Prevalence of autism spectrum disorder symptomatology and related behavioural characteristics in persons with Down syndrome.

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**Abstract**

We evaluated the proportion of individuals with Down syndrome (DS: N=108) who met criteria for autism spectrum disorder (ASD) on the Social Communication Questionnaire (SCQ) and the severity of ASD related symptomatology in this group. The proportion of individuals with DS meeting the cut off for ASD and autism in this sample was 19% and 8% respectively. We then evaluated the behavioural profile of individuals with DS who scored above cut off for ASD (DS+ASD; N=17) compared to those with DS only (N=17) and individuals with idiopathic ASD (N=17), matched for adaptive behaviour skills and ASD symptom severity (ASD group only). Individuals in the DS+ASD and ASD only groups showed more stereotyped behaviour, repetitive language, overactivity and self-injury than the DS only group (p<.001). Individuals in the DS+ASD and DS only groups appeared less withdrawn from their surroundings than those with ASD (p <.004). These findings indicate differences in the behavioural and cognitive profile of individuals with DS+ASD compared to those with DS only, when controlling for adaptive behaviour skills. Individuals with DS+ASD show broad similarities with individuals with idiopathic ASD with regard to ASD and behavioural characteristics but may also show some areas of subtle difference to this group.

**Keywords**

Down syndrome, autism spectrum disorder, repetitive behaviour, challenging behaviour, mood, behavioural phenotype

**Introduction**
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In recent years, there has been increasing interest into the association between autism spectrum disorder (ASD) and a range of genetic disorders. The presence of ASD or autistic like characteristics have now been reported in a large number of genetic syndromes including: Angelman, Cohen, Williams, Fragile X, Rett, Cornelia de Lange, 22q11 deletion and Prader Willi syndromes and Tuberous Sclerosis Complex (for reviews see Fombonne, 1999; Gillberg & Coleman, 2000; Moss & Howlin, 2009; Moss, Howlin & Oliver, 2011). Recent advances in genetic technologies have resulted in further expansion of this list to include a number of microdeletion syndromes such as 8p23 deletion (Fisch et al., 2010), 3q29 deletion (Quintero-Rivera et al., 2010) and 9p partial duplication syndrome (Abu-Amero et al., 2010) which are considered, by some researchers, to be key to developing our understanding of the causes of ASD.

The study of the association between ASD and genetic syndromes has raised considerable debate within the ASD and behavioural phenotypes fields. While it is acknowledged that recognition and accurate identification of ASD characteristics among individuals with genetically determined syndromes is important for providing appropriate educational and behaviour management programmes (Howlin et al., 1995; Moss & Howlin, 2009), a number of conceptual and methodological issues have consistently been raised. At the forefront of this debate is the question regarding the role that intellectual disability (ID) plays in the association between genetic syndromes and ASD. Identification of ASD like characteristics in individuals with severe and profound levels of ID and those with complex behavioural and cognitive profiles is particularly difficult (Moss & Howlin, 2009). Many of the core diagnostic features of ASD are developmentally weighted and consequently an individual may meet certain diagnostic criteria because they have not yet reached the developmental level required for that behaviour to be achieved. Moreover, the clinical tools that have been developed to aid the diagnosis of ASD are generally not designed to be able to distinguish between these very subtle differences and complex patterns of behaviour and thus may have more limited sensitivity and
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specificity when applied to individuals with genetic syndromes associated with ID (for a review see Moss, Howlin & Oliver, 2011). Careful attention should be paid to the role of ID when evaluating the strength of association between ASD and a specific genetic syndrome.

Caution is also required when considering the level at which to interpret research and clinical findings within this population. While the prevalence of ASD symptomatology has been shown to be heightened in a range of syndromes, evaluation of the specific ASD symptomatology associated with a given syndrome group has often identified profiles of ASD related behaviour that are different to that observed in individuals with idiopathic ASD. Amongst others, this has been the case in Fragile X, Rett, Cornelia de Lange and Angelman syndromes (Hall et al., 2010; Moss et al., 2008; Mount et al., 2003; Trillingsgaard & Østergaard, 2004). These findings clearly have important implications for the conceptualisation of the triad of impairments within genetic syndromes and highlight the importance of detailed behavioural description, beyond the level of clinical cut off scores, in order to illustrate accurately, the profile of ASD phenomenology in genetic syndromes. These findings also emphasize the need for appropriate comparison groups when evaluating ASD symptomatology in genetic syndrome groups. Single syndrome description is no longer sufficient to accurately evaluate the strength and nature of association between a given genetic syndrome and ASD symptomatology.

Comparison of genetic syndrome groups with individuals with idiopathic ASD and careful attention to degree of ID, is required in order to further progress research in this field.

One syndrome in which an interesting association with ASD has begun to emerge in recent years is Down syndrome (DS). DS is the most common chromosomal cause of ID, occurring in approximately 10.3 in 10,000 live births (Bell et al., 2003). Typically, DS is caused by the presence of a full or partial trisomy of chromosome 21, although occasionally an unbalanced translocation involving chromosome
21 has been identified (Dykkens et al., 2000). Intellectual disability in DS ranges from mild to severe (Capone et al., 2005).

