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Characteristics of Autism Spectrum Disorder in Cornelia de Lange Syndrome

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Abstract

Background: The prevalence of Autism Spectrum Disorder (ASD) symptomatology is comparatively high in Cornelia de Lange Syndrome (CdLS). However, the profile and developmental trajectories of these ASD characteristics are potentially different to those observed in individuals with idiopathic ASD. In this study we examine the ASD profile in CdLS in comparison to a matched group of individuals with ASD.

Method: The Autism Diagnostic Observation Schedule (ADOS) was administered to 20 individuals with CdLS (mean age = 11.34; range = 6yrs to 13yrs) and 20 individuals with idiopathic ASD (mean age = 10.42; range = 8yrs to 11yrs). Participants were matched according to adaptive behaviour skills and receptive language.

Results: Sixty-five per cent (N= 13) of individuals with CdLS met the cut off score for autism on the total ADOS score. Further analysis at domain and item level indicated that individuals with CdLS showed significantly less repetitive behaviour, (specifically sensory interests); more eye contact, more gestures and less stereotyped speech than the ASD group. The CdLS group also showed higher levels of anxiety.

Conclusions: The comparison between CdLS and idiopathic ASD indicates subtle group differences in the profile of ASD symptomatology that are not accounted for by degree of intellectual disability or receptive language skills. These differences may not be evident when relying solely upon clinical and domain level scores, but may be distinguishing features of the ASD presentations in the two disorders. The findings have implications for the conceptualisation and assessment of ASD in individuals with genetic syndromes.

Key words: Autism Spectrum Disorder, Cornelia de Lange Syndrome, behavioural phenotypes, genetic syndromes, neurodevelopmental disorders.

Abbreviations: Cornelia de Lange syndrome (CdLS).

Introduction

Autism Spectrum Disorders occur in approximately 1% of children in the general population (Baird et al., 2006) and up to 40% of individuals with severe to profound levels of intellectual disability (La Malfa, Lassi, Bertelli, Salvini & Placidi, 2004). ASD related symptomatology or 'autistic-like' characteristics have been reported in a 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 molecular genetics have seen this list expand to include several microdeletion syndromes[1] such as: 8p23 deletion (Fisch, Grossfeld, Youngblom, Simensen & Battaglia, 2010), 3q29 deletion (Quintero-Rivera, Sharifi-Hannauer & Martinez-Agosto, 2010) and 9p partial duplication syndrome (Abu-Amero et al., 2010). Persico and Bourgeron (2006) suggest that understanding the association between ASD and various genetic syndromes may be helpful in determining the underlying genetic and neurological pathways within the wider ASD population.

The study of ASD symptomatology in genetic syndromes raises a number of methodological and conceptual issues. Firstly, intellectual disability (ID) may play a role in the association between genetic syndromes and ASD. Skuse (2007) suggests that impaired intellectual ability largely accounts for the increased prevalence of ASD symptomatology in genetic syndromes. Moreover, identification of autistic-like characteristics in individuals with severe and profound ID and those with complex behavioural and cognitive profiles is difficult (Moss & Howlin, 2009). Many of the core diagnostic features of ASD are developmentally influenced and consequently an individual may meet certain diagnostic criteria because he/she has not yet reached the required developmental level. The clinical tools that have been developed to aid the diagnosis and assessment of ASD were not designed for individuals with specific genetic disorders and ID, and thus may have limited sensitivity and specificity when used with these groups (for a review see Moss, et al., 2011).

