that all information collected during the study will be confidential. Only members of the research team at the Cerebra Centre for Neurodevelopmental disorders will know who has participated in the study. All information collected during the study will be stored in locked cabinets that only members of the research team will have access to. No names will be published in any reports.	
I would like to give my 'informed' consent to take part in the typical and atypical social development study	

Name: _____

Signature: _____

Date: _____

Section 2: This section is to be completed by the PARENT/LEGAL GUARDIAN of PARTICIPANTS UNDER 16 YEARS OLD who have made the informed decision that they would like to participate in the research and completed section 1 above.

I have read and understood the typical and atypical social development information sheet.	
I understand that I can withdraw my consent for the person I care for to participate in the study at any time and that this will not affect the future access that I/this child has to services.	

I understand that all information collected during the study will be confidential. Only members of the research team at the Cerebra Centre for Neurodevelopmental Disorders will know who has participated in the study. All information collected during the study will be stored in locked cabinets that only members of the research team will have access to. No names will be published in any reports.	
--	--

I would like to give my 'informed' consent for the person I care for to take part in the typical and atypical social development study.	
---	--

Name: _____

Signature: _____

Date: _____ **Telephone number:** _____



CONSENT FORM B FOR TYPICAL AND ATYPICAL SOCIAL DEVELOPMENT: On behalf of someone with Smith Magenis syndrome who has communicated their informed consent

Section 1a: Please read the following statement and tick to show that you agree.

I have read and understood the typical and atypical social development information sheet on behalf of someone that I care for. I have discussed the information with the person that I care for. I feel that the person I care for understands what the study is trying to find out and why, and what they would have to do if they take part. The person that I care for has made an informed decision about whether or not they wish to participate and they have communicated this decision to me.	
---	--

Section 1b: Please read the following statements and tick EACH ONE on behalf of the person you care for to show that they agree

I understand that it is up to me whether or not I take part in the study	
--	--

I understand that even after consent has been given, participants can withdraw from the study at any time simply by telling the researchers of their decision or by asking someone else to tell the researchers for them	
--	--

I understand that all information collected during the study will be confidential. Only members of the research team at the Cerebra Centre for Neurodevelopmental disorders will know who has participated in the study. All information collected during the study will be stored in locked cabinets that only members of the research team will have access to. No names will be published in any reports.	
--	--

I would like to give my 'informed' consent to take part in the typical and atypical social development study	
--	--

Note: As you are completing this form on behalf of someone who you care for who has communicated to you their informed decision that they would like to participate, please write the participant's name but sign yourself on the participant's behalf.

Name: _____

Signature: _____

Date: _____

Section 2: This section is to be completed by the PARENT/LEGAL GUARDIAN of PARTICIPANTS UNDER 16 YEARS OLD who have made the informed decision that they would like to participate in the research and had section 1 above completed on their behalf.

I have read and understood the social behaviour in children with genetic syndromes information	
--	--

sheet.	
--------	--

I understand that I can withdraw my consent for my child to participate in the study at any time and that this will not affect the future access that I/my child has to services.	
---	--

I understand that all information collected during the study will be confidential. Only members of the research team at the Cerebra Centre for Neurodevelopmental Disorders will know who has participated in the study. All information collected during the study will be stored in locked cabinets that only members of the research team will have access to. No names will be published in any reports.	
--	--

I would like to give my 'informed' consent for my child to take part in the social behaviour in children with genetic syndromes study.	
--	--

Name: _____

Signature: _____

Date: _____ **Telephone number:** _____



UNIVERSITY OF
BIRMINGHAM

lvw894@bham.ac.uk

0121 414 2855

CONSENT FORM C FOR TYPICAL AND ATYPICAL SOCIAL DEVELOPMENT: For those acting as a personal/nominated consultee for someone with Smith Magenis syndrome

Section 1: Please read the following statements and tick EACH ONE to show that you agree.

I have read and understood the typical and atypical social development information sheet on behalf of someone that I care for. I feel that the person that I care for <i>does not</i> have the capacity to make an informed decision about whether or not they wish to participate in the study or that they cannot communicate this decision to me.	
--	--

I have read and understood the 'Personal Consultee Information sheet or if I am acting as a 'Nominated Consultee' then I have read and understood the 'Personal Consultee Information Sheet' and the 'Nominated Consultee Information Sheet'.	
--	--

I agree to act as a personal consultee for the person that I care for and will advise the researchers about what I feel would be that person's wishes throughout the study or there is no appropriate person able/willing to act as a personal consultee for the person that I care for (in a professional capacity) so I agree to act as a nominated consultee for the person that I care for and will advise the researchers about what I feel would be that person's wishes throughout the study.	
---	--

I understand that if I feel that the wishes of the person that I care for have changed at any point during the study then I must advise the researchers so that they can act accordingly.	
---	--

I will complete the rest of this form to advise the researchers of what I feel would be the wishes/interests of the person that I care for in my capacity as a personal consultee or nominated consultee.	
--	--

Name: _____

Signature: _____ Date: _____

Participants name: _____ Relationship to participant: _____

Section 2: Please read the following statements and tick EACH ONE to show that you agree.

I have read and understood the typical and atypical social development information sheet.	
---	--

I understand that it is up to me to advise on whether or not the person that I care for would want to take part.	
--	--

I can advise the researchers if I feel that the person that I care for would want to withdraw from the study at any time.	
---	--

I understand that all information collected during the study will be confidential. Only members of the research team at the Cerebra Centre for Neurodevelopmental disorders will know who has participated in the study. All information collected during the study will be stored in locked cabinets that only members of the research team will have access to. No names will be published in any reports.	
--	--

I would like to advise the researchers that in my opinion the person that I care for would wish to provide their consent to take part in the study.	
---	--

As you are acting as a consultee for the person that you care for who you feel *does not* have the capacity to make an informed decision about whether or not to participate, please fill in your own name and signature.

Name: _____

Signature: _____

Date: _____ **Telephone number:** _____



PERSONAL CONSULTEE INFORMATION SHEET

Please read this information sheet if you care for a person who you have judged *is not* able to make an ‘informed’ decision about whether or not they would like to take part in the study or *is not* able to communicate that decision to you.

We would like to invite you to act as a personal consultee for the person that you care for.

What is a Personal Consultee?

In order to understand illness and disability, and to improve treatment and care, research is essential. That research may focus on the people with the illness or disability or on children under the age of 16, and may invite those people to participate. Some people will have capacity to make their own decision whether to take part in the research.

Others, possibly the youngest children or those most affected by the illness or disability, may not have that capacity. They may not be able to understand enough of the research to be able to give ‘informed consent’. They may not be able to communicate a decision. The research provisions of the Mental Capacity Act are designed to allow such people to take part in research even though they cannot give valid consent of their own.

First, the research has to be approved by a Research Ethics Committee. Then, instead of asking the research participant for consent, the researcher must ask a consultee for an opinion whether the research participant would have wished to take part in the research.

Who can be a personal consultee?

Any person interested in the welfare of the proposed participant, for example:

- A family member, unpaid carer or friend
- A person acting under a Lasting Power of Attorney
- A court appointed deputy

Who cannot be a personal consultee?

- Paid carers and professionals
- People connected with the research (e.g. members of the research team)

Why have I been asked?

You have been asked to act as a personal consultee by a researcher because the researcher thinks you might be willing and able to do this because of your close relation with the proposed research participant.

If I agree to be a personal consultee, what will I have to do?

You will need to think about what the proposed participant’s wishes and feelings about the research would be if they had capacity to make an informed decision and decide whether in your view the person should be involved in the research or not. This means you need to

- Look at the study information sheet.
- Think about whether or not the person would want to be involved in the research project if he or she had the capacity to make that decision.

You should not put forward your personal views on participation in the specific project or research in general, you must consider only what the person's views and interests are or would likely be. You should think about:

- What the broad aims of the research and the practicalities of taking part will mean for the proposed participant.
- How the specific activities in the research might impact the participant. For example, if the study involves activities in the afternoon when the person is most tired they might find it a strain or the research might involve an activity that the person particularly enjoys and thus would give them more pleasure.
- Any view previously expressed by the person on the overall nature of the research.

If you advise that the proposed participant would not have wanted to be involved in the research, they cannot be included in the research.

If you advise that the proposed participant would want to be involved, they may be included in the research. If the research commences but the person shows any sign at any stage that they are not happy to be involved in the research you can change your advice at any time without giving a reason, whereby the researcher must withdraw the person from the research. If the person seems unhappy at any point or shows any signs of objection, then they will be withdrawn from the research.

The research project has been approved by the University of Birmingham Research Ethics Committee. If you wish to see proof of approval from this body, or you wish to discuss any concerns about acting as a personal consultee for the person that you care for, please contact Lucy Wilde on 0121 414 2855 or by email at lvw894@bham.ac.uk

I don't want to be a personal consultee/ I am a paid carer and so cannot be a personal consultee- what do I do?

Please try to suggest an alternative person who might like to act as a personal consultee for the potential participant, please pass the project information pack on to that person.

Where can I get more information and guidance?

More information is available from:

Department for Constitutional Affairs (2007) *Mental Capacity Act 2005 Code of Practice*

<http://www.dca.gov.uk/legal-policy/mental-capacity/mca-cp.pdf>

Department of Health (2007) *Guidance on nominating a consultee for research involving adults who lack capacity to consent* (consultation)

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_076207

Mental Capacity Implementation Programme (2007) *Making Decisions: a guide for family, friends and unpaid carers. Second edition*

<http://www.dca.gov.uk/legal-policy/mental-capacity/mibooklets/booklet02.pdf>

A printed copy of this booklet is available by telephoning 023 80878038.



NOMINATED CONSULTEE INFORMATION SHEET

Please read this information if you are a **paid carer** for a person who you have judged *is not* able to make an ‘informed’ decision about whether or not they would like to take part in the study or *is not* able to communicate that decision to you. If this person does not have any family members, unpaid carers or friends who are in regular contact and are able and willing to act as a personal consultee, does not have anyone acting under Lasting Power of Attorney or a court appointed deputy, then we would like to invite you to act as a nominated consultee for the person that you care for.

What is a Nominated Consultee?

In order to understand illness and disability, and to improve treatment and care, research is essential. That research may focus on the people with the illness or disability or on children under the age of 16, and may invite those people to participate. Some people will have capacity to make their own decision whether to take part in the research.

Others, possibly the youngest children or those most affected by the illness or disability, may not have that capacity. They may not be able to understand enough of the research to be able to give ‘informed consent’. They may not be able to communicate a decision. The research provisions of the Mental Capacity Act are designed to allow such people to take part in research even though they cannot give valid consent of their own.

First, the research has to be approved by a Research Ethics Committee. Then, instead of asking the research participant for consent, the researcher must ask a consultee for an opinion whether the research participant would have wished to take part in the research.

Who can be a nominated consultee?

- Any person interested in the welfare of the proposed participant who works with the participant in a professional capacity.

Who cannot be a nominated consultee?

- People connected with the research (e.g. members of the research team)

Why have I been asked?

You have been asked to act as a nominated consultee by a researcher because the researcher thinks you might be willing and able to do this because of your professional relationship with the proposed research participant.

If I agree to be a nominated consultee, what will I have to do?

You will need to think about what the proposed participant's wishes and feelings about the research would be if they had capacity to make an informed decision and decide whether in your view the person should be involved in the research or not. This means you need to

- Look at the study information sheet.
- Think about whether or not the person would want to be involved in the research project if he or she had the capacity to make that decision.
- You may need to seek the advice of friends/ family/ other paid carers of the person you care for in order for you to best advise us on what the person's wishes and feelings would be.

You should not put forward your personal views on participation in the specific project or research in general, you must consider only what the person's views and interests are or would likely be. You should think about:

- What the broad aims of the research and the practicalities of taking part will mean for the proposed participant.
- How the specific activities in the research might impact the participant. For example, if the study involves activities in the afternoon when the person is most tired they might find it a strain or the research might involve an activity that the person particularly enjoys and thus would give them more pleasure.
- Any view previously expressed by the person on the overall nature of the research.

If you advise that the proposed participant would not have wanted to be involved in the research, they cannot be included in the research.

If you advise that the proposed participant would want to be involved, they may be included in the research. If the research commences but the person shows any sign at any stage that they are not happy to be involved in the research you can change your advice at any time without giving a reason, whereby the researcher must withdraw the person from the research. If the person seems unhappy at any point or shows any signs of objection, then they will be withdrawn from the research.