Previously, ASD in persons with DS has been considered to be relatively rare. However, several case studies of individuals with DS who met ASD criteria have now been reported (Bregman & Volkmar, 1988; Ghaziuddin et al., 1992; Howlin et al., 1995; Wakabayashi, 1979) and, more recently, studies that have used standardized, ASD specific assessments have indicated that co-morbidity may be more common than previously thought with prevalence rates ranging from 5% to 39% (Capone et al., 2005; DiGuiseppi et al., 2010; Ghaziuddin et al., 1992; Gillberg et al., 1986; Hepburn et al., 2008; Kent et al., 1999; Lowenthal et al., 2007; Lund, 1988; Reilly, 2009; Starr et al., 2005; Turk & Graham, 1997). Although Hepburn et al. (2008) suggest that the presentation of the triad of impairments in DS may be atypical, with fewer impairments in the domain of social relatedness. Higher rates of impaired social skills have also been reported in family members of individuals with DS and ASD in comparison to individuals with DS without ASD (Lowenthal et al., 2007; Reilly, 2009), indicating a potentially heightened susceptibility for the broader autism phenotype in families of children with DS and ASD.

Recent research has focused on what might distinguish individuals with DS and ASD from those with ‘typical DS’ and findings indicate that there may be differences between these two subgroups. Capone et al. (2005), Carter et al. (2007) and Molloy et al. (2009) have reported that those with ASD and DS have a greater degree of ID relative to those with DS who do not meet ASD criteria. Molloy et al. (2009) propose that the presence of ASD like impairments in those with DS and ASD is not solely accounted for by the greater degree of ID. Additionally, higher rates of behaviour difficulties including: stereotyped behaviours, hyperactivity and inappropriate speech have been reported in individuals with DS and ASD relative to those with DS only (Capone et al., 2005; Carter et al., 2007 & Molloy et al. 2009). However, none of these studies have employed matched comparison groups in order to
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evaluate whether these differences in behavioural profile are accounted for by the greater degree of ID and whether this behaviour profile is similar to that observed in individuals with idiopathic ASD who show similar levels of ASD symptomatology.

This is the first study to evaluate the profile of ASD symptomatology, repetitive behaviour, hyperactivity and mood in individuals with DS who score above the cut off for ASD on the Social Communication Questionnaire (SCQ; Rutter et al., 2003) compared to a contrast group of individuals with DS matched for chronological age and estimates of ID who do not score above the cut off for ASD and individuals with idiopathic ASD (also matched for severity of ASD symptomatology). In this study we address the following research questions:

1. What is the prevalence of ASD symptomatology in individuals with DS?
2. What is the profile of ASD symptomatology, hyperactivity, challenging behaviour, mood and repetitive behaviour in individuals with DS who score above the SCQ cut off for ASD compared to individuals with DS who do not score highly on the SCQ and individuals with idiopathic ASD who are matched on estimates of ID and ASD symptom severity (ASD group only)?
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Methods

This study was conducted as part of a larger project comparing aspects of the behavioural phenotypes of individuals with a range of genetic syndromes (see anonymised for blind review., 2011; anonymised for blind review, 2010; anonymised for blind review., 2009; anonymised for blind review., 2011).

Participants

This study was conducted in two stages:

Stage 1: Investigation of the prevalence and phenomenology of ASD symptomatology in a sample of 108 individuals with DS. Participants were recruited via the UK Down Syndrome Association. 500 families caring for people with DS were contacted and invited to participate. 144 (28.8 %) individuals returned questionnaires. Participants were included if information regarding participant’s date of birth and diagnosis of DS from a professional (Physician, Clinical Geneticist, Paediatrician or other) was present, if at least 75% of the SCQ (Rutter et al., 2003) had been completed and if the participant with DS was at least four years of age. Eleven participants (7.6%) were excluded from the study because they did not provide information regarding age or date of birth, 12 (8.3%) were excluded because they did not have a confirmed diagnosis and 13 (9.0%) were excluded because they had not completed at least 75% of the SCQ. This left a total sample of 108 participants.

Stage 2: Investigation of the behaviour profile of individuals with DS who score above the cut off for ASD on the SCQ (DS+ASD) compared to individuals with DS who do not meet this criteria (DS only) and individuals with idiopathic ASD (ASD only). Participants with DS meeting the suggested cut off for ASD on the SCQ who could be matched to those with DS who did not score above this cut off and those with idiopathic ASD were selected into the DS +ASD group (N=17; 4 participants with DS who met the ASD cut off were excluded as they could not be matched to individuals in the contrast groups). Seventeen participants with DS who did not score above the ASD cut off on the SCQ were selected.
into the DS only group based on matching criteria of +/- 2 points on the self help subscale of the Wessex questionnaire (Kushlick, Blunden & Cox, 1973). For the purposes of analysis, a comparison group of 17 individuals with idiopathic ASD were selected from a larger participant sample that had been collected as part of a large study of individuals with ASD (anonymised for blind review et al., In Press). Participants with ASD were included in the study if information regarding diagnosis of ASD by a relevant professional (Paediatrician, G.P., Psychiatrist, Clinical Psychologist, Educational Psychologist) was present and they scored above the ASD cut off on the SCQ. The ASD group were matched to the DS+ASD group using the SCQ total score (+/- two points on total score) and estimates of ID (+/- 2 points on the self help subscale of the Wessex Questionnaire; Kushlick, Blunden & Cox, 1973). Participant characteristics for the total DS sample, the DS+ASD and DS only subsamples and the ASD comparison group are reported in Table 1.