Secondly, there is debate regarding the interpretation of findings from autism specific assessments within this population and specifically, whether evaluation of clinical cut offs is sufficient or whether more detailed inspection of the behavioural presentation is required. This is important because the

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[1] Syndromes caused by a genetic mutation that is too small to be seen using conventional cytogenetic methods.

profile of ASD related behaviours, as identified on autism specific measures, may be different to that of individuals with idiopathic ASD. For example, social impairments in Fragile X syndrome have been shown to be characterised by social anxiety and gaze avoidance, but accompanied by apparent willingness to interact with others (Cornish, Turk & Levitas, 2007; Hall, de Benardis & Reiss, 2006; Lesniak-Karpiak, Mazzocco & Ross, 2003; Roberts, Weisenfeld, Hatton, Heath, & Kaufmann., 2007). Other atypical ASD profiles have been described in Rett and Angelman syndromes (Hall, Lightbody, Hirt, Rezvani & Reiss, 2010; Mount, Hastings, Reilly, Cass & Charman, 2003; Trillingsgaard & Østergaard, 2004). These findings have important implications for the conceptualisation of the triad of impairments within genetic syndromes and highlight the importance of description beyond the level of clinical cut off scores. They also emphasize the need for appropriate comparison groups when assessing ASD symptomatology in genetic syndromes. Single syndrome description is no longer sufficient to 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 are also essential.

One syndrome in which an association with ASD has been described is Cornelia de Lange syndrome (CdLS). CdLS has an estimated prevalence of one in 40 000 live births (Beck 1976; Beck & Fenger 1985) and is caused by a deletion in the NIPBL gene on chromosome 5 (locus 5p13) in 20 to 50% of cases (Gillis et al., 2004; Krantz et al., 2004; Miyake et al., 2005; Tonkin, Wang, Lisgo, Bamshad & Strachan, 2004). Additional mutations on the SMC3 gene on chromosome 10 (Deardorff et al., 2007) and X linked SMC1 gene (Musio et al., 2006) are reported to account for 5% of cases. CdLS is characterized by developmental delay, delayed growth, distinctive facial features and limb abnormalities (Jackson, Kline, Barr & Koch, 1993).

Estimates of the prevalence of ASD symptomatology in CdLS, using autism specific informant and direct assessments, range from 50 – 67% (Basile, Villa, Selicorni & Molteni, 2007; Berney, Ireland & Burn, 1999; Bhyuian et al., 2006; Moss et al., 2008; Oliver, Arron, Sloneem & Hall, 2008; Oliver, Berg, Burbidge, Arron & Moss, 2011). Previous studies, using matched comparison groups of individuals with Cri du Chat syndrome (Moss et al., 2008) and individuals with ID of heterogeneous cause (Oliver, Arron, Sloneem & Hall, 2008), have indicated that the association between ASD and CdLS is not solely accounted for by the degree of ID that is characteristic of the syndrome. However, it has been suggested that the profile of ASD impairments in CdLS may not be typical of that observed in idiopathic ASD. Social impairments in CdLS are characterized by selective mutism, extreme shyness

and social anxiety (Goodban, 1993; Collis, Oliver & Moss, 2006; Moss et al., 2008; Richards, Moss, O'Farrell, Kaur & Oliver, 2009). Additionally, Oliver, Berg, Burbidge, Arron & Moss (2011) demonstrate that repetitive behaviours contribute less to the ASD profile of individuals with CdLS than impairments in communication and social interaction.

To date, there have been no studies that have compared directly the presentation of ASD symptomatology in CdLS to that of individuals with idiopathic ASD. Therefore, in the present study we examined the profile of ASD symptomatology in individuals with CdLS compared to a sample of individuals with idiopathic ASD, matched for adaptive behaviour and receptive language skills.

Methods

Recruitment:

Data were collected as part of two larger independent studies. The first was a study by Moss et al. (2008) evaluating ASD symptomatology in individuals with CdLS and Cri du Chat syndrome (Moss et al. 2008). The second was a longitudinal study evaluating outcomes in children with ASD who had been involved in autism-specific interventions in their pre-school and early school years (either home based behavioural programmes (n=11) or autism-specific community based educational provisions (n=9; Magiati, Charman & Howlin, 2007; Magiati, Moss, Charman & Howlin, 2011; Moss et al., 2008).