The research project has been approved by the University of Birmingham Research Ethics Committee. If you wish to see proof of approval from this body, or you wish to discuss any concerns about acting as a personal consultee for the person that you care for, please contact Lucy Wilde on 0121 414 2855 or by email at lvw894@bham.ac.uk

I don't want to be a nominated consultee - what do I do?

Please try to suggest an alternative person who might like to act as a nominated consultee for the potential participant, please pass the project information pack on to that person.

If no-one can be found who is willing and able to act as a consultee for the person you care for then the person will not be able to participate in the research study.

Where can I get more information and guidance?

More information is available from:

Department for Constitutional Affairs (2007) *Mental Capacity Act 2005 Code of Practice*
<http://www.dca.gov.uk/legal-policy/mental-capacity/mca-cp.pdf>

Department of Health (2007) *Guidance on nominating a consultee for research involving adults who lack capacity to consent* (consultation)
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_076207

Mental Capacity Implementation Programme (2007) *Making Decisions: a guide for family, friends and unpaid carers. Second edition*
<http://www.dca.gov.uk/legal-policy/mental-capacity/mibooklets/booklet02.pdf>
A printed copy of this booklet is available by telephoning 023 80878038.

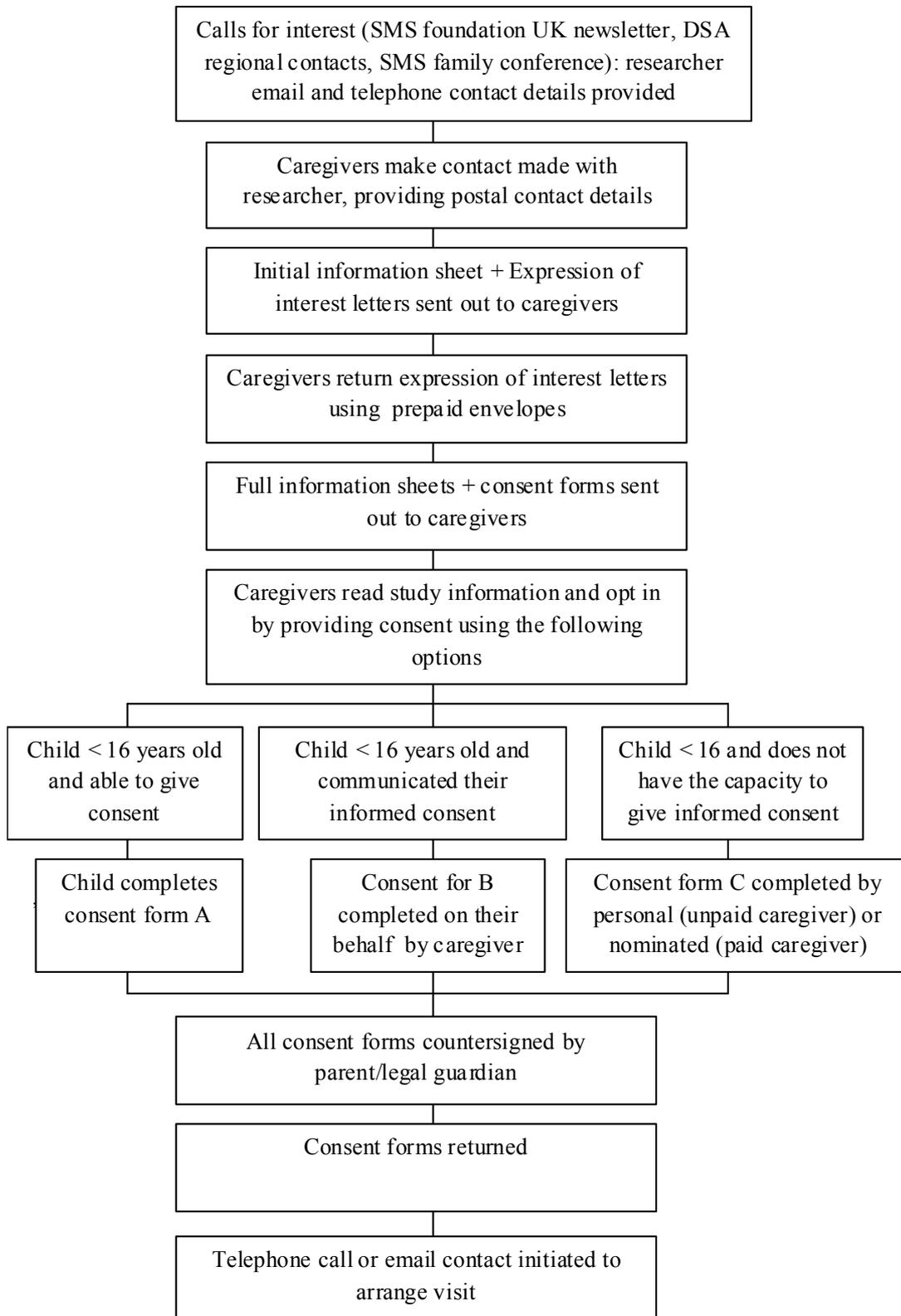
I have decided that I want to be a nominated consultee - what do I do?

Please go back to the typical and atypical social development information sheet and continue reading.

APPENDIX E

Opt in consent process for initial samples of chapter four, five
and six studies

Opt in consent flowchart



APPENDIX F
Questionnaire measures

APPENDIX F1: Demographic questionnaire

ID _____

BACKGROUND INFORMATION

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

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

Uni-parental disomy	<input type="checkbox"/>	Sequence repetition	<input type="checkbox"/>
Deletion	<input type="checkbox"/>	Translocation	<input type="checkbox"/>
Unknown	<input type="checkbox"/>	Other _____	
7. When was the person you care for diagnosed? _____
8. Who diagnosed the person you care for?

Paediatrician	<input type="checkbox"/>	Clinical Geneticist	<input type="checkbox"/>
GP	<input type="checkbox"/>	Other _____	
9. Has the person you care for had any medical/health difficulties in the last six months? If yes, please give details:

APPENDIX F2: Wessex questionnaire

WESSEX QUESTIONNAIRE

These items refer to the person you care for. For each question (A, B, C, D etc ...), please enter the appropriate code in each box.

- | | | | | |
|----------------------------|----------------|-------------------|--------------------------------|--------------------------|
| A) <u>Wetting (nights)</u> | 1 = frequently | 2 = occasionally | 3 = never | <input type="checkbox"/> |
| B) <u>Soiling (nights)</u> | 1 = frequently | 2 = occasionally | 3 = never | <input type="checkbox"/> |
| C) <u>Wetting (days)</u> | 1 = frequently | 2 = occasionally | 3 = never | <input type="checkbox"/> |
| D) <u>Soiling (days)</u> | 1 = frequently | 2 = occasionally | 3 = never | <input type="checkbox"/> |
| E) <u>Walk with help*</u> | 1 = not at all | 2 = not up stairs | 3 = up stairs
and elsewhere | <input type="checkbox"/> |

*(note: if this person walks *by himself/herself* upstairs and elsewhere, please also code '3' for 'walk with help')

- | | | | | |
|---------------------------|---------------------|--------------------------|--------------------------------|--------------------------|
| F) <u>Walk by himself</u> | 1 = not at all | 2 = not up stairs | 3 = up stairs and
elsewhere | <input type="checkbox"/> |
| G) <u>Feed himself</u> | 1 = not at all | 2 = with help | 3 = without help | <input type="checkbox"/> |
| H) <u>Wash himself</u> | 1 = not at all | 2 = with help | 3 = without help | <input type="checkbox"/> |
| I) <u>Dress himself</u> | 1 = not at all | 2 = with help | 3 = without help | <input type="checkbox"/> |
| J) <u>Vision</u> | 1 = blind or almost | 2 = poor | 3 = normal | <input type="checkbox"/> |
| K) <u>Hearing</u> | 1 = deaf or almost | 2 = poor | 3 = normal | <input type="checkbox"/> |
| L) <u>Speech</u> | 1 = never a word | 2 = odd words only | 3 = sentences and normal | <input type="checkbox"/> |
| | | 4 = can talk but doesn't | | <input type="checkbox"/> |

If this person talks in sentences, is his/her speech:

1 = Difficult to understand even by acquaintances, impossible for strangers?

2 = Easily understood for acquaintances, difficult for strangers?

3 = Clear enough to be understood by anyone?

- | | | | | |
|------------------|-------------|--------------|------------------------------|--------------------------|
| M) <u>Reads</u> | 1 = nothing | 2 = a little | 3 = newspapers and/or books | <input type="checkbox"/> |
| N) <u>Writes</u> | 1 = nothing | 2 = a little | 3 = own correspondence | <input type="checkbox"/> |
| O) <u>Counts</u> | 1 = nothing | 2 = a little | 3 = understands money values | <input type="checkbox"/> |

Please check your answers and go on to the next questionnaire.

APPENDIX F3: Autism Screening measure

SOCIAL COMMUNICATION QUESTIONNAIRE © Rutter et al 2003

Please circle 'yes' if any one of the following behaviours is present. Although you may be uncertain about whether some behaviours are present or not, please do answer 'yes' or 'no' to every question on the basis of what you think.

- | | | |
|---|-----|----|
| 1. Is she/he now able to talk using short phrases or sentences? If no, skip to question 8. | Yes | No |
| 2. Can you have a to and fro "conversation" with her/him that involves taking turns or building on what you have said? | Yes | No |
| 3. Has she/he ever used odd phrases or said the same thing over and over in almost exactly the same way (either phrases that she/he has heard other people use or ones that she/he has made up)? | Yes | No |
| 4. Has she/he ever used socially inappropriate questions or statements? For example, has she/he ever regularly asked personal questions or made personal comments at awkward times? | Yes | No |
| 5. Has she/he ever got her/his pronouns mixed up (e.g., saying you or she/he for I)? | Yes | No |
| 6. Has she/he ever used words that she/he seemed to have invented or made up her/himself; put things in odd, indirect ways; or used metaphorical ways of saying things (e.g., saying hot rain for steam)? | Yes | No |
| 7. Has she/he ever said the same thing over and over in exactly the same way or insisted that you say the same thing over and over again? | Yes | No |
| 8. Has she/he ever had things that she/he seemed to have to do in a very particular way or order or rituals that she/he insisted that you go through? | Yes | No |
| 9. Has her/his facial expression usually seemed appropriate to the particular situation, as far as you could tell? | Yes | No |
| 10. Has she/he ever used your hand like a tool or as if it were part of her/his own body (e.g., pointing with your finger, putting your hand on a doorknob to get you to open the door)? | Yes | No |
| 11. Has she/he ever had any interests that preoccupy her/him and might seem odd to other people (e.g., traffic lights, drainpipes, or timetables)? | Yes | No |
| 12. Has she/he ever seemed to be more interested in parts of a toy or an object (e.g., spinning the wheels of a car), rather than using the object as it was intended? | Yes | No |
| 13. Has she/he ever had any special interests that were unusual in their intensity but otherwise appropriate for her/his age and peer group (e.g., trains, dinosaurs)? | Yes | No |
| 14. Has she/he ever seemed to be unusually interested in the sight, feel, sound, taste, or smell of things or people? | Yes | No |
| 15. Has she/he ever had any mannerisms or odd ways of moving her/his hands or fingers, such as | Yes | No |

flapping or moving her/his fingers in front of her/his eyes?