+++/Insert Table 1 about here+++

Measures

Demographic Information. The demographic questionnaire provided information regarding date of birth, gender, mobility (able to walk unaided), verbal ability (more than 30 signs/words) and diagnostic status (whether or not a diagnosis had been made, the precise diagnosis made, when and by whom).

Assessment of Autism Spectrum Disorder Symptomatology: The Social Communication Questionnaire (SCQ; Rutter, Bailey, Lord & Berument, 2003) was used to screen for the presence of ASD symptomatology in individuals of all age groups. The measure consists of forty items that comprise three subscales: communication, social interaction and repetitive and stereotyped patterns of behaviours. The authors suggest a cut-off point for ASD of fifteen. This score was found to differentiate individuals with Pervasive Developmental Disorders from other diagnoses (excluding
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those with ID) with a specificity of .80 and a sensitivity of .96 and differentiated individuals with autism from individuals with ID with a specificity of .67 and a sensitivity of .96. A higher cut-off point of 22 or more is required to differentiate individuals with autism from other Pervasive Developmental Disorders with a sensitivity of .75 and a specificity of .60. The SCQ has also been shown to have good concurrent validity with the Autism Diagnostic Interview and with the Autism Diagnostic Observation Schedule (Berument et al., 1999; Bishop & Norbury, 2002). Internal consistency is also good (Berument et al., 1999). Howlin and Karpf (2004) report good internal consistency and concurrent validity with the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview in individuals with Cohen syndrome and propose that this supports the validity of using this screening tool for evaluating ASD symptomatology in individuals with genetic syndromes.

Estimates of ability, hyperactivity, repetitive behaviour, mood and challenging behaviour: Full details of these assessments are provided in anonymised for blind review et al. (2011); anonymised for blind review et al. (2010); anonymised for blind review et al. (2002); anonymised for blind review et al. (2009); anonymised for blind review et al., (2011) and anonymised for blind review (2003).

The Wessex (Kushlick, et al., 1973) is an informant based measure of adaptive behaviour for children and adults with ID and was used as an estimate of degree of ID. The Wessex is an informant questionnaire designed to assess social and physical abilities in children and adults with ID. Subscales include continence, mobility, self help skills, speech and literacy and information on vision and hearing is also included. The Wessex Scale has good inter-rater reliability at subscale level for both children and adults (Kushlick et al., 1973; Palmer and Jenkins, 1982).

The Mood Interest and Pleasure Questionnaire-Short (MIPQ-S; anonymised for blind review, 2003; anonymised for blind review et al., 2011) is a twelve item informant questionnaire used to assess two
con structs related to depression, mood and, interest and pleasure. It is designed for use with people with ID including those with severe or profound intellectual disabilities. There are two subscales: Mood, and Interest and Pleasure. The MIPQ-S shows good internal consistency (Cronbach’s alpha coefficients: total = .88, Mood = .79, Interest and Pleasure = .87), test-retest (.97) and inter-rater reliability (.85).

The Activity Questionnaire (TAQ; anonymised for blind review, 2010) is an eighteen item informant questionnaire designed to evaluate hyperactivity and impulsivity and is appropriate for use with people with ID including those with severe or profound ID. Item level inter-rater reliability ranges from .31 to .75 (mean .56) and test-retest reliability ranges from .60 to .90 (mean .75). Inter-rater and test-retest reliability indices for subscales and total score exceed .70.

The Challenging Behaviour Questionnaire (CBQ; anonymised for blind review et al., 2002) was used to evaluate the presence or absence of self-injury, physical aggression, verbal aggression, destruction of property and inappropriate vocalizations over the last month. Previous examination of the psychometric properties of the questionnaire has demonstrated good inter-rater reliability with reliability coefficients ranging from .61 to .89 (anonymised for blind review, 2002).

The Repetitive Behaviour Questionnaire (RBQ; anonymised for blind review, 2009) was used to assess the frequency of a range of repetitive behaviours. There are five subscales: stereotyped behaviour, compulsive behaviour, restricted preferences, insistence on sameness and repetitive use of language. The RBQ is an informant questionnaire for use with children and adults with a range of intellectual abilities. Examination of the psychometric properties of the RBQ indicates that item level inter-rater and test-retest reliability and validity are good (anonymised for blind review et al., 2009).
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**Procedure**

Questionnaires were distributed to families and carers of individuals with DS and individuals with ASD via the relevant family support groups that were local to the research bases in two cities in the UK.

**Data Analysis**

All data were tested for normality using Kolmogorov-Smirnov tests. Non-parametric tests were employed where data were not normally distributed.

*Stage 1 analysis.* The proportion of individuals with DS scoring above the cut offs for ASD and Autism on the SCQ were assessed using the total sample of individuals with DS (N=108). Independent t tests and Chi squared tests (for categorical data) were conducted to evaluate differences in chronological age, self help skills, verbal ability and mobility between individuals who scored above and below these cut off scores.