For the purposes of the current study, twenty participants with CdLS were selected from the larger sample of 34 individuals in the Moss et al (2008) study[2]. Participants with CdLS had been recruited through family support groups or had previously participated in research at the University of Birmingham and had agreed to be contacted by the researchers with information about future studies (for full details of recruitment of original sample see Moss et al., 2008). Twenty participants with ASD, who did not have a known genetic syndrome, were selected from the larger sample of children who had participated in the Magiati et al. (2007; 2011) and Moss et al. (2008) studies. Participants with ASD were initially recruited through local education authorities, specialist schools, diagnostic centres and

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[2] Analysis indicated that the selected participants with CdLS were broadly representative of the larger CdLS sample.

the UK National Autistic Society (for full details of recruitment see Magiati, et al., 2007; 2011 Moss et al., 2008). Data for the ASD sample included for analysis in the current study were collected in the most recent follow up of this cohort (Magiati et al., 2011).

Participants were selected for this study if:

(a). they had a confirmed diagnosis of either ASD or CdLS from an appropriate professional (relevant professionals for a diagnosis of CdLS included: GP, Paediatrician, Clinical Geneticist; relevant professionals for ASD diagnosis included: Psychologist, Psychiatrist, Paediatrician, GP). Individuals with ASD also met criteria for autism or ASD (Risi et al., 2006) on the ADI-R at initial recruitment;

and

(b). if they could be matched to an individual in the corresponding comparison group based on the following matching criteria: 1. Receptive language age equivalence (according to BPVS) +/- two years; 2. Adaptive behaviour age equivalence (according to VABS) +/- two years

Participants:

Table 1 presents the characteristics of the two matched participant samples. Statistical comparisons confirmed that there were no group differences with regard to receptive language and adaptive behaviour. As expected, there were significantly fewer males in the CdLS group compared to the ASD group ($p < .001$). The difference between chronological age approached significance (medium effect size), with the CdLS group being slightly older than the ASD group.

++++++Insert Table 1 here++++++

Measures:

<u>ASD symptomatology</u> was assessed using the *Autism Diagnostic Observation Schedule* (ADOS; Lord, Rutter, DiLavore, & Risi, 2000). The ADOS is a semi-structured, standardized, observational assessment of communication and social interaction skills, play and imaginative skills and repetitive behaviour. It correlates well with informant based measures of autism symptomatology and concurrent validity with the Autism Diagnostic Interview-Revised and the Social Communication Questionnaire is good (Howlin & Karpf, 2002; Lord et al., 2000; Rutter et al., 2003). Sensitivity, specificity and inter-rater reliability are reported to be robust (Lord et al., 2000). The ADOS incorporates planned social 'presses' that provide optimum opportunity for the participant to display certain behaviours or

responses. It comprises four separate modules appropriate for a range of developmental abilities, chronological ages and language skills. Scores on individual items range from 0 (no evident abnormalities) to 3 (marked abnormality) and each module provides four domain scores: communication, social interaction, imagination and creativity, and repetitive behaviour as well as a total social-communication score. There are separate cut off scores for autism and ASD which differ slightly from module to module (see Table 2).

++++Insert Table 2 about here++++

Selection of a module is based on the individual's expressive language and developmental age. All participants in the current study were assessed using Modules 1, (ASD N =14; CdLS N =11), 2 (ASD N=4; CdLS N = 8) or 3 (ASD N=2; CdLS N =1).

Adaptive behaviour was assessed using the *Vineland Adaptive Behavior Scales* (VABS, Survey form; Sparrow, Balla, & Chicchetti, 1984; the VABS-II was not available when the study began). Standard and age equivalent scores were obtained on the VABS Composite Score (VABS ABC) and each of the three domains (communication, daily living skills, socialization). Participants in the two groups were matched according to VABS ABC age equivalent scores (+/- 2 years).

Receptive language was evaluated using the *British Picture Vocabulary Scales* (BPVS 2nd Edition; Dunn, Dunn, Whetton, & Burley, 1997). This assessment requires the participant to select the picture matching the stimulus word presented orally by the examiner. Split–half reliability and internal consistency are good. Raw, age equivalent and standard scores are provided. Participants in the two groups were matched according to BPVS age equivalent scores (+/- 2 years).