- | | | |
|--|-----|----|
| 16. Has she/he ever had any complicated movements of her/his whole body, such as spinning or repeatedly bouncing up and down? | Yes | No |
| 17. Has she/he ever injured her/himself deliberately, such as by biting her/his arm or banging her/his head? | Yes | No |
| 18. Has she/he ever had any objects (other than a soft toy or comfort blanket) that she/he had to carry around? | Yes | No |
| 19. Does she/he have any particular friends or a best friend? | Yes | No |
| 20. When she/he was 4 to 5, did she/he ever talk with you just to be friendly (rather than to get something)? | Yes | No |
| 21. When she/he was 4 to 5, did she/he ever spontaneously copy you (or other people) or what you were doing (such as vacuuming, gardening, or mending things)? | Yes | No |
| 22. When she/he was 4 to 5, did she/he ever spontaneously point at things around her/him just to show you things (not because she/he wanted them)? | Yes | No |
| 23. When she/he was 4 to 5, did she/he ever use gestures, other than pointing or pulling your hand, to let you know what she/he wanted | Yes | No |
| 24. When she/he was 4 to 5, did she/he nod her/his head to mean yes? | Yes | No |
| 25. When she/he was 4 to 5, did she/he shake her/his head to mean no? | Yes | No |
| 26. When she/he was 4 to 5, did she/he usually look at you directly in the face when doing things with you or talking with you? | Yes | No |
| 27. When she/he was 4 to 5, did she/he smile back if someone smiled at her/him? | Yes | No |
| 28. When she/he was 4 to 5, did she/he ever show you things that interested her/him to engage your attention? | Yes | No |
| 29. When she/he was 4 to 5, did she/he ever offer to share things other than food with you? | Yes | No |
| 30. When she/he was 4 to 5, did she/he ever seem to want you to join in her/his enjoyment of something? | Yes | No |
| 31. When she/he was 4 to 5, did she/he ever try to comfort you if you were sad or hurt? | Yes | No |
| 32. When she/he was 4 to 5, when she/he wanted something or wanted help, did she/he look at you and use gestures with sounds or words to get your attention? | Yes | No |
| 33. When she/he was 4 to 5, did she/he show a normal range of facial expressions? | Yes | No |
| 34. When she/he was 4 to 5, did she/he ever spontaneously join in and try to copy the actions in social games, such as The Mulberry Bush or London Bridge Is Falling Down? | Yes | No |

- | | | |
|---|------------|-----------|
| 35. When she/he was 4 to 5, did she/he play any pretend or make-believe games? | Yes | No |
| 36. When she/he was 4 to 5, did she/he seem interested in other children of approximately the same age whom she/he did not know? | Yes | No |
| 37. When she/he was 4 to 5, did she/he respond positively when another child approached her/him? | Yes | No |
| 38. When she/he was 4 to 5, if you came into a room and started talking to her/him without calling her/his name, did she/he usually look up and pay attention to you? | Yes | No |
| 39. When she/he was 4 to 5, did she/he ever play imaginative games with another child in such a way that you could tell that they each understood what the other was pretending? | Yes | No |
| 40. When she/he was 4 to 5, did she/he play cooperatively in games that required joining in with a group of other children, such as hide-and-seek or ball games? | Yes | No |

APPENDIX F4: Activity questionnaire

ACTIVITY QUESTIONNAIRE

Instructions:

- Please read each item carefully and circle the appropriate number on the scale, for the person you care for.
- Please ensure that you indicate a response for every item. If the particular behaviour does not apply, for example, if the person is not verbal or not mobile, please circle 0 on the scale.

	Never/ almost never	Some of the time	Half of the time	A lot of the time	Always/ almost all the time
1. Does the person wriggle or squirm about when seated or lying down?	0	1	2	3	4
2. Does the person fidget or play with their hands and/or feet when seated or lying down?	0	1	2	3	4
3. Does the person find it difficult holding still?	0	1	2	3	4
4. Does the person find it difficult to remain in their seat even when in situations where it would be expected?	0	1	2	3	4
5. Does the person prefer to be moving around or become frustrated if left in one position for too long?	0	1	2	3	4
6. When the person is involved in a leisure activity (e.g. watching TV, playing a game etc.) do they make a lot of noise?	0	1	2	3	4
7. When the person is involved in an activity, are they boisterous and/or rough?	0	1	2	3	4
8. Does the person act as if they are “driven by a motor” (i.e. often very active)?	0	1	2	3	4
9. Does the person seem like they need very little rest to recharge their battery?	0	1	2	3	4
10. Does the person often talk excessively?	0	1	2	3	4
11. Does the person’s behaviour seem difficult to manage/contain whilst out and about (e.g. in town, in supermarkets etc.)?	0	1	2	3	4
12. Do you feel that you need to “keep an eye” on the person at all times?	0	1	2	3	4
13. Does the person you care for seem to act/do things without stopping to think first?	0	1	2	3	4
14. Does the person blurt out answers before questions have been completed?	0	1	2	3	4
15. Does the person start to respond to instructions before they have been fully given or without seeming to understand them?	0	1	2	3	4
16. Does the person want things immediately?	0	1	2	3	4
17. Does the person find it difficult to wait?	0	1	2	3	4
18. Does the person disturb others because they have difficulty waiting for things or waiting their turn?	0	1	2	3	4

APPENDIX F5: Sociability questionnaire for people with intellectual disabilities

THE SOCIABILITY QUESTIONNAIRE FOR PEOPLE WITH INTELLECTUAL DISABILITIES © Collis, Oliver & Moss 2006

Instructions:

This questionnaire asks you how the person you care for typically behaved in social situations over the LAST TWO MONTHS. Each situation will involve one of the following:

1. *The person's main caregiver*: Someone that provides the main support and care for the person, e.g. a parent or carer.
2. *A familiar adult or someone familiar of the same age*: Someone that knows the person relatively well but does *not* provide the main care for the person, e.g. a relative *not* in the immediate family, a friend of the family, a support worker at school/college, a friend at school/college etc.
3. *An adult or someone of the same age that the person does not know*: Someone the person has *never* met before, e.g. a stranger, a new teacher, a new support worker at school/college, someone new of the same age at school/college etc.

The person may appear 'sociable', 'shy' or somewhere in between in the situations given below.

- If the person is 'sociable' (s)he may show one or more of the following behaviours: looks pleased; starts to speak or sign to others; turns face and/or body towards others or tries to gain other people's attention in some way.
- If the person is 'shy' (s)he may show one or more of the following behaviours: looks a little sad or distressed; reluctant to speak or sign to others; turns head and/or body away from others; tries to avoid or remove himself/herself from situations when other people are present.

Read each question and circle the response that best describes the behaviour of the person in the situation described.

For example, for question 4 if you think that when the person is spending time with a familiar adult (s)he would be 'very sociable' then your answer would look like this:-

4. (S)he is spending time with a familiar adult? 1 2 3 4 5 6 7

	Very shy	Moderately shy	A little shy	Neither	A little sociable	Moderately sociable	Very sociable
How would the person you care for appear if...							
1. Her/his main caregiver walks up to her / him?	1	2	3	4	5	6	7
2. (S)he is spending time with an adult (s)he does <i>not</i> know?	1	2	3	4	5	6	7
3. Someone (s)he does <i>not</i> know that is her/his own age walks up to her /him?	1	2	3	4	5	6	7
4. (S)he is spending time with a familiar adult?	1	2	3	4	5	6	7
5. (S)he is the focus of attention in a group of adults (s)he knows?	1	2	3	4	5	6	7
6. (S)he is spending time with someone (s)he does <i>not</i> know that is her/his own age?	1	2	3	4	5	6	7

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7. Someone familiar that is her/his own age walks up to her /him?	1	2	3	4	5	6	7
8. (S)he has just been separated from her/his main caregiver to be with an adult (s)he does not know?	1	2	3	4	5	6	7
9. An adult (s)he does not know walks up to her/him?	1	2	3	4	5	6	7
10. (S)he is the focus of attention in a group of people her/his own age that (s)he does not know?	1	2	3	4	5	6	7
11. (S)he is spending time with someone familiar that is her/his own age?	1	2	3	4	5	6	7
12. (S)he is the focus of attention in a group of people her/his own age that (s)he knows? ...	1	2	3	4	5	6	7
	Very shy	Moderately shy	A little shy	Neither	A little sociable	Moderately sociable	Very sociable
How would the person you care for appear if...							
13. (S)he is with her/his main caregiver and then someone her / his own age that (s)he does not know starts to talk to her/him?	1	2	3	4	5	6	7
14. A familiar adult walks up to her/him?	1	2	3	4	5	6	7
15. (S)he is with her/his main caregiver and then an adult (s)he does not know starts to talk to her/him?	1	2	3	4	5	6	7
16. (S)he is spending time with her/his main caregiver?	1	2	3	4	5	6	7
17. (S)he is the focus of attention in a group of adults (s)he does not know?	1	2	3	4	5	6	7
	Never or very rarely	Rarely	Sometimes	About half the time	Often	Very often	Nearly Always
18. When there are only familiar people around, how often does (s)he try to make contact with them in any way (by talking, signing, vocalising, using gestures, moving towards them in any way etc.)?	1	2	3	4	5	6	7
19. When familiar people and people are around who (s)he does not know, how often does (s)he try to make contact with the people (s)he does not know in any way (by talking, signing, vocalising, using gestures, moving towards them in any way etc.)?	1	2	3	4	5	6	7
20. When familiar people and people are around who (s)he does not know, how often does (s)he try to make contact with the familiar people in any way (by talking, signing, vocalising, using gestures, moving towards them in any way etc.)?	1	2	3	4	5	6	7
21. When there are only people around who (s)he does not know, how often does (s)he try to make contact with them in any way (by talking, signing, vocalising, using gestures, moving towards them in any way etc.)?	1	2	3	4	5	6	7

Appendices

YES NO

22. Does the person you care for speak or sign **more** than 30 words?

If you answered 'yes' to this question, please complete the rest of the questionnaire. If you answered 'no', please complete the box at the end of the questionnaire if there is anything else you think we should know.

23. Does the person speak *less* than (s)he used to?

24. Does the person *only* speak or sign in some settings and not others?

If 'yes' please describe

.....
.....
.....

25. Does the person *only* speak or sign to some people and not others?

If 'yes' please describe

.....
.....
.....

<p>Is there anything else you want to tell us about how the person you care for appears in social situations with other people (s)he knows or doesn't know, when separated from you, in a group setting or is the centre of attention in a group of people?</p> <p>.....</p>

APPENDIX F6: Behavior Rating Inventory of Executive Function: Preschool

BRIEF-P © Gioia Espy & Isquith 2003

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

N if the behaviour is never a problem
S if the behaviour is sometimes a problem
O if the behaviour is often a problem

	Never	Sometimes	Often
During the past 6 months, how often has each of the following behaviours been a problem?			
1. Over-reacts to small problems	N	S	O
2. When given two things to do, remembers only the first or last	N	S	O
3. Is unaware of how his/her behaviour affects or bothers others	N	S	O
4. When instructed to clean up, puts things away in a disorganised, random way	N	S	O
5. Becomes upset with new situations	N	S	O
6. Has explosive, angry outbursts	N	S	O
7. Has trouble carrying out the actions needed to complete tasks (such as, trying one puzzle piece at a time, cleaning up to earn a reward)	N	S	O
8. Does not stop laughing at funny things or events when others stop	N	S	O
9. Needs to be told to begin a task even when willing to do it	N	S	O
10. Has trouble adjusting to new people (such as babysitter, teacher, friend or day care worker)	N	S	O
11. Becomes upset too easily	N	S	O
12. Has trouble concentrating on games, puzzles or activities	N	S	O
13. Has to be more closely supervised than similar peers	N	S	O
14. When sent to get something, forgets what he/she is supposed to get	N	S	O
15. Is upset by a change in plans or routine (for example, order of daily activities, adding last minute errands to schedule, change in driving route to shop)	N	S	O
16. Has outbursts for little reason	N	S	O
17. Repeats the same mistakes over and over even after help is given	N	S	O
18. Acts wilder or sillier than others in groups (such as, birthday parties, class at school/college, family gatherings)	N	S	O
19. Cannot find clothes, shoes, toys or books even when he/she has been given specific instructions	N	S	O
20. Takes a long time to feel comfortable in new places or situations (such as visiting distant relatives or new friends)	N	S	O
21. Mood changes frequently	N	S	O
22. Makes silly mistakes on things he/she can do	N	S	O
23. Is fidgety, restless or squirmy	N	S	O
24. Has trouble following established routines for sleeping, eating or activities	N	S	O

25.	Is bothered by loud noises, bright lights or certain smells	N	S	O
26.	Small events trigger big reactions	N	S	O
27.	Has trouble with activities or tasks that have more than one step	N	S	O
28.	Is impulsive	N	S	O
29.	Has trouble thinking of a different way to solve a problem or complete an activity when stuck	N	S	O
30.	Is disturbed by changes in the environment (such as, new furniture, things in room moved around or new clothes)	N	S	O
During the past 6 months, how often has each of the following behaviours been a problem?		Never	Sometimes	Often
31.	Angry or tearful outbursts are intensive but end suddenly	N	S	O
32.	Needs help from adult to stay on task	N	S	O
33.	Does not notice when his/her behaviour causes negative reactions	N	S	O
34.	Leaves messes that others have to clean up even after instruction	N	S	O
35.	Has trouble changing activities	N	S	O
36.	Reacts more strongly to situations than other peers	N	S	O
37.	Forgets what he/she is doing in the middle of an activity	N	S	O
38.	Does not realise that certain actions bother others	N	S	O
39.	Gets caught up in the small details of a task or situation and misses the main idea	N	S	O
40.	Has trouble "joining in" at unfamiliar social events (such as, birthday parties, picnics, holiday gatherings)	N	S	O
41.	Is easily overwhelmed or over stimulated by typical daily activities	N	S	O
42.	Has trouble finishing tasks (such as, games, puzzles or other activities)	N	S	O
43.	Gets out of control more than peers	N	S	O
44.	Cannot find things in room even when given specific instructions	N	S	O
45.	Resists change of routine, foods, places etc.	N	S	O
46.	After having a problem, will stay disappointed for a long time	N	S	O
47.	Cannot stay on the same topic when talking	N	S	O
48.	Talks or plays too loudly	N	S	O
49.	Does not complete tasks even after given directions	N	S	O
50.	Acts overwhelmed or over stimulated in crowded, busy situations (such as, lots of noise, activity or people)	N	S	O
51.	Has trouble getting started on activities or tasks even after instructed	N	S	O
52.	Acts too wild or out of control	N	S	O
53.	Does not try as hard as his/her ability on activities	N	S	O
54.	Has trouble putting the brakes on his/her actions even after being asked	N	S	O
55.	Unable to finish describing an event, person or story	N	S	O
56.	Completes tasks or activities too quickly	N	S	O
57.	Is unaware when he/she does well and not well	N	S	O
58.	Gets easily sidetracked during activities	N	S	O
59.	Has trouble remembering something, even after a brief period of time	N	S	O
60.	Becomes too silly	N	S	O
61.	Has a short attention span	N	S	O
62.	Behaves carelessly or recklessly in situations where he/she could be hurt (such as, playground, swimming pool)	N	S	O
63.	Is unaware when he/she performs a task right or wrong	N	S	O