*Stage 2 analysis.* One way ANOVA’s (or Kruskal Wallis tests where data were not normally distributed) and Chi squared tests for categorical data (or Fisher’s exact where required) were conducted to determine differences between the DS+ASD, DS only and ASD only groups with regard to chronological age, self help skills, verbal ability and mobility. Differences between the three groups (DS+ASD, DS, ASD) on measures of mood, repetitive behaviour, levels of hyperactivity and impulsivity and challenging behaviour were also conducted in this way at both subscale and item level. Post hoc differences were investigated using Scheffé post hocs (or pairwise Mann Whitney U tests). A conservative $p$ value of $\leq .01$ was used for all main analysis, while Bonferonni corrected $p$ values were used for item level analysis due to the number of comparisons. All post hoc tests used a significance level of $p < .05$. 
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Results

Stage 1 analysis - Prevalence of ASD symptomatology in DS:

21 participants in the total DS sample (N=108) scored above the cut off for ASD on the SCQ (cut off score 15; 19.4%). Of these, nine participants scored above the more stringent cut off for autism (cut off score 22; 8.3%). Those who scored above the cut off for autism and/or ASD did not differ significantly from those with DS who did not score above these criteria on chronological age (autism cut off vs. not: t(97) = .63, p = .53; ASD cut off vs. not: t(97)=.75, p = .46) or gender (autism cut off vs. not: Fisher’s Exact; p = .49; N males meeting autism cut off = 5 (55.6%); ASD cut off vs. not: χ² (1) =1.02; p = .35; N males meeting ASD cut off = 11 (52.4%)) but did have significantly lower self help skills (above autism cut off vs. not: t(105) = 4.50, p < .001; above ASD cut off vs. not: t(105) = 4.01, p < .001) and lower levels of verbal ability (above autism cut off vs. not: Fisher’s exact, p < .001; above ASD cut off vs. not: Fisher’s exact, p =.02). Those scoring above the cut off for ASD were also less mobile than those who did not meet this criteria (Fisher’s exact, p=.02).

A comparison between individuals with DS who met the cut off for autism and those who met the ASD cut off only, showed no differences in chronological age (t(17)=.25, p=.80). A difference in self help scores between these groups approached significance (t(18)=2.15, p =.05), with those scoring above cut off for ASD showing greater self help skills than those scoring above cut off for autism.

Stage 2 analysis - Profile of autism spectrum symptomatology, hyperactivity, repetitive behaviour, mood and challenging behaviour

For the next stage of analysis, participants were matched on estimates of ID (+/-2 points; measured by the Wessex self help score) and SCQ total score (ASD group only; +/- 2 points). Accordingly, participants did not differ significantly on self help scores (F(50,2) = 1.13; p = .33) and the DS+ASD and ASD only groups did not differ on SCQ total score (t(32)=-.02; p = .98). There were also no
significant differences between the groups on chronological age (F(50,2) =2.45; \(p = .10\)), verbal ability (>30 words/signs Fisher’s exact = 1.65, \(p = .58\)), mobility (walks unaided; Fisher’s exact = 1.65, \(p = .58\)) and gender (\(\chi^2 (2) =4.39; p = .15\)). Details of participant characteristics can be seen in Table 1.

Table 2 describes the profiles of ASD symptomatology, hyperactivity, repetitive behaviour, mood and challenging behaviour across the three participant groups.

+++Insert Table 2 about here+++ 

In order to investigate the profile of ASD phenomenology in DS, the scores on the SCQ subscales were compared across the three groups. The DS only group scored significantly lower than both the DS+ASD and ASD only groups on all domains of the SCQ (all \(p\) values \(\leq .001\)), while no significant differences were identified between the DS+ASD and ASD only groups on any of the SCQ domains (all \(p\) values \(> .20\)), suggesting no differences between these groups with regard to the profile of domain scores on this measure.

Scores on assessments of hyperactivity, repetitive behaviour, mood and challenging behaviour were compared at subscale and item level across the three matched participant groups. Analysis at subscale level revealed that the DS only group evidenced significantly higher levels of interest and pleasure than the ASD only group. The DS + ASD and ASD only groups engaged in significantly more stereotyped behaviour and showed greater levels of overactivity than the DS only group. The DS+ASD group also showed significantly more repetitive language than the DS only group. The ASD only group was significantly more impulsive than the DS only group. There were no significant differences between the groups on measures of compulsive behaviour, insistence on sameness, restricted preferences,
aggression or property destruction. Self-injurious behaviour was more frequent in the DS+ASD and ASD only groups compared to the DS only group.

Item level analysis showed significant differences between the groups on the frequency of hand stereotypies (DS+ASD, ASD>DS), repetitive phrases (DS+ASD, ASD>DS), echolalia (DS+ASD, ASD>DS), positive vocalisations (DS>DS+ASD, ASD), flat affect (DS>ASD), interest in surroundings (DS,DS+ASD> ASD), expressing enjoyment in activities (DS >ASD) and preference to be moving around (DS+ASD,ASD>DS). See Table 3 for a description of item level scores. For conciseness, only group scores on items on which there were significant differences are reported.