Reliability:

Inter-rater reliability for ADOS scores was completed for 20% of the sample (25% CdLS group; 15% ASD group). Two raters independently (and blind to initial scoring) observed and scored videotaped ADOS assessments. The mean Intra-class correlation at domain level was .65 (range across domains = .55 to .88). Kappa scores for reaching diagnostic cut off for autism on the communication and social interaction domains and the total social-communication score for the CdLS group were .71, .60 and .71 respectively. Kappa could not be calculated for ASD cut off scores as all individuals included in the inter-rater reliability sample scored above this cut off.

Procedure:

The VABS (Sparrow et al., 1984) was conducted with the primary caregiver either by telephone or face to face. All participants were visited at their school/day centre where the ADOS and BPVS assessments were completed in a quiet, distraction free room and were video recorded. ADOS assessments were scored immediately after administration using a combination of live and video recorded observations.

Data analysis:

Analysis of ADOS scores was conducted at three levels: algorithm cut off score, domain/total and item level scores. Item level scores of 3 were converted to 2 and scores of 8 (indicating items that are not applicable or where there is insufficient evidence) were converted to 0 for the domain and algorithm scores, as stated in the ADOS manual. All data were tested for normality using Kolmogorov Smirnov tests. Chi squared tests (or Fisher's exact where appropriate) were used to assess differences between the CdLS and ASD groups with regard to the proportions meeting clinical cut off scores. Group differences on item and domain/total scores were compared using t-tests [3]. The p value was set at <.05, as this was primarily an explorative study. Effect sizes were also calculated for all group comparisons. Pearson's correlation coefficient (r) was used to determine effect size (Field, 2005). Effect sizes between .10 and .29 were considered to be small; .30-.49 medium and .50+ large (cf Field, 2005). Due to scoring differences across modules a subset of items that are common across modules 1 to 3 were selected for item analysis[4]. (See Figures 2 & 3)

Results

Meeting clinical cut off in the ADOS:

+++++Insert Table 3 here++++++

Significantly more participants in the ASD group met the cut off for autism on the communication, social interaction domains and total score compared to the CdLS group (See Table 3). There were no significant group differences in the proportions meeting the cut off for ASD.

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[3] Item level data were not normally distributed. However, results using non-parametric tests mirrored those identified using parametric tests. Thus, the results from the parametric tests are reported here.
[4] Three algorithm items and four non-algorithm items are common to modules one and two only. For analysis of these items, individuals with CdLS and ASD who completed a module three assessment and their matched pair were excluded from analysis. Thus, 18 participants from each group were included in analysis of these items.

ADOS Domain Level Scores:

+++++++Insert Figure 1 here+++++++

Mean domain scores are presented in Figure 1. The ASD group scored significantly higher on the repetitive behaviour domain than the CdLS group (t (38) = 2.14; *p* =.04; r=.33). There were no significant group differences on the communication (t (38) = 1.43; *p* =.16; r =.23), social interaction (t (30.23) = 1.75; *p* =.09; r=.27) and imagination and creativity (t (38) = .68; *p* = .50; r=.11) domains, nor on the total social-communication score (t (30.23) = 1.75; *p* =.09; r=.27).

ADOS Item Level Scores:

Item level scores are shown in Figures 2 and 3. The ASD group was significantly more impaired on algorithm items related to stereotyped words/phrases (t (22.27) = 2.26; *p* =.03; r=.34), gestures (t (36) = 23.14; *p* =.03; r=.34), eye contact (t (26.03) = 3.21; *p* = .004; r=.46) and sensory interests (t (38) = 2.45; *p* = .02; r=.37),

On non-algorithm items, there was a significant group difference on the anxiety item (t (29.70) = -2.23; *p* = .03; r=.34), with the CdLS group showing greater anxiety than the ASD group. The group difference on scores for echolalia approached significance, with the ASD group showing more frequent echolalia than the CdLS group (t (32) =1.93; *p* = .06; r=.30). No other significant differences were identified (r ranged from .09 to .26 on all other items).