APPENDIX F7: Repetitive behaviour questionnaire

THE RBQ © Moss & Oliver 2003

INSTRUCTIONS:

1. The questionnaire asks about 19 different behaviours.
2. Each behaviour is accompanied by a brief definition and examples. The examples given for each behaviour are not necessarily a complete list but may help you to understand the definitions more fully.
3. Please read the definitions and examples carefully and circle the appropriate number on the scale to indicate how frequently the person you care for has engaged in each of the behaviours WITHIN THE LAST MONTH.
4. If a particular behaviour does not apply to the person you care for because they are not mobile or verbal please circle the number 0 on the scale

	Never	Once a month	Once a week	Once a day	More than once a day
1. Object stereotypy: Repetitive, seemingly purposeless movement of objects in an unusual way <i>E.g. twirling or twiddling objects, twisting or shaking objects, banging or slapping objects.</i>	0	1	2	3	4
2. Body stereotypy: Repetitive, seemingly purposeless movement of whole body or part of body (other than hands) in an unusual way. <i>E.g. body rocking, or swaying or spinning, bouncing, head shaking, body posturing.</i> Does not include self-injurious behaviour.	0	1	2	3	4
3. Hand stereotypy: Repetitive, seemingly purposeless movement of hands in an unusual way. <i>E.g. finger twiddling, hand flapping, wiggling or flicking fingers, hand posturing.</i> Does not include self-injurious behaviour.	0	1	2	3	4
4. Cleaning: Excessive cleaning, washing or polishing of objects or parts of the body <i>E.g. polishes windows and surfaces excessively, washes hands and face excessively.</i>	0	1	2	3	4
5. Tidying up: Tidying away any objects that have been left out. This may occur in situations when it is inappropriate to put the objects away. Objects may be put away into inappropriate places. <i>E.g. putting cutlery left out for dinner in the bin, removes all objects from surfaces.</i>	0	1	2	3	4
6. Hoarding: Collecting, storing or hiding objects to excess, including rubbish, bits of paper, and pieces of string or any other unusual items.	0	1	2	3	4
7. Organising objects: Organising objects into categories according to various characteristics such as colour, size, or function. <i>E.g. ordering magazines according to size, ordering toy cars according to colour, ordering books according to topic.</i>	0	1	2	3	4
8. Attachment to particular people: Continually asking to see, speak or contact a	0	1	2	3	4

particular ‘favourite’ person. <i>E.g. continually asks to see or speak to particular friend, carer, babysitter or schoolteacher.</i>					
9. Repetitive questions: Asking specific questions over and over. <i>E.g. always asking people what their favourite colour is, asking who is taking them to school the next day over and over.</i>	0	1	2	3	4
10. Attachment to objects: Strong preference for a particular object to be present at all times. <i>E.g. carrying a particular piece of string everywhere, taking a particular red toy car everywhere, attachment to soft toy or particular blanket.</i>	0	1	2	3	4
	Never	Once a month	Once a week	Once a day	More than once a day
11. Repetitive phrases/signing: Repeating particular sounds, phrases or signs that are unrelated to the situation over and over. <i>E.g. repeatedly signing the word ‘telephone’.</i>	0	1	2	3	4
12. Rituals: carrying out a sequence of unusual or bizarre actions before, during or after a task. The sequence will always be carried out when performing this task and will always occur in the same way. <i>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.</i>	0	1	2	3	4
13. Restricted conversation: Repeatedly talks about specific, unusual topics in great detail. <i>E.g. conversation restricted to: trains, buses, dinosaurs, particular film, country or sport.</i>	0	1	2	3	4
14. Echolalia: Repetition of speech that has either just been heard or has been heard more than a minute earlier. <i>E.g. Mum: ‘Jack don’t do that’ Jack: ‘Jack don’t do that’.</i>	0	1	2	3	4
15. Preference for routine: Insists on having the same household, school or work schedule everyday. <i>E.g. likes to have the same activities on the same day at the same time each week, prefers to eat lunch at exactly the same time every day, wearing the same jumper everyday.</i>	0	1	2	3	4
16. Lining up or arranging objects: Arrangement of objects into lines or patterns. <i>E.g. placing toy cars in a symmetrical pattern, precisely lining up story books.</i>	0	1	2	3	4
17. Just right behaviour: Strong insistence that objects, furniture and toys always remain in the same place. <i>E.g. all chairs, pictures and toys have a very specific place that cannot be changed.</i>	0	1	2	3	4
18. Completing behaviour: Insists on having objects or activities ‘complete’ or ‘whole’. <i>E.g. Must have doors open or closed not in between, story must be read from beginning to end, not left halfway through.</i>	0	1	2	3	4
19. Spotless behaviour: Removing small, almost unnoticeable pieces of lint, fluff, crumbs or dirt from surfaces, clothes and objects. <i>E.g. picking fluff off a jumper, removing crumbs from the kitchen table.</i>	0	1	2	3	4

APPENDIX G

Recruitment process for study ‘The nature of social preference and interactions in Smith Magenis syndrome’

Recruitment

Expressions of interest for participation were gained from caregivers involved in an existing research project (see 5.3.2 for full details of this sample). Nineteen of 21 parents of children with SMS expressed an interest in participating in a study of social behaviour in schools.

Of these 11 met the inclusion criteria of being children of school age (over 4 years old and under 16 years) and having completed the cognitive assessment in the previous study which enabled mental age matching in the current study. All of these parents were contacted and 10 confirmed participation. Of the 17 parents of children with DS who met inclusion criteria and indicated that they would like to part in this study, parents were contacted in the order which reflected the best mental age matches for the SMS sample until 10 participants had been recruited.

Following initial expressions of interest, consent for participation was obtained from children's parents. Children's schools were then contacted in order to gain their consent for researchers to visit.

APPENDIX H

Full list of codes and operational definitions and associated
Kappa values: The nature of social preference and interactions
in Smith-Magenis syndrome

Codes and operational definitions and associated Kappa values

E/D	Attention from adult	Definition	Kappa
D	Adult touches child (AdTouch)	Adult initiated touching any part of the participant (including clothing) as a result of deliberately moving part of their body towards them e.g. hugging, patting, kissing, tapping.	.67
D	Adult verbalises to child (AdVerb)	Adult speech directed towards the participant; These may be utterances (e.g. ‘erm’), words, phrases or sentences.	.59
E	Adult makes non verbal communication to child (AdNVerb)	Adult use of signing (Makaton or British Sign Language), gestures e.g., pointing, or making non verbal response (responds question, statement, comment or prompt by nodding or shaking their head) directed toward the participant	.48
	Attention to adult		
D	Child touches adult (ChTouAd)	Child initiated touching any part of an adult (including clothing) as a result of deliberately moving part of their body towards them e.g. hugging, patting, kissing, tapping. Does not include aggressive pulling or grabbing or movements of legs or feet.	.65
D	Child verbalises to adult (ChVerbAd)	Participant’s speech; These may be utterances (e.g. ‘erm’), words, phrases or sentences.	.61
E	Non verbal communication to adult (ChNVerbAd)	Participant use of signing (Makaton or British Sign Language), gestures e.g., pointing, or making non verbal response (responds question, statement, comment or prompt by nodding or shaking their head) directed towards an adult	.6
D	Child looks towards adult	Child looks in the direction of an adult’s eyes or face	.63

	face (ChLookAd)		
	Attention to peer		
D	Child touches peer (ChTouPr)	Participant initiated touching any part of another child (including clothing) as a result of deliberately moving part of their body towards them e.g. hugging, patting, kissing, tapping. Does not include aggressive pulling or grabbing or movements of legs or feet.	.74
D	Child verbalises to peer (ChVerbPr)	Participant's speech directed to another child; These may be utterances (e.g. 'erm'), words, phrases or sentences.	.49
E	Non verbal communication to peer (ChNVerbPr)	Participant use of signing (Makaton or British Sign Language), gestures e.g., pointing, or making non verbal response (responds question, statement, comment or prompt by nodding or shaking their head) directed towards another child	.68
D	Child looks towards peer face (ChLookPr)	Child looks in the direction of a peer's eyes or face	.7
	Positive affect		
D	Positive facial expression (PosAff)	Facial expressions or vocalisations with clear positive tone e.g., smiling or laughing	.75
	Negative affect		
D	Negative affect (NegAff)	Facial expressions or vocalisations with clear negative tone e.g., frowning, turning down of mouth, crying, whining	.81
	Challenging		

	behaviour		
D	Self injury (SIB)	The participant engages in non-accidental self-directed injurious behaviours which produce temporary marks or reddening of the skin or cause bruising, bleeding or other temporary or permanent tissue including hair pulling, picking, biting, tapping, hitting, banging, scratching.	.75
D	Aggression (Agg)	Any physical aggression directed towards another person ie hitting, kicking, grabbing, scratching	.78
D	Property destruction (PropDest)	Destructive behaviour ie tearing, tipping furniture, pulling items off walls, throwing/swiping items away	.93
D	Other CB (OthCB)	Any other behaviour that would be considered harmful to the participant, challenging for carers or objectionable to the public e.g swearing, spitting	.68
	Other codes		
D	Fatigue (Fatg)	Any occurrences of yawning and/or laying down	.8
E	Error (Error)		-
E	Flag (Flag)	Potentially important environmental event	-
E	Approach Observer (ApprOb)	Child approaches observer includes talking to observer and touching observer	.78
D	One to one attention* (OneTOne)	Child is receiving one to one attention from an adult	.78
D	Shared attention* (Shared)	Child is receiving shared attention from an adult – other children are present and adult is interacting with them	.88
D	Free play* (FPlay)	Child is engaged in free play and is not the focus of adult directed attention	.91

Reliability of combined variables

The mean and range of the Kappa values of the target variables were: Adult attention to child; 0.65 (-0.03 – 1.00), Child attention to adult 0.69 (-0.02 – 1.00), child attention to peer 0.65 (-0.03 – 1.00), child look at adult 0.63 (-0.11 – 1.00), child look at peer 0.70 (-0.02 – 1.00), positive affect 0.75 (0.00– 1.00), negative affect 0.81 (0.00– 1.00). Kappa values of 0.4 - 0.6 are considered 'fair' and 0.6 - 0.75 'good' (Fleiss, 1981), thus the mean reliability of all of the variables can be considered 'good'.

APPENDIX I

Protocols: child leaving testing situation, child showing
challenging behaviour

Child leaving the room

If the child left the testing room the person interacting with them during that set of conditions was prompted to return them to the room. If the child could not be encouraged to return (i.e. was very resistant/showed challenging behaviour) by the end of the current condition then the protocol was implemented in their present location.

Challenging behaviour

In the social contact conditions if the child showed prolonged/severe challenging behaviour (self-injury, verbal/physical aggression or property destruction) about which either unfamiliar adults or parents expressed concern, social contact was discontinued until 30 seconds clear of challenging behaviour. In the non contact condition social contact was given by the person in background until 30 seconds clear of challenging behaviour.