+++Insert Table 3 here+++
In this study we assessed the prevalence of ASD symptomatology in a large group of individuals with DS. Following this analysis, the profile of ASD symptomatology, repetitive behaviour, hyperactivity and mood in individuals with DS who met the cut off for ASD on the SCQ (DS+ASD) was evaluated relative to two matched contrast groups of individuals with DS who did not meet these criteria (DS only; matched on estimates of adaptive behaviour) and individuals with idiopathic ASD (ASD only; matched on estimates of adaptive behaviour and severity of ASD symptomatology). This is the first study to have evaluated the behavioural profile of individuals with DS+ASD relative to others with DS who do not meet these criteria and individuals with idiopathic ASD, using matched comparison groups to control for differences in adaptive behaviour skills. Furthermore, this is the first study to consider whether the presentation of ASD symptomatology and the behavioural profile of those with DS+ASD are similar to that of individuals with idiopathic ASD, who are matched for ASD symptom severity.

Prevalence and profile of ASD symptomatology in DS

Of the total DS sample (108), the proportion of individuals with DS who met the cut off for ASD and autism was 19% (N=21) and 8% (N=9) respectively. These figures are broadly consistent with the majority of previous prevalence estimates reported within the DS population (Capone et al., 2005; Hepburn et al., 2008; Kent et al., 1999; Lowenthal et al., 2007; Lund, 1988; Turk & Graham, 1997). However, they are higher than that reported by Gillberg et al. (1986) and Ghaziuddin et al. (1992; both 5%) and lower than that reported by Starr et al., 2005 (39%). This variability is likely to reflect differences in assessment measures, sample characteristics and changes in diagnostic criteria over time.

Although some previous case reports and studies of individuals with DS+ASD have indicated a male bias in individuals with DS+ASD (see Reilly 2009 for a review), this was not identified in the current study. The proportion of males with DS meeting the cut off for ASD and autism was 52% (N=11) and
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55.6% (N=5) respectively. These figures are consistent with the findings of Kent et al. (1999), Rasmussen et al. (2001) and Lowenthal (2007).

Further analysis indicated that individuals with DS who met the cut off for ASD/autism on the SCQ had lower levels of self help skills, were less mobile and had fewer verbal abilities compared to the total sample of individuals with DS who did not score above the SCQ cut off. These findings are consistent with reports from Capone et al. (2005), Carter et al. (2007), Hepburn et al. (2008) and Molloy et al. (2009). A comparison of individuals with DS scoring above the cut off for ASD to those meeting the more stringent criteria for autism was limited by the small sample size but indicated that those scoring above the cut off for ASD only were more able than those who scored above the cut off for autism. This difference approached significance ($p = .05$). Given that the ability to assess ASD symptomatology becomes more difficult as the severity of the ID increases, it is not clear whether the association between DS and ASD simply reflects a lack of specificity of autism specific measures to accurately screen individuals with more severe ID. Molloy et al. (2009) argue that this association is unlikely to be solely accounted for by degree of ID.

In order to evaluate the role of ID further, we considered the scores within the domains of the SCQ across three groups of participants (DS+ASD, DS only, ASD only) who were matched on estimates of adaptive behaviour and SCQ scores (ASD only group). Individuals in the DS+ASD group scored significantly higher than the DS only group on all three domains of the SCQ, and showed a similar profile of scores on these domains to individuals with ASD only. These findings indicate that the DS+ASD group demonstrated impairments across all domains of ASD symptomatology, with similar levels of severity to individuals with idiopathic ASD. This is in contrast to reports of an atypical presentation, as has been identified in toddlers with DS who met criteria for ASD (Hepburn et al., 2008) and several other genetic syndromes (Moss & Howlin, 2009). While the similarities between the
DS+ASD and ASD only group are perhaps not surprising, given that these groups were matched on total SCQ scores, it indicates that the presentation of ASD symptomatology and the contribution of each domain score towards the total SCQ score, is similar in those with DS who meet the cut off for ASD on the SCQ and those with idiopathic ASD. These findings are consistent with that of Capone et al. (2005) who also report impairments within all domains of the triad and support Molloy et al.’s (2009) conclusion that this association cannot be solely accounted for by degree of ID.

Profile of hyperactivity, repetitive behaviour, challenging behaviour and mood
Previous studies have reported that those with DS and ASD are different from those with ‘typical’ DS, showing higher rates of behaviour difficulties including: hyperactivity, stereotyped behaviour and inappropriate speech (Capone et al., 2005; Carter et al., 2007 & Molloy et al. 2009). In this study, we evaluated whether these differences were evident when adaptive behaviour was controlled for, and whether this behaviour profile was also evident in individuals with idiopathic ASD. Similar to previous findings by Capone et al. (2005), Carter et al. (2007) and Molloy et al. (2009), our results indicated that individuals in the DS+ASD group showed significantly more stereotyped behaviour (specifically hand stereotypies), repetitive use of language (including repetitive phrases and echolalia) and overactivity than those in the DS only group. No differences between the DS+ASD and DS only groups were identified with regard to impulsivity, although the ASD only group showed significantly more impulsivity than the DS only group. Interestingly, the repetitive interests, rituals, preference for routine and attachment to objects, previously reported in some of the single case studies of individuals with DS+ASD (Ghazzudin et al., 1992; Ghazzudin, 1997; Howlin et al., 1995; Kent et al., 1998) were not highlighted in this study as being particularly prominent of this group relative to individuals with DS only.
This study extended previous findings to evaluate levels of mood and challenging behaviour (self-injurious behaviour, physical aggression and destruction of property) in individuals with DS+ASD relative to those with DS only and ASD only. Analysis indicated that individuals with DS only had higher levels of interest and pleasure than those with ASD only. Item level analysis of this questionnaire indicated that both the DS only and DS+ASD groups showed significantly more interest in their surroundings compared to the ASD only group, while the DS+ASD and ASD only groups showed fewer positive vocalizations than the DS only group. Additionally, the DS only group showed significantly less flat affect and expressed greater enjoyment in activities compared to the ASD only group. Self-injury was significantly more likely to occur in individuals with DS+ASD and ASD only, relative to those with DS only. No other differences in challenging behaviour were observed.