Discussion

To our knowledge, this is the first study that has compared the prevalence and profile of ASD symptomatology in CdLS as compared to a group of individuals with idiopathic ASD, matched for overall levels of adaptive behaviour and receptive language skills using the ADOS (Lord et al., 2000).

The proportion of individuals with CdLS meeting the cut off for autism on the total ADOS score was 65%, broadly consistent with previous findings (Basile et al., 2007; Berney et al., 1999; Bhyuian et al., 2006; Oliver et al., 2008; Oliver et al., 2011). Eighty-five per cent of the CdLS group met the total ADOS cut-off score for ASD, which was higher than expected and may reflect the limited sensitivity of the ADOS for individuals with more severe levels of ID (Moss & Howlin, 2009). Significantly more individuals in the ASD group scored above the cut-off for autism, although there were no differences in

the proportions meeting ASD cut off, suggesting that individuals with CdLS may be more likely to show a "milder" presentation of ASD symptomatology than those with ASD.

At domain level, 90% of individuals with CdLS met the cut off for ASD on both the communication and social interaction domain; 60% and 65% scored above the autism cut off on the communication and social interaction domains respectively. Consistent with findings from other studies involving larger samples of individuals with CdLS and different assessments of ASD (Oliver et al., 2011; Moss et al., 2010), the CdLS group was significantly less likely to show repetitive and stereotyped behaviours compared to the ASD group, in particular fewer sensory related behaviours, indicating subtle differences in the nature and severity of repetitive behaviours between the two groups.

The CdLS group used eye contact and gestures significantly more and stereotyped phrases significantly less, while they also obtained higher anxiety ratings compared to individuals with ASD. Less impaired eye contact in the CdLS group is particularly interesting and is consistent with Nelson (2010) who described frequent and prolonged eye gaze in CdLS compared to Down syndrome. Increased anxiety in CdLS is also consistent with previous reports of increased levels of social anxiety in the syndrome (Goodban, 1993; Collis et al., 2006; Moss et al., 2008; Richards et al., 2009) and suggests that the nature (and possibly the underlying causes) of social impairments in CdLS may be different to those observed in ASD. Taken together, these findings suggest that individuals with CdLS have motivation or desire to engage with others (indicated by frequent eye contact), combined with a lack of skill/ability to engage (indicated by social and communication impairments) and anxiety relating to social encounters (indicated by the higher rates of anxiety). The differences between individuals with CdLS and ASD in repetitive behaviour and the subtle differences in other aspects of the triad of impairments are masked when evaluating clinical cut off and domain level scores alone. A more detailed approach is required in order to identify the precise nature of ASD symptomatology in individuals with genetic syndromes.

Understanding the similarities and differences in the presentation of the ASD triad of impairments in genetic syndromes may be helpful in furthering our understanding of the underlying aetiology of ASD (Persico & Bourgeron, 2006). Other syndromes in which subtle differences in ASD symptom presentation have been reported include Fragile X, Angelman and Rett syndromes and Tuberous Sclerosis Complex (see Cornish, Turk & Levitas, 2007; Hall, Lightbody, Hirt, Rezvani & Reiss, 2010; Mount, Hastings, Reilly, Cass & Charman, 2003; Moss & Howlin, 2009; Trillingsgaard & Østergaard,

2004). Mandy and Skuse (2008) also describe several studies reporting children with a diagnosis of autism who do not demonstrate the full triad of impairments. Others have reported large individual differences in developmental trajectories and response to intervention in the different domains of the ASD triad (i.e. Charman et al., 2005; Charman & Swettenham, 2001; Happé, Plomin & Ronald, 2006), while genetic studies have shown some level of independence between these diagnostic domains in ASD (i.e. Happé et al., 2006; Happé & Ronald, 2008). The apparent "fractionation" of the triad of impairments in individuals with different genetically defined disorders and even in individuals with diagnoses of ASD themselves raises difficulties regarding the conceptualisation of Autism as a spectrum disorder and the way in which its boundaries can and should be defined. Syndromes such as CdLS in which fractionation of ASD presentation is evident may prove to be particularly important in this pursuit, particularly when making comparisons with other genetic syndromes that have divergent ASD profiles.