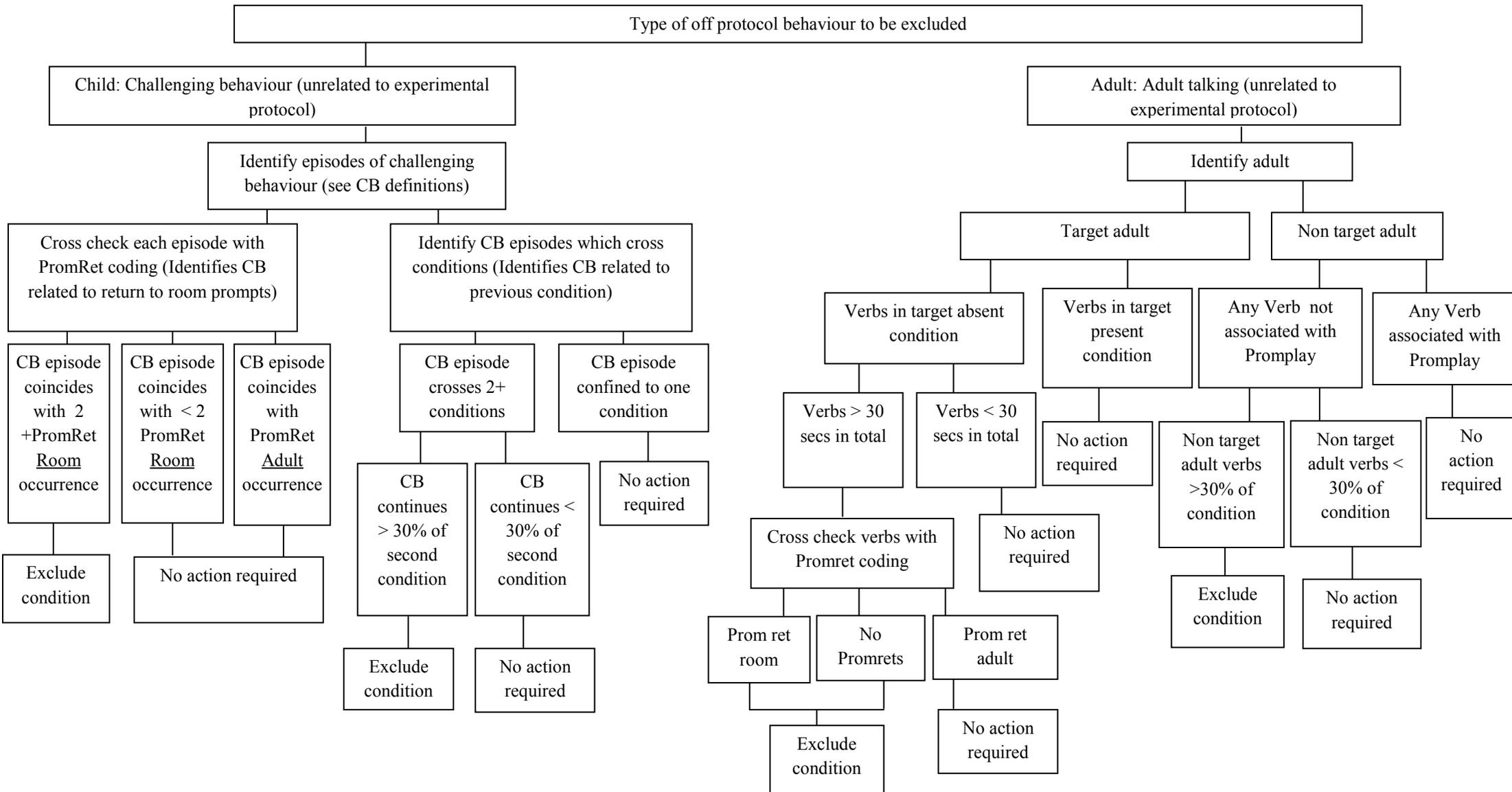
APPENDIX J

Exclusion process explanation and flowchart, definitions of episodes of challenging behaviour, record of resulting exclusions

Exclusion of off protocol episodes

For the low attention conditions percentage of time either adult spent verbalising to the child was recorded. Where adults verbalised to the child exceed a specified amount of time in low attention conditions (unless was a prompt to return to the room from the interacting absent adult which was determined to be related to child leaving to access attention from that adult or a prompt to return to play from the unresponsive adult) conditions were excluded.

Conditions where challenging behaviour and/or negative affect was shown which coincided with prompts to return to the room from the interacting absent adult that were determined to be unrelated to child leaving to access attention from that adult (e.g. was to access a tangible reward such as television) were excluded. Similarly conditions where episodes of challenging behaviour/negative affect were carried on from the previous condition (i.e. there was a less than 20 second gap between the offset of challenging behaviour or negative affect in one condition and the onset of those behaviours in the next) and continued for over 30 percent of that condition were excluded.



Episodes of challenging behaviour (CB)

An episode of CB can consist of the following:

- 1) Any incidence of aggression (agg) or self injury (SIB)
- 2) Any destruction which co-occurs with negative affect (neg aff) which includes incidents of screaming, shouting, crying (not solely whinging/frowning) or which exceeds 20 seconds in duration (either solidly or re-occurs at less than 20 seconds intervals and exceeds 20 seconds)
- 3) Negative affect which exceeds 30 seconds duration and includes incidents of screaming, shouting, crying (not solely whinging/frowning)

Do not describe the negative affect that accompanies destruction (dest), agg or SIB unless it meets the 30 second duration and not just whinging/frowning criteria above (important for working out total length of cb episode)

Defining separate episodes

Burst are separated by 20 second periods of clear (i.e. no neg aff, SIB, agg or dest) or if footage shows a new antecedent is introduced (child/adult behaviour)

Describing each episode using Obswin

- 1) identify which behaviours are involved (prolonged neg aff, agg, dest, sib)
- 2) identify how long the burst goes on for in total (from start first example of CB included to the end)
- 3) identify the total duration of each behaviour involved during the episode
- 4) identify the mean occurrence length of each behaviour
- 5) identify the number of occurrences of each behaviour within the episode (onset)
- 6) identify the when the behaviour starts and when it finishes

Excluded conditions

Reason for exclusion

- 1) Child: Challenging behaviour (unrelated to experimental protocol)

Final exclusion process

Identify episodes of challenging behaviour (see CB definitions) - Cross check each episode with PromRet coding (Identifies CB related to return to room prompts) - CB episode coincides with 2 +PromRet Room occurrence - CB episode coincides with 2 +PromRet Room occurrence -CB continues > 30% of second condition: SMS 12 conditions (6 participants), DS: 2 conditions (1 participant): **SMS; 12 conditions (6 participants), DS: 2 conditions (1 participant)**

Identify episodes of challenging behaviour (see CB definitions) - Identify CB episodes which cross conditions (Identifies CB related to previous condition) - CB episode crosses 2+ conditions

- CB continues > 30% of second condition: **SMS; 12 conditions (9 participants), DS; 3 conditions (2 participants)**

- 2) Adult: Adult talking (unrelated to experimental protocol)

Final exclusion process

Identify adult - Target adult - Verbs in target absent condition - Verbs > 30 secs in total - Cross check verbs with Promret coding

- Prom ret room or No Promrets: **SMS: 11 conditions (6 participants), DS: 5 conditions (3 participants)**

Identify adult - Non target adult - Any Verb not associated with Promplay

- Non target adult verbs >30% of condition: **SMS: 3 conditions (2 participants), DS: no events**

Syndrome group total number of conditions excluded: SMS: 32 (8.7%) 366, DS: 8 (2.11%)

Overall total number of conditions excluded: 40 (5.37%)

Note: conditions can be excluded for multiple reasons this the total number of excluded conditions may equal less than those excluded for each individual reason

APPENDIX K

Full list of codes and operational definitions and associated Kappa values: Effect of adult familiarity and level of attention on social behaviours in Smith-Magenis syndrome study

Codes and operational definitions and associated Kappa values

E/D	Eye Contact	Definition	Mean Kappa
D	Looking at mother (lookatmum)	The participant looks in the direction of the mother's eyes or face. Mother has to be on camera.	.81
D	Looking at researcher (lookatres)	The participant looks in the direction of the researcher's eyes or face. Researcher has to be on camera	.8
D	Participant's face not on camera (noface)	The participant's face cannot be seen on camera.	.7
D	Looking at camera (lookatcam)	The participant looks in the direction of the camera.	.86
	Non Verbal Behaviours		
D	Reaching for mother (childreachmum)	Moving arms towards the body or head of the mother but not able to make contact with them	.86
D	Reaching for researcher (childreachres)	Moving arms towards the body or head of the researcher but not able to make contact with them	.97
D	Touching mother (childtouchmum)	Child initiated touching of any part of the mother (including clothing) as a result of deliberately moving part of their body towards them e.g. hugging, patting, kissing, tapping. Does not include or aggressive pulling/ grabbing or movements of legs or feet.	.87
D	Touching researcher (childtouchres)	Child initiated touching any part of the researcher (including clothing) as a result of deliberately moving part of their body towards them e.g. hugging, patting, kissing, tapping. Does not include aggressive pulling/grabbing or movements of legs or feet.	.87
E	Approach mother (apprmum)	Child physically approaches mother (code at point when approach is complete or if following and mother leaves room at point of exit) includes following them – does not have to make physical contact.	.85
E	Approach researcher	Child physically approaches	.95

	(appres)	researcher (code at point when approach is complete or if following and researcher leaves room at point of exit) includes following them— does not have to make physical contact.	
E	Approach to camera person (apprcam)	Child physically approaches camera person (code at point when approach is complete)	1
E	Removal behaviour from mother (removemum)	Child physically moves away from interaction with the mother, includes attempts to leave room.	1
E	Removal behaviour from researcher (removers)	Child physically moves away from interaction with the researcher, includes attempts to leave room.	.76
E	Non verbal communication to mother (nonverbmum)	Signing (use of Makaton or British Sign Language for the purpose of communicating with mother), gestures e.g., pointing, or makes non verbal response (responds question, statement, comment or prompt by nodding or shaking their head) directed toward mother	.71
E	Non verbal communication to researcher (nonverbres)	Signing (use of Makaton or British Sign Language for the purpose of communicating with mother), gestures e.g., pointing, or makes non verbal response (responds question, statement, comment or prompt by nodding or shaking their head) directed toward researcher	.74
	Verbal Behaviours	Definition	
D	Verbalisation to mother (verbtomum)	The participant’s speech directed towards mother; These may be utterances (e.g. ‘erm’), words, phrases or sentences. Does not include negative verbalisations.	.77
D	Verbalisation to researcher (verbtiores)	The participant’s speech directed towards researcher; These may be utterances (e.g. ‘erm’), words, phrases or sentences. Does not include negative verbalisations.	.76
D	Verbalisation to camera person	The participant’s speech directed towards camera person; These may	.88

	(verbtocam)	be utterances (e.g. 'erm'), words, phrases or sentences. Does not include negative verbalisations	
D	Verbalisation no target (verbnotarget)	Participant's speech used when the person is talking to themselves. These may be utterances (e.g. 'erm'), words, phrases or sentences. Does not include negative verbalisations	.73
E	Negative verbalisation to mother (negverbtomum)	Verbalisations expressing a clear lack of enjoyment, negative emotion towards the mother or a wish to terminate an interaction. Will co-occur with verbalisation codes, code after each phrase	.58
E	Negative verbalisation to researcher (negverbttores)	Verbalisations expressing a clear lack of enjoyment, negative emotion towards the researcher or a wish to terminate an interaction. Will co-occur with verbalisation codes, code after phrase	-
	Challenging Behaviour		
D	SIB (SIB)	The participant engages in non-accidental self-directed injurious behaviours which produce temporary marks or reddening of the skin or cause bruising, bleeding or other temporary or permanent tissue including hair pulling, picking, biting, tapping, hitting, banging, scratching.	.83
D	Aggression (Agg)	Any physical aggression directed towards another person ie hitting, kicking, grabbing, scratching	1
D	Destruction (Dest)	Destructive behaviour ie tearing, tipping furniture, pulling items off walls, throwing/swiping items away	.82
	Facial expression		
D	Positive affect (posaffect)	Facial expressions or vocalisations with clear positive tone e.g., smiling laughing.	.71
D	Negative affect (negaffect)	Facial expressions or vocalisations with clear negative tone e.g.,	.87

		frowning, turning down of mouth, crying, whining	
	Other		
D	Child off screen (Offscreen)	Child is temporarily out of shot	.8