Overall, these results support previous findings showing differences between individuals with DS only and those with DS+ASD. Specifically, individuals with DS who meet the cut off for ASD on the SCQ show greater levels of stereotyped behaviour, repetitive language, self-injurious behaviour, overactivity and fewer positive vocalizations than those with DS only. These differences are not accounted for by degree of ID. Furthermore, the DS+ASD group show a similar profile of ASD symptomatology and a similar behavioural profile to those with idiopathic ASD. Again, this does not appear to be accounted for by degree of ID. However, the DS+ASD group are reported to be less withdrawn from their environment than those with idiopathic ASD, suggesting some subtle differences between these groups with regard to the quality of the social impairments. It is well established that the DS population, as a whole, experience significantly fewer behaviour difficulties relative to other individuals with ID (Dykens et al., 2000; Reilly, 2009) and this has been suggested by some to be indicative that DS is, in some way, protective of such difficulties. The findings from this study suggest that this apparent ‘protection’ may be reduced by the presence of ASD symptomatology.
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Limitations of the study

The findings from the current study should be considered alongside a number of limitations. The presence of ASD symptomatology was identified through the use of an informant screening tool, the SCQ (Rutter et al., 2003). Consequently, there is a limit to what we are able to infer regarding the prevalence of ASD within this DS sample. Scoring highly on the SCQ alone is not sufficient to indicate a diagnosis and further detailed observation and interview is required for diagnosis. However, previous studies have reported very good convergent validity for the SCQ and other ‘gold standard’ diagnostic assessments of ASD, suggesting that this measure provides a very good indicator of ASD symptomatology. Reliance upon the Wessex self help scale to provide an estimate of adaptive behaviour skills is a further limitation of the study. In future studies, direct assessments of ID and adaptive skills such as the Vineland Adaptive Behavior Scales (Sparrow et al., 2005) would provide a more accurate account of degree of ID. However, it is important to note that the Wessex, although brief, has been reported to show good reliability (Kushlick et al., 1973; Palmer & Jenkins, 1979). Furthermore, this is the first study to consider the role of ID, in any way, when evaluating the association between ASD and DS. Given the difficulties in identifying ASD in individuals with ID this is clearly an important confound to take into account. The overall response rate of the DS group was relatively low (28.8%) and this is likely to be due to the fact that this syndrome group has been extensively researched and thus may reflect participant fatigue. While this may have introduced some bias in the sample, the study was presented to families as a project evaluating the characteristics of DS and this is likely to have avoided a bias towards more severely affected individuals. The sample size of the three matched participants groups was small and this may have resulted in limited statistical power. However, the size of the samples was largely driven by the proportion of individuals with DS who met the cut off for ASD. Furthermore, inclusion of matched comparison groups addresses the threat to internal validity and enables more precise characterisation of the behavioural profile of individuals with DS+ASD. One potential drawback of the matched DS only group is that our analyses identified that
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those individuals with DS who scored above cut off for ASD on the SCQ had significantly lower levels of ability compared to the total DS sample. This confound was accounted for in the subsequent matched groups comparisons, although it may suggest that the individuals selected into the matched DS only group were those who were less able and therefore may not be representative of the wider DS population. However, the fact that our findings are consistent with those reported in previous studies, where matched comparison groups have not been employed, suggests that our findings are valid. Finally, diagnosis of DS was not confirmed by genetic karyotyping in this study. Given the age range of the sample (4-62 yrs) it is unlikely that this information would be available for a significant proportion of individuals and thus reliance upon a confirmed clinical diagnosis, which is highly accurate in this syndrome, was considered to be sufficient.

Conclusions

Consistent with previous findings, we identified the proportion of individuals meeting cut off scores for ASD and autism in a sample of 108 individuals with DS to be 19% and 8% (respectively). Individuals with DS+ASD showed a different profile of behaviour difficulties compared to individuals with DS only, that was not accounted for by level of adaptive behaviour skills. This provides support for previous reports that have suggested that individuals with DS and ASD comprise a subgroup of individuals with DS. Individuals with DS+ASD performed similarly to individuals with ASD on a range of measures however, this was not always the case, suggesting that individuals with ASD+DS may show some areas of subtle difference compared to those with idiopathic ASD. Further detailed study of these subgroups using larger samples and direct assessments is required in order to progress our understanding of the association between ASD and DS.
Footnotes

1 The reference ‘DS+ASD’ is used here and throughout the paper to describe participants scoring above the cut off on the SCQ for ASD, it does not imply that these individuals have a confirmed diagnosis of co-morbid ASD.