APPENDIX L
Social behaviour rating scales

PARTICIPANT SOCIAL BEHAVIOUR RATING SCALES

GENERAL BEHAVIOURS	0	1	2	3	4
<p>Positive emotional affect (E.g. positive <u>facial expressions</u>, <u>vocalisations</u> and <u>manner</u> such as <u>smiling</u>, <u>laughing</u>, <u>clapping hands</u>.)</p>	<p><u>No</u> examples of positive affect at any stage.</p>	<p><u>Some</u> examples of positive affect but only <u>tentative</u> or <u>occasional</u>.</p>	<p>Affect positive about <u>half of the time</u>. May consist of brief expressions of positive affect in response to <u>particular activities</u> for example, but affect <u>not sustained</u> between these instances.</p>	<p>Affect positive <u>most of the time</u>. May consist of brief expressions of positive affect in response to <u>particular activities</u> for example, but also <u>sometimes sustained</u> between these instances.</p>	<p>Affect generally positive <u>throughout</u> and <u>often sustained</u> between expressions of positive affect in response to particular activities.</p>
<p>Negative emotional affect (E.g. negative <u>facial expressions</u>, <u>vocalisations</u> and <u>manner</u> such as <u>crying</u> and <u>frowning</u>. Participant may appear <u>distressed</u> or <u>angry</u>.)</p>	<p><u>No</u> examples of negative affect at any stage.</p>	<p><u>Some</u> examples of negative affect but only <u>tentative</u> or <u>occasional</u>.</p>	<p>Affect negative about <u>half of the time</u>. May cry in response to <u>particular activities</u> for example, but affect <u>not sustained</u> between these instances.</p>	<p>Affect negative <u>most of the time</u>. May cry in response to <u>particular activities</u> for example, but also <u>sometimes sustained</u> between these instances.</p>	<p>Affect generally negative <u>throughout</u> and <u>often sustained</u> between expressions of negative affect in response to particular activities.</p>
<p>Frequency of challenging behaviour *Challenging behaviour includes any of the following: Self injurious behaviour: Non-accidental behaviours producing temporary marks or reddening of the skin or cause bruising, bleeding or other temporary or permanent tissue damage. Aggression: A non-accidental, physical act involving physical contact with another person likely to result in pain or distress. Property destruction: A non-accidental physical act which results in disruption damage to any property or the environment. Rate the occurrence of <u>any</u> of the preceding behaviours.</p>	<p>No challenging behaviour* shown.</p>	<p>Occasional, brief episodes of challenging behaviour* shown</p>	<p>Frequent brief episodes of challenging behaviour* shown</p>	<p>Frequent brief episodes brief AND occasionally sustained episodes of challenging behaviour* shown</p>	<p>Frequent, sustained challenging behaviour* shown</p>

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<p>Severity of challenging behaviour</p> <p>*Challenging behaviour (CB) includes any of the following</p> <p>Self injurious behaviour (SIB): Non-accidental behaviours producing marks or reddening of the skin or cause bruising, bleeding or other temporary or permanent tissue damage.</p> <p>Aggression: A non-accidental, physical act involving physical contact with another person likely to result in pain or distress.</p> <p>Property destruction: A non-accidental physical act which results in disruption damage to any property or the environment.</p> <p>**Degree of injury to others defined using same criteria as SIB</p> <p>Rate the occurrence of <u>any</u> of the preceding behaviours, rate the most severe instance of CB</p>	<p>No challenging behaviour* shown.</p>	<p>Challenging behaviour* shown but unlikely to have impact on self, others or environment</p> <p><u>SIB</u> unlikely to cause injury to self (no marks, bruising, cuts or tissue damage)</p> <p><u>Aggression</u> unlikely to cause injury** to others</p> <p>Attempt at <u>property destruction</u> unlikely to cause disruption or damage (item does not require repair or replacement)</p>	<p>Challenging behaviour* shown likely to have minor impact on self, others or environment</p> <p><u>SIB</u> likely to cause minor, temporary injury, such as reddening of the skin, but <i>no</i> bruising or tissue damage</p> <p><u>Aggression</u> likely to cause minor injury to others</p> <p><u>Property destruction</u> likely to cause minor disruption or damage to property (item requires repair but can be used)</p>	<p>Challenging behaviour* shown likely to have moderate impact on self, others or environment</p> <p><u>SIB</u> likely to result in moderate injury, tissue damage such as bruising, cuts or abrasions lasting less than a day</p> <p><u>Aggression</u> likely to cause moderate injury to others</p> <p><u>Property destruction</u> likely to cause moderate disruption or damage to property (item requires repair and cannot be used)</p>	<p>Challenging behaviour* shown likely to have significant impact on self, others or environment</p> <p><u>SIB</u> likely to result in significant tissue damage such as severe bruising, cuts or abrasions lasting more than a day</p> <p><u>Aggression</u> likely to cause significant injury to others</p> <p><u>Property destruction</u> likely to cause significant disruption or damage to property (item requires replacement and cannot be used or repaired)</p>
<p>TARGET ADULT DIRECTED BEHAVIOURS</p>	<p>0</p>	<p>1</p>	<p>2</p>	<p>3</p>	<p>4</p>
<p>Frequency of spontaneous physical contact with target adult</p> <p>(Include all <u>participant initiated</u> physical contact, regardless of nature of contact or intent)</p>	<p><u>No</u> spontaneous physical contact initiated with the target adult</p>	<p><u>One or two</u> examples of spontaneous initiation of physical contact.</p>	<p><u>Several</u> examples of spontaneous initiation of physical contact.</p>	<p>Spontaneous physical contact initiated <u>frequently</u> but not to an <u>excessive</u> or <u>socially inappropriate</u> degree.</p>	<p>Spontaneous physical contact initiated <u>frequently</u> to an <u>excessive</u> or <u>socially inappropriate</u> degree.</p>
<p>Nature of physical contact initiated with target adult</p> <p>(Rate nature of instances of spontaneous contact observed in previous item regardless of frequency.)</p>	<p>EITHER <u>No</u> spontaneous physical contact initiated with the target adult OR Contact <u>mostly negative or aggressive</u> in nature (e.g. hair pulling or hitting).</p>	<p>Physical contact <u>mostly negative or aggressive</u> in nature (e.g. hair pulling or hitting) but <u>one or two instances</u> of positive physical contact (e.g. hugging, climb onto lap, tapping to gain attention) also observed.</p>	<p>Contact generally <u>neither negative nor positive</u> in nature and <u>does not appear socially motivated</u>. May be for personal demands only or for sensory stimulation/interest (e.g. sniffing or peering at examiner).</p>	<p>Contact is mostly <u>positive</u> in nature (e.g. hug, climb onto lap, tapping to gain attention) but one or two <u>instances of negative physical contact</u> (e.g. hair pulling or hitting) also <u>observed</u>.</p>	<p>Physical contact always <u>positive</u> in nature and appears <u>socially motivated and affectionate</u> (e.g. hug, climb onto lap, tapping to gain attention).</p>

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<p>Spontaneous initiation of interaction with target adult</p> <p>* Initiation of interaction may be verbal or non-verbal (e.g. <u>approaching</u> the target adult, <u>offering</u> or <u>requesting</u> objects, <u>speaking</u> or <u>signing</u>, <u>touching</u> the target adult to attempt to gain their attention (aggressively or otherwise), <u>gesturing</u> or <u>pointing</u> to an object while looking at target adult.</p>	<p>No clear spontaneous initiation of interaction* with the target adult.</p>	<p>One or two examples of spontaneous initiation of interaction* with target adult but for <u>personal demands</u> or other unclear purpose only.</p>	<p>Three or more examples of spontaneous initiation of interaction* with the target adult but for <u>personal demands</u> or unclear purpose only.</p>	<p>One or two examples of spontaneous initiation of interaction* with the target adult which appears to be <u>socially motivated</u> (e.g. for the purpose of being friendly) and not merely for personal demands (e.g. giving or showing an object).</p>	<p>Three or more examples of spontaneous initiation of interaction* with the target adult which appear to be <u>socially motivated</u> (e.g. for the purpose of being friendly) and not merely for personal demands (e.g. giving or showing an object).</p>
<p>Motivation for target adult engagement (in <u>adult absent</u> conditions ONLY)</p> <p>* Interaction attempts may be verbal or non-verbal. E.g. <u>approaching</u> the location of the absent adult (i.e. door), <u>offering</u> or <u>requesting</u> objects, <u>speaking</u> or <u>signing</u>, <u>touching</u> the target adult to attempt to gain their attention (aggressively or otherwise), <u>gesturing</u> or <u>pointing</u> to an object while looking at target adult, asking where the absent adult is, <u>attempting to exit the room with clear intent to locate target adult</u>.</p>	<p>The participant <u>does not</u> attempt to initiate interaction*. Either <u>sits passively</u> or <u>entertains self</u> (e.g. plays with the toys or passively).</p>	<p>The participant makes <u>one or two</u> attempts to initiate interaction* but when attention is not given they <u>give up quickly</u> and <u>entertain self</u>.</p>	<p>The participant makes <u>three or more</u> attempts to initiate interaction* but <u>eventually gives up</u> and <u>entertains self</u>. May subsequently return for renewed attempt to engage with target adult but there must be a <u>clear gap</u> in their efforts.</p>	<p>The participant makes <u>persistent</u> attempts to initiate interaction* throughout the observation but stays <u>within socially appropriate limits</u> (e.g. approaching, vocalising (not high volume)).</p>	<p>The participant makes <u>persistent</u> attempts to initiate interaction* throughout the observation and through <u>several different means</u>, to the extent of using <u>socially inappropriate methods</u> (e.g. through engaging in challenging behaviour)***</p>
<p>Avoidance of social interaction</p> <p>* Aversion includes aversion to gaze or touch, turning back on examiner, pushing examiner's hand away or removing self from proximity of target adult (not as part of a game e.g. hide and seek), or to retrieve a object to show or for play. <u>N/A for adult absent conditions</u></p>	<p><u>Consistently</u> shows aversion* to <u>all</u> target adult approaches.</p>	<p>Shows aversion* to <u>most</u> but <u>not all</u> target adult approaches.</p>	<p>Shows aversion* to <u>about half</u> the target adult approaches.</p>	<p><u>Occasionally</u> shows aversion* to target adult approaches.</p>	<p>Shows aversion* to <u>none</u> of the target adult approaches.</p>

Appendices

	0	1	2	3	4
<p>Social responsiveness to target adult * Responds to specific behavioural requests, suggestions, questions or their name (if used). ** Elaboration is defined as when the participant <u>spontaneously</u> builds on what is expected of them E.g gets a new book to read, finds different crayon for target adult to colour with. <u>N/A for adult absent conditions</u></p>	<p><u>Unresponsive</u> and <u>disinterested</u>. <u>Does not respond</u>*. Largely <u>ignores</u> what the target adult is doing.</p>	<p><u>Unresponsive</u> but <u>some interest</u>. <u>May not respond</u>* but <u>attends</u> to what target adult is doing (this must be <u>more than a fleeting glance</u>).</p>	<p><u>Interested</u> and <u>occasionally responsive</u>. Responds* at <u>least once</u> but interactions are <u>target adult led</u> and <u>not reciprocal</u>. Participant <u>mostly attentive</u> to target adult.</p>	<p><u>Interested</u> and <u>highly responsive</u>. Responds* <u>more often than not</u>. Interactions are <u>reciprocal</u>. At least one or two examples of a back and forth exchange of <u>several steps</u> but participant <u>does not elaborate</u>** beyond initial target adult suggestions (interaction <u>not necessarily verbal</u>)</p>	<p><u>Interested</u> and <u>elaborately responsive</u>. Responds* <u>more often than not</u>. <u>More than two</u> examples of back and forth exchanges of <u>several steps</u>. Participant <u>elaborates</u>** on initial examiner suggestions (interaction <u>not necessarily verbal</u>).</p>
<p>Focus of attention with target adult (objects focus vs. people focus) <u>N/A for adult absent conditions</u></p>	<p>Focus of the participant's attention either <u>unclear</u> or <u>entirely object focussed</u>. Participant does <u>not</u> attend to or show any interest in the target adult</p>	<p>Focus of the participant's attention <u>mostly on objects</u>. <u>Some</u> attention paid to <u>target adult</u> even if only for <u>monitoring purposes</u>.</p>	<p>Focus of the participant's attention <u>shared</u> between <u>target adult</u> and <u>objects</u>.</p>	<p>Focus of the participant's attention <u>mostly on target adult</u>. Attention appears to be <u>socially motivated</u> at least <u>some of the time</u> and <u>not</u> simply for purpose of <u>monitoring</u>.</p>	<p>Focus of the participant's attention almost <u>entirely</u> on target adult perhaps to an excessive degree. Attention appears to be mostly <u>socially motivated</u>.</p>
<p>Social communication style with target adult (Rate the majority of examples of social communication demonstrated by the participant rather than the best example)</p>	<p><u>Little</u> or <u>no</u> verbal or non-verbal communication at all to target adult.</p>	<p><u>Some</u> vocalisations or gestures <u>mostly indicating affect</u> (e.g. laughing or crying sounds indicating excitement) and <u>not</u> specifically <u>communicative</u> or directed at others AND/OR attempts to communicate through <u>grabbing/touching</u> or other physical means that has clear communicative intent.</p>	<p><u>Some clearly communicative</u> vocalisations (verbal or non-verbal) or gestures (e.g. pointing, nodding and shaking head). Makes attempts to communicate <u>specific desires</u> but <u>does not</u> use speech or signing.</p>	<p><u>Some clearly communicative</u> vocalisations (verbal or non-verbal) or gestures (e.g. pointing, nodding and shaking head). Makes attempts to communicate <u>specific desires</u> AND shows <u>some</u> use of speech or signing which may be <u>infrequent</u> or <u>unclear</u> (not full sentences).</p>	<p><u>Regular clear</u> speech and or signing (e.g. BSL or Makaton). Makes attempts to communicate <u>specific desires</u> which may be for the purpose of being friendly or otherwise.</p>

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<p>Frequency of eye contact with target adult</p> <p>*Eye contact defined as the participant looking up/at the target adult, fixating on their eyes or face.</p>	<p><u>No</u> eye contact* made with target adult.</p>	<p><u>Occasional, fleeting</u> eye contact* made with target adult.</p>	<p><u>Frequent, fleeting OR occasionally sustained</u> eye contact* made with target adult</p>	<p><u>Frequent fleeting AND occasionally sustained</u> eye contact* made with target adult.</p>	<p><u>Frequent, sustained</u> eye contact* made with target adult.</p>
<p>Nature of eye contact with target adult</p> <p>* Appropriate integration of eye contact with other social-communication skills including gesture, pointing or facial expressions e.g. participant checks what target adult is looking at, or points, then follows target adult 's gaze to check point has been registered. *Inappropriate e.g. staring or avoidant.</p>	<p><u>No</u> eye contact made with target adult.</p>	<p>Eye contact <u>obviously awkward or inappropriate*</u> in nature on <u>all occasions</u> - <u>not naturally integrated</u> with other behaviours during interaction. Includes participants who show prolonged eye contact (e.g. staring)</p>	<p>Eye contact <u>somewhat awkward or inappropriate*</u> in nature - <u>not naturally integrated</u> with other behaviours on every occasion but on <u>some</u>.</p>	<p>Eye contact <u>slightly awkward or inappropriate*</u> in nature - <u>mostly naturally integrated</u> with other behaviours during interaction but <u>not always</u>.</p>	<p>Eye contact <u>consistently naturally and appropriately integrated*</u> with other behaviours during social interaction.</p>
<p><u>NON TARGET ADULT DIRECTED BEHAVIOURS</u></p>	<p>0</p>	<p>1</p>	<p>2</p>	<p>3</p>	<p>4</p>
<p>Frequency of spontaneous physical contact with non target adult</p> <p>(Include all <u>participant initiated</u> physical contact, regardless of nature of contact or intent.)</p>	<p><u>No</u> spontaneous physical contact initiated with the non target adult</p>	<p><u>One or two</u> examples of spontaneous initiation of physical contact.</p>	<p><u>Several</u> examples of spontaneous initiation of physical contact.</p>	<p>Spontaneous physical contact initiated <u>frequently</u> but not to an <u>excessive</u> or <u>socially inappropriate</u> degree.</p>	<p>Spontaneous physical contact initiated <u>frequently</u> to an <u>excessive</u> or <u>socially inappropriate</u> degree.</p>
<p>Nature of physical contact initiated with non target adult</p> <p>(Rate nature of instances of spontaneous contact observed in previous item regardless of frequency.)</p>	<p>EITHER <u>No</u> spontaneous physical contact initiated with the non target adult OR Contact <u>mostly negative or aggressive</u> in nature (e.g. hair pulling or hitting).</p>	<p>Physical contact <u>mostly negative or aggressive</u> in nature (e.g. hair pulling or hitting) but <u>one or two instances</u> of positive physical contact (e.g. hugging, climb onto lap, tapping to gain attention) also observed.</p>	<p>Contact generally <u>neither negative nor positive</u> in nature and <u>does not appear socially motivated</u>. May be for personal demands only or for sensory stimulation/interest (e.g. sniffing or peering at examiner)</p>	<p>Contact is <u>mostly positive in nature</u> (e.g. hug, climb onto lap, tapping to gain attention) but <u>one or two instances of negative physical contact</u> (e.g. hair pulling or hitting) also <u>observed</u></p>	<p>Physical contact always <u>positive</u> in nature and appears <u>socially motivated and affectionate</u> (e.g. hug, climb onto lap, tapping to gain attention).</p>

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<p>Spontaneous initiation of interaction with non target adult</p> <p>* Initiation of interaction may be verbal or non-verbal (e.g. <u>approaching</u> the non target adult, <u>offering or requesting</u> objects, <u>speaking</u> or <u>signing</u>, <u>touching</u> the non target adult to attempt to gain their attention (aggressively or otherwise), <u>gesturing</u> or <u>pointing</u> to an object while looking at non target adult.</p>	<p><u>No</u> clear spontaneous initiation of interaction* with the non target adult</p>	<p><u>One or two examples</u> of spontaneous initiation of interaction* with non target adult but for <u>personal demands</u> or other unclear purpose only.</p>	<p><u>Three or more examples</u> of spontaneous initiation of interaction* with the non target adult but for <u>personal demands</u> or unclear purpose only</p>	<p><u>One or two examples</u> of spontaneous initiation of interaction* with the non target adult which appears to be <u>socially motivated</u> (e.g. for the purpose of being friendly) and not merely for personal demands (e.g. giving or showing an object).</p>	<p><u>Three or more examples</u> of spontaneous initiation of interaction* with the non target adult which appear to be <u>socially motivated</u> (e.g. for the purpose of being friendly) and not merely for personal demands (e.g. giving or showing an object).</p>
<p>Motivation for non target adult engagement</p> <p>* Interaction may be verbal or non-verbal (e.g. <u>approaching</u> the target adult, <u>offering or requesting</u> objects, <u>speaking</u> or <u>signing</u>, <u>touching</u> the target adult to attempt to gain their attention (aggressively or otherwise), <u>gesturing</u> or <u>pointing</u> to an object while looking at target adult.</p>	<p>The participant <u>does not</u> attempt to initiate interaction*. Either <u>sits passively</u> or <u>entertains self</u> (e.g. plays with the toys or passively).</p>	<p>The participant makes <u>one or two</u> attempts to initiate interaction* but when attention is not given they <u>give up quickly</u> and <u>entertain self</u>.</p>	<p>The participant makes <u>three or more</u> attempts to initiate interaction* but <u>eventually gives up</u> and <u>entertains self</u>. May subsequently return for renewed attempt to engage with non target adult but there must be a <u>clear gap</u> in their efforts.</p>	<p>The participant makes <u>persistent</u> attempts to initiate interaction* throughout the observation but stays <u>within socially appropriate limits</u> (e.g. approaching, vocalising (not high volume)).</p>	<p>The participant makes <u>persistent</u> attempts to initiate interaction* throughout the observation and through <u>several different means</u>, to the extent of using <u>socially inappropriate methods</u> (e.g. through engaging in challenging behaviour).**</p>
<p>Focus of attention with non target adult (objects focus vs. people focus)</p>	<p>Focus of the participant's attention either <u>unclear</u> or <u>entirely object focussed</u>. Participant does <u>not</u> attend to or show any interest in the non target adult</p>	<p>Focus of the participant's attention <u>mostly</u> on <u>objects</u>. <u>Some</u> attention paid to <u>non target adult</u> even if only for <u>monitoring</u> purposes.</p>	<p>Focus of the participant's attention <u>shared</u> between <u>non target adult</u> and <u>objects</u>.</p>	<p>Focus of the participant's attention <u>mostly</u> on <u>non target adult</u>. Attention appears to be <u>socially motivated</u> at least <u>some of the time</u> and <u>not</u> simply for purpose of <u>monitoring</u>.</p>	<p>Focus of the participant's attention almost <u>entirely</u> on <u>non target adult</u> perhaps to an excessive degree. Attention appears to be mostly <u>socially motivated</u>.</p>
<p>Social communication style with non target adult</p> <p>(Rate the majority of examples of social-communication demonstrated by the participant rather than the best example)</p>	<p><u>Little</u> or <u>no</u> verbal or non-verbal communication at all to non target adult.</p>	<p><u>Some</u> vocalisations or gestures <u>mostly indicating affect</u> (e.g. laughing or crying sounds indicating excitement) and <u>not</u> specifically <u>communicative</u> or directed at others AND/OR attempts to communicate through <u>grabbing/touching</u> or other physical means that has clear communicative intent.</p>	<p><u>Some clearly communicative</u> vocalisations (verbal or non-verbal) or gestures (e.g. pointing, nodding and shaking head). Makes attempts to communicate <u>specific desires</u> but <u>does not</u> use speech or signing.</p>	<p><u>Some clearly communicative</u> vocalisations (verbal or non-verbal) or gestures (e.g. pointing, nodding and shaking head). Makes attempts to communicate <u>specific desires</u> AND shows <u>some</u> use of speech or signing which may be <u>infrequent</u> or <u>unclear</u> (not full sentences).</p>	<p><u>Regular clear</u> speech and or signing (e.g. BSL or Makaton). Makes attempts to communicate <u>specific desires</u> which may be for the purpose of being friendly or otherwise.</p>

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	0	1	2	3	4
<p>Frequency of eye contact with non target adult</p> <p>*Eye contact defined as the participant looking up/at the non target adult, fixating on their eyes or face.</p>	<p><u>No</u> eye contact* made with non target adult.</p>	<p><u>Occasional, fleeting</u> eye contact* made with non target adult.</p>	<p><u>Frequent, fleeting OR occasionally sustained</u> eye contact* made with non target adult</p>	<p><u>Frequent fleeting AND occasionally sustained</u> eye contact* made with non target adult.</p>	<p><u>Frequent, sustained</u> eye contact* made with target adult.</p>
<p>Nature of eye contact with non target adult</p> <p>* Appropriate integration of eye contact with other social-communication skills including gesture, pointing or facial expressions e.g. participant checks what target non adult is looking at, or points, then follows non target adult 's gaze to check point has been registered. *Inappropriate e.g. staring or avoidant.</p>	<p><u>No</u> eye contact made with non target adult.</p>	<p>Eye contact <u>obviously awkward or inappropriate*</u> in nature on <u>all occasions</u> - <u>not naturally integrated</u> with other behaviours during interaction. Includes participants who show prolonged eye contact (e.g. staring)</p>	<p>Eye contact <u>somewhat awkward or inappropriate*</u> in nature - <u>not naturally integrated</u> with other behaviours on every occasion but on <u>some</u>.</p>	<p>Eye contact <u>slightly awkward or inappropriate*</u> in nature - <u>mostly naturally integrated</u> with other behaviours during interaction but <u>not always</u>.</p>	<p>Eye contact <u>consistently naturally and appropriately integrated*</u> with other behaviours during social interaction.</p>

Notes

Target adult = adult who is playing with child (and who leaves the room in adult absent condition) in any set of 3 conditions
 Non target adult = adult in the background in any set of three conditions

APPENDIX M

Rating reliability and correlations with real time coding

Inter rater reliability for rating scales

Rating item	Spearman's rho
Positive affect	.43
Negative affect	.765
Frequency of challenging behaviour	.818
Severity of challenging behaviour	.811
Frequency of spontaneous physical contact with interacting adult	.463
Nature of spontaneous physical contact with interacting adult	.472
Spontaneous initiation of interaction with interacting adult	.66
Motivation for interacting adult attention	.748
Avoidance of interacting adult attention	.418
Responsiveness to interacting adult	.629
Focus of attention with the interacting adult	.467
Social communication style with interacting adult	.799
Frequency of eye contact with interacting adult	.7
Nature of eye contact with interacting adult	.657
Frequency of spontaneous physical contact with unresponsive adult	.721
Nature of spontaneous physical contact with unresponsive adult	.686
Spontaneous initiation of interaction with unresponsive adult	.849
Focus of attention with the unresponsive adult	.744
Motivation for unresponsive adult attention	.61
Social communication style with unresponsive adult	.737
Frequency of eye contact with unresponsive adult	.537
Nature of eye contact with unresponsive adult	.52

Spearman's correlations between rating and coding

(positive affect (rating) and positive affect (coding) = .7; negative affect (rating) and negative affect (coding) = .66; frequency of challenging behaviour (rating) and challenging behaviour (coding) = .51;

spontaneous initiation of physical interaction (rating) and physical initiation (coding) for interacting adult = .4; spontaneous initiation of physical interaction (rating) and physical initiation (coding) for unresponsive adult = .5) The mean correlation was .55.