2 It was important to match the DS+ASD and ASD only groups according to SCQ scores in order to ensure that any difference in the profile of ASD symptomatology and other behavioural characteristics could clearly be attributed to group membership rather than differences in the severity of ASD symptomatology of the two groups.
References


ASD symptomatology and related characteristics in Down syndrome


ASD symptomatology and related characteristics in Down syndrome


ASD symptomatology and related characteristics in Down syndrome


Table 1: Age, Gender, Ability, Mobility and Speech characteristics for the total DS group, DS+ASD subsample group, DS only subsample and ASD group.

<table>
<thead>
<tr>
<th></th>
<th>DS total group</th>
<th>DS only</th>
<th>DS+ASD</th>
<th>ASD group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>108</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>22.16 (12.51)</td>
<td>20.53 (11.72)</td>
<td>21.14 (11.79)</td>
<td>13.65 (8.90)</td>
</tr>
<tr>
<td>Range</td>
<td>4.00 – 62.00</td>
<td>5.00-43.00</td>
<td>4.00-39.00</td>
<td>4.00-32.00</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% male (N)</td>
<td>42.59 (46)</td>
<td>35.29 (6)</td>
<td>47.06 (8)</td>
<td>70.01 (12)</td>
</tr>
<tr>
<td>Total Self Help Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.87 (1.41)</td>
<td>7.53 (1.62)</td>
<td>6.71 (1.76)</td>
<td>6.88 (1.65)</td>
</tr>
<tr>
<td>Range</td>
<td>4.00-9.00</td>
<td>5.00-9.00</td>
<td>4.00-9.00</td>
<td>4.00-9.00</td>
</tr>
<tr>
<td>Mobility</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% mobile (N)</td>
<td>96.30 (104)</td>
<td>94.12 (16)</td>
<td>88.2 (15)</td>
<td>88.24 (15)</td>
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<tr>
<td>Speech</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% verbal (N)</td>
<td>93.52 (101)</td>
<td>88.24 (15)</td>
<td>70.59 (12)</td>
<td>76.47 (13)</td>
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</tbody>
</table>
### Table 2: Mean scores and percentage displayed on subscales of MIPQ, RBQ, TAQ and CBQ for DS, DS + ASD and ASD groups.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Subscale</th>
<th>DS Mean (SD)</th>
<th>DS + ASD Mean (SD)</th>
<th>ASD Mean (SD)</th>
<th>χ²/F df p</th>
<th>Post hoc analyses (Scheffe/Mann Whitney U)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCQ</td>
<td>Communication</td>
<td>3.58 (2.03)</td>
<td>7.31 (2.27)</td>
<td>7.24 (1.82)</td>
<td>17.71 49,2 .001</td>
<td>DS+ASD, ASD&gt;DS</td>
</tr>
<tr>
<td></td>
<td>Restricted and repetitive behavior</td>
<td>1.24 (.97)</td>
<td>3.97 (2.33)</td>
<td>5.00 (1.73)</td>
<td>20.47 50,2 .001</td>
<td>DS+ASD, ASD&gt;DS</td>
</tr>
<tr>
<td></td>
<td>Reciprocal social interaction</td>
<td>2.74 (1.74)</td>
<td>9.94 (2.59)</td>
<td>8.94 (3.88)</td>
<td>31.35 50,2 .001</td>
<td>DS+ASD, ASD&gt;DS</td>
</tr>
<tr>
<td></td>
<td>Mood</td>
<td>21.60 (2.48)</td>
<td>20.35 (2.74)</td>
<td>19.29 (2.31)</td>
<td>3.58 50,2 .04</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Interest and Pleasure</td>
<td>19.12 (3.67)</td>
<td>16.35 (5.15)</td>
<td>12.53 (4.37)</td>
<td>9.44 50,2 .001</td>
<td>DS&gt; ASD</td>
</tr>
<tr>
<td>MIPQ</td>
<td>Mood</td>
<td>21.60 (2.48)</td>
<td>20.35 (2.74)</td>
<td>19.29 (2.31)</td>
<td>3.58 50,2 .04</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Interest and Pleasure</td>
<td>19.12 (3.67)</td>
<td>16.35 (5.15)</td>
<td>12.53 (4.37)</td>
<td>9.44 50,2 .001</td>
<td>DS&gt; ASD</td>
</tr>
<tr>
<td>RBQ</td>
<td>Stereotyped Behavior</td>
<td>1.56 (3.16)</td>
<td>7.00 (4.56)</td>
<td>6.19 (5.00)</td>
<td>17.06 2 .001</td>
<td>DS+ASD, ASD &gt; DS</td>
</tr>
<tr>
<td></td>
<td>Compulsive Behavior</td>
<td>4.74 (6.48)</td>
<td>7.47 (8.97)</td>
<td>8.53 (5.64)</td>
<td>1.16 48,2 .323</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Insistence on Sameness</td>
<td>1.94 (2.98)</td>
<td>2.94 (3.25)</td>
<td>4.06 (2.16)</td>
<td>2.32 49,2 .110</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Restricted Preferences*</td>
<td>3.14 (2.63)</td>
<td>4.42 (3.58)</td>
<td>4.85 (2.64)</td>
<td>1.22 38,2 .308</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Repetitive use of Language*</td>
<td>1.64 (1.65)</td>
<td>5.50 (4.50)</td>
<td>4.62 (3.10)</td>
<td>5.23 38,2 .010</td>
<td>DS+ASD&gt; DS</td>
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<tr>
<td>TAQ</td>
<td>Impulsivity</td>