APPENDIX N

Analysis and interpretation of communication results in Effect of adult familiarity and level of attention on social behaviours in Smith-Magenis syndrome study

Attention

Hypotheses

No formal hypothesis/predictions were generated for communicative behaviours; this was an exploratory analysis of an area of interest (both groups been reported to have expressive language impairments), focussing on identifying differences in communication skills children demonstrate once interaction is initiated.

No significant between syndrome group differences in patterns of behaviour with mothers as the unresponsive adult compared to the unfamiliar adult were found for communication in either high or low attention.

While no effects of attention were found for affect or motivation with either mothers or the unfamiliar adult, between syndrome patterns of communication with the interacting adults differed significantly across levels of attention, both for mothers and the unfamiliar adult.

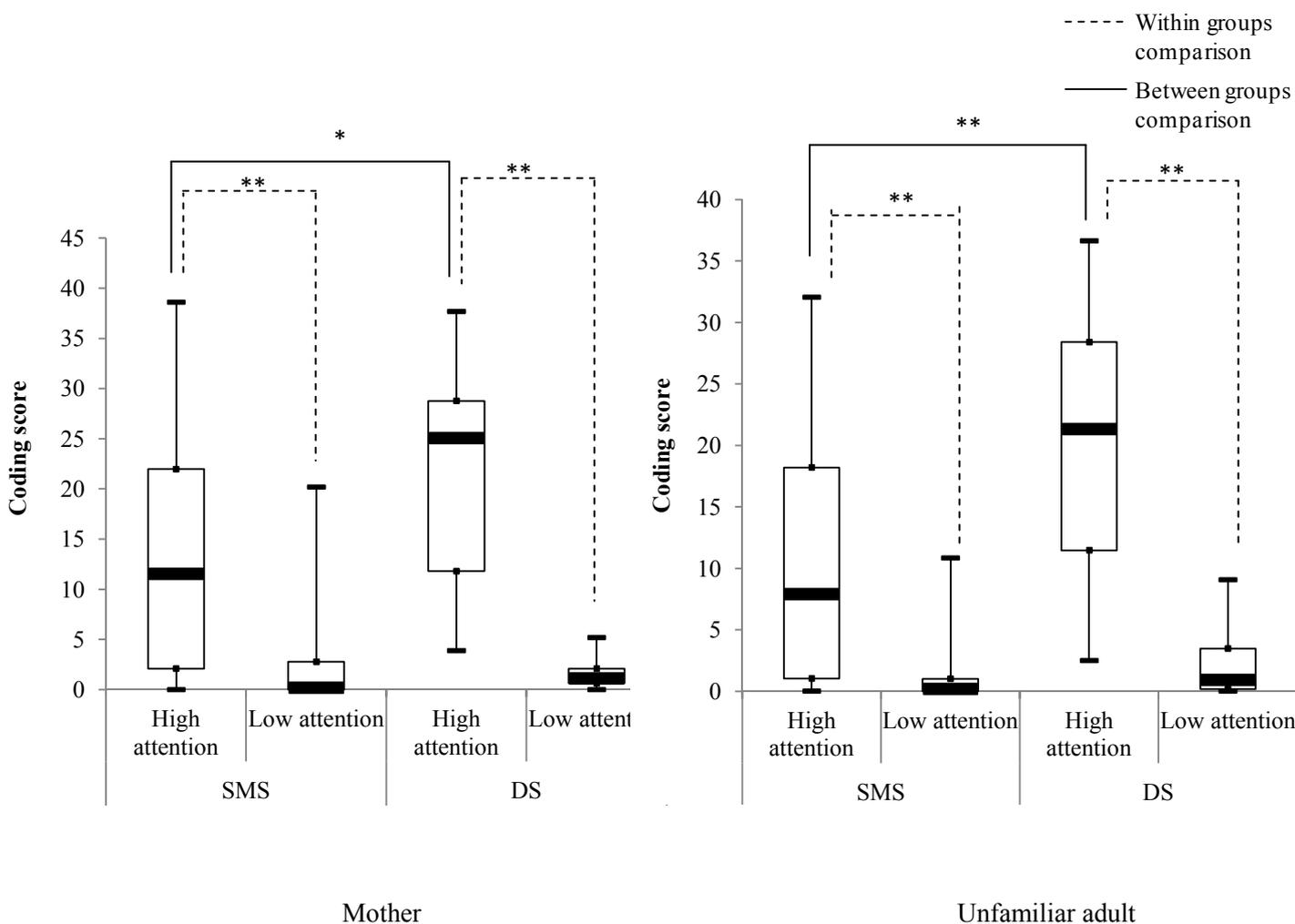


Figure 1 Communication scores with the interacting adults (* $p \leq .01$, ** $p \leq .001$)

The figure shows reduced communication of the SMS group in high attention with both adults, shown by the difference between syndrome groups in this condition and also the similarity of patterns of results for mothers and the unfamiliar adult.

Significantly greater differences between high and low attention conditions were found in DS than SMS for communication with mothers ($U = 92.5$, $p = .002$, two tailed) and also with the unfamiliar adult ($U = 94$, $p = .001$, one tailed).

Post hoc analyses of communication with both interacting mothers ($U = 153.5$, $p = .140$, two tailed) and the interacting unfamiliar adult ($U = 150$, $p = .113$, two tailed) indicated that SMS and DS did not differ in attempts to communicate with either adult when they were absent from the room (e.g. calling out to them, approaching to talk to them). When the interacting adult was present, SMS communicated with them significantly less than DS, regardless of whether the adult was their mother ($U = 109.5$, $p = .008$, two tailed) or the unfamiliar adult ($U = 89$, $p = .001$, two tailed). Analyses of within syndrome differences of communication with the interacting adult found the same pattern of results for both SMS and DS, with significantly more communication occurring in high attention than low attention, with both mothers (SMS: $z = -3.636$, $p < .001$ two tailed, DS: $z = -3.920$, $p < .001$ two tailed) and the unfamiliar adult (SMS: $z = -3.823$, $p < .001$ two tailed, DS: $z = -3.920$, $p < .001$ two tailed).

No significant differences were found for communication with the unresponsive adult.

Summary

Effects of attention were found for behaviours directed towards both the *interacting adult* and the *unresponsive adult*. Both syndrome groups communicated more with the interacting adult (unfamiliar adult and mother) when they were giving high attention than low. However, in high attention children with SMS communicated with adults less than those with DS.

Interpretation

No effect of familiarity on communication with adults was found. This suggests that while children with SMS may have greater drive to interact with their mother, this was not reflected by increased communication with them. This is similar to lack of differences in affect shown when interacting with their mother and again suggests that a disparity may exist between social motivation and behaviours actually shown during interaction. Communicative elements of social skills has been identified by Gesten, Weissberg, Amish, and Smith (1987) who describe social skills as “highly specific patterns of learned observable behaviour, both verbal and non-verbal, through which people meet their needs, avoid unpleasant circumstances and influence others”, suggesting that within social skills macro-skills include “engaging in conversation”. This definition alludes to the role of communication as a skill demonstrated during social interactions. In SMS these social communication skills may not have matched their level of social motivation in the current study.

The only effect of attention on behaviours towards the *interacting adult* was for communication. Children with SMS showed smaller increases in communication from low attention to high than those with DS. As groups were well matched on expressive language it seems unlikely that this is due to deficits in *ability* to communicate; rather may reflect reduced demonstration of this skill in social situations. As alluded to previously, this deficit may make social interactions less rewarding as adult may be less able to respond for children with SMS, possibly resulting in increased initiations to get more attention to achieve the level of reward required. The lack of increased affect in high attention supports the proposal that children may not find interactions with preferred adult as rewarding as would be expected from their levels of motivation to interact with them. While this is entirely speculative at this stage, it is an avenue for exploration which could potentially account some of aspects of attention seeking in SMS.

APPENDIX O

Assessment and matching criteria for inclusion: Inhibition and impulsivity in children with Smith-Magenis syndrome study

Assessing inclusion

Children were included in the final sample if they were able to follow simple instructions necessary for engagement in the task. This was assessed during the warm up phase for the first task, the Bear dragon task, where children are required to copy actions demonstrated by the researcher. If a child was clearly engaged with this task (looking at researcher and following their movements) but was unable to follow the copying instructions then the rest of the battery was not administered. If other assessments of ability suggested that the child was able to follow instructions similar to those needed to participate in the inhibition tasks, or the caregiver indicated that they would usually be able to do a similar activity, then the task was repeated at a later time and all other items in the battery were given. For all inhibition tasks if the child refused to respond to a request then the request was repeated after 10 seconds. If the child still did not respond (or left the test situation) then after a further 10 seconds the request was repeated at which point if there was no response the testing was terminated for that task. If a test was terminated due to disengagement then it was repeated later in the session.

Matching

Participants with DS were individually matched to the SMS participants based on mental age estimates derived from IQ assessments described in the materials section. Participants from the resulting SMS and DS sample were then separately and individually matched to participants from the normative comparison groups based on mental age. As the normative sample excluded any children with intellectual disability chronological age was used as a proxy for mental age. Groups were found to be well matched, with no differences between mental age for any matched groups. Additionally SMS and DS groups did not differ on chronological age: both syndrome groups were significantly older than the normative contrast group.

APPENDIX P

Detailed description of inhibition battery

Inhibition battery

Bear dragon task

The task started with the researcher asking the child to copy a series of nine actions which are later used in the task. The researcher then introduced the child to a “nice bear” puppet using a soft voice; they were told that they should do what the nice bear tells them to do. Next they were introduced to a “naughty dragon” puppet using a deep, gruff voice and told that they should not do what the naughty dragon tells them to do. Children’s understanding of the task was checked with a practice trial where the child performed or suppressed a response to a command made by each of the puppets according to the rules outlined previously, feedback was given after each practice trial. If the participant made an error during this practice stage, they were reminded of the rules and the practice was repeated. If the participant still made an error on the practice they were asked who they should not listen to and if they answered incorrectly were given the correct answer. All children then proceeded to the test phase where bear/dragon commands were given in a previously determined pseudorandom order. Eight test trials were then performed at which point a rule reminder was given and a further eight trials were then administered. At the end of the trial a rule check was performed where the child was asked who they do not listen to.

Responses were coded from video footage. Performance of the commanded action was given a score of 1 if given by the bear, 0 if from the dragon. No movement was scored as 0 for the bear command and 1 for the dragon. Total scores, out of 16, were calculated by summing the bear and dragon scores.

Reverse categorisation

Children were shown two buckets which were placed in front of them, one red, one blue and a bag containing 12 balls, six red and six blue. Children were required to sort the balls according to the rule red balls go into the blue bucket and blue balls go into the red bucket. The balls were given to the child in a previously determined pseudorandom order.

The researcher started by demonstrating the rule, placing a red ball in the blue bucket, explaining that red balls go in that bucket, and then placing a blue ball in the red bucket stating that blue balls go in

that bucket. A practice trial was then given where children were given a blue ball and then a red ball to sort. If the child failed the first practice trial then practice was repeated. All children then continued to the test trials. The children were then given six balls to sort without any feedback. After six balls a rule reminder was given, where the researcher demonstrated the rule with a verbal reminder. The child is then asked to sort the remaining six balls. On completion the buckets were emptied in front of the child and the child was asked to sort the balls into the matching coloured buckets to check their colour knowledge. Scores were derived from the number of correctly sorted balls, with a maximum of 12. Where children changed their response on a trial their first response was recorded.

Black white Stroop

Participants were first shown a large rectangular board with a square white card on one side and a square black card on the opposite side. A colour knowledge check was carried out first where the child was asked to point to the white card and then to the black card. If an error was made corrective feedback was given and the knowledge check was repeated. Children were then told that were going to play a special game, where when the researcher says “black” they need to point to the white card, and when the researcher says “white” they need to point to the black card. A practice trial was then given where the researcher first called “black” and then “white” and gave feedback if the child made an error. If an error was made this practice was repeated. All children then continued to the test trials. Sixteen trials were completed in total with a midway verbal rule reminder. Colours were called in a pseudorandom order determined prior to testing. On completion a rule check was given where children were asked to identify which colour the researcher wanted them to point to first when they said “black” and then when they said “white”. Scores, out of a total of 16, were coded from footage as a 0 for an incorrect response (no reversal) and a 1 for a correctly reversed response. Where children change their response on a trial their first response was recorded.