<td>7.82 (6.37)</td>
<td>11.26 (6.86)</td>
<td>16.60 (5.80)</td>
<td>5.83 49,2 .005</td>
<td>ASD &gt; DS</td>
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<td>Overactivity</td>
<td>5.47 (5.95)</td>
<td>13.06 (10.71)</td>
<td>15.59 (11.97)</td>
<td>5.19 50,2 .009</td>
<td>DS+ASD, ASD &gt; DS</td>
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<td>Impulsive Speech*</td>
<td>3.07 (3.53)</td>
<td>3.91 (4.13)</td>
<td>6.39 (3.64)</td>
<td>2.14 38,2 .132</td>
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<tr>
<td>CBQ</td>
<td>Aggression (% showing behavior)</td>
<td>23.53 (11.76)</td>
<td>43.75 (13.33)</td>
<td>58.82 (6.38)</td>
<td>4.38 2 .112</td>
<td>-</td>
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<tr>
<td></td>
<td>Self-injurious behavior (%</td>
<td>5.88 (3.53)</td>
<td>37.50 (4.13)</td>
<td>52.94 (3.64)</td>
<td>8.98 2 .011</td>
<td>DS+ASD, ASD &gt; DS</td>
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<tr>
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<td>showing behavior)</td>
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<tr>
<td></td>
<td>Property Destruction (%</td>
<td>11.76 (10.34)</td>
<td>13.33 (3.64)</td>
<td>47.06 (6.38)</td>
<td>6.38 2 .039</td>
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<td>showing behavior)</td>
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* = Subscale only calculated for verbal participants
### Table 3: Median scores and interquartile range on items of the MIPQ, RBQ and TAQ in which significant differences were identified.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Item</th>
<th>DS</th>
<th>DS + ASD</th>
<th>ASD</th>
<th>$\chi^2$</th>
<th>$p$ value</th>
<th>Post hoc</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Median (Inter-quartile range)</td>
<td>Median (Inter-quartile range)</td>
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<tr>
<td>RBQ</td>
<td>Hand stereotypies</td>
<td>0.00</td>
<td>1.50</td>
<td>3.00</td>
<td>18.92</td>
<td>&lt;.001</td>
<td>DS+ASD, ASD&gt;DS</td>
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<tr>
<td></td>
<td></td>
<td>(0.00)</td>
<td>(4.00)</td>
<td>(1.50)</td>
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<td></td>
<td>Repetitive phrases</td>
<td>0.00</td>
<td>0.00</td>
<td>1.00</td>
<td>11.49</td>
<td>.003</td>
<td>DS+ASD, ASD&gt;DS</td>
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<tr>
<td></td>
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<td>(0.00)</td>
<td>(3.75)</td>
<td>(3.00)</td>
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<td></td>
<td>Echolalia</td>
<td>0.00</td>
<td>3.00</td>
<td>2.00</td>
<td>12.81</td>
<td>.002</td>
<td>DS+ASD, ASD&gt;DS</td>
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<tr>
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<td>(0.00)</td>
<td>(4.00)</td>
<td>(3.00)</td>
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<td>MIPQ</td>
<td>Positive vocalisations</td>
<td>3.00</td>
<td>3.00</td>
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<td>14.01</td>
<td>.001</td>
<td>DS&gt;DS+ASD, ASD</td>
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<td>Flat affect</td>
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<td>3.00</td>
<td>15.22</td>
<td>.001</td>
<td>DS&gt;ASD</td>
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<td>(0.50)</td>
<td>(1.00)</td>
<td>(1.50)</td>
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<td>Interested in surroundings</td>
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<td>4.00</td>
<td>3.00</td>
<td>14.43</td>
<td>.001</td>
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<td></td>
<td></td>
<td>(0.50)</td>
<td>(1.00)</td>
<td>(1.00)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Enjoyment in activities</td>
<td>3.00</td>
<td>3.00</td>
<td>2.00</td>
<td>16.10</td>
<td>&lt;.001</td>
<td>DS&gt;ASD</td>
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<td></td>
<td>(1.00)</td>
<td>(2.75)</td>
<td>(1.50)</td>
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<td>TAQ</td>
<td>Prefers to be moving around</td>
<td>0.00</td>
<td>1.00</td>
<td>3.00</td>
<td>12.76</td>
<td>.002</td>
<td>DS+ASD, ASD&gt;DS</td>
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<td></td>
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<td>(1.00)</td>
<td>(3.00)</td>
<td>(2.50)</td>
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</table>