What remains less clear are the clinical implications of these atypicalities. There is currently little, if any, evidence to show that children with 'atypical autism' are any different to those with ASD with regard to the difficulties they face, the interventions they need and their prognoses (Mandy & Skuse, 2008). In the case of genetic syndromes, we are not aware of any studies that have reported on the effectiveness of autism specific interventions, although anecdotal descriptions indicate that such programmes may be helpful to an individual's progress (see Moss & Howlin, 2009 for example case studies). A combination of autism specific programmes and more targeted intervention in the specific areas of difficulty (i.e. social anxiety in the case of CdLS) may prove to be most helpful in children with genetic syndromes and atypical ASD presentations.

The above findings should be considered alongside the study's limitations. Sample size was relatively small and thus may have limited statistical power. However, the groups were closely matched for degree of ID and receptive language skills, ensuring greater control over these confounds than previous studies of ASD in CdLS. While the matching criteria may have impacted on the representativeness of the sample, analysis indicated that the selected CdLS group were broadly similar to the non-selected individuals in the larger sample on overall levels of adaptive behaviour and receptive language skills. The item-level results should be treated with caution, given the relatively small group sizes and the risk of some differences occurring by chance. Although the ADOS is considered the "gold standard" assessment tool in the diagnosis of ASD, only this, single direct observational measure of ASD symptomatology was employed in our study. Furthermore, the validity of the ADOS assessment in

individuals with genetic conditions such as CdLS is still not well understood. Future studies might consider using both direct and indirect assessments in addition to assessments which consider broader social abilities and not simply ASD specific measures. Access to early intervention programmes in approximately half of the ASD sample may have influenced the severity of ASD symptomatology in this group. However, Magiati et al. (2007; 2011) found no significant effect of intervention on the severity of ASD in the larger sample from which the current participants were selected. Finally, there were fewer males in the CdLS group. Given the strong influence of gender identified in the wider ASD population (Baird et al., 2006), it is possible that this may have impacted on the findings. However, if this gender discrepancy were a relevant confound, then one might argue that this would result in greater heterogeneity in the presentation of ASD in the CdLS group.

Conclusions:

Our findings support previous reports of subtle but significant differences in ASD symptomatology between CdLS and individuals with idiopathic ASD. The current study indicates that there may be distinguishing topographies of repetitive behaviours (specifically sensory interests) between individuals with CdLS and ASD. Further, other specific distinguishing features possibly include less stereotyped speech, less impaired gestures and eye contact and higher levels of anxiety compared to the ASD group. Finally, this study highlights that the use of clinical cut off scores and total scores alone may mask more subtle, but potentially significant, differences in the precise nature of ASD symptomatology in genetic syndromes. Carefully matched participants and a more detailed approach at item level is required to more accurately describe and identify ASD-related difficulties and to ensure that any interventions are appropriately targeted and thus more likely to be effective.

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Table 1: Participant characteristics

	CdLS Mean (SD) *range*	ASD Mean (SD) *range*	t/χ²	*p* value	Effect size
CA	11.34 (1.94) *6.74 – 13.98*	10.42 (0.86) *8.88-11.79*	-1.93	.06	.30
N Male	7	18	12.91	<.001	.57
VABS AE *Communication*	31.60 (23.32) *9.00-95.00*	33.50 (26.69) *11.00-97.00*	0.24	.81	.04
Daily living skills	34.65 (18.60) *7.00-66.00*	38.95 (17.29) *19.00-76.00*	0.76	.45	.12
Socialisation	37.35 (29.99) *10.00-124.00*	26.75 (14.03) *12.00-69.00*	-1.43	.16	.23
Adaptive Behavior Composite AE	34.52 (23.18) *9.60-94.00*	33.65 (18.48) *14.00-79.00*	-0.13	.90	.02
Adaptive Behavior Composite raw	99.10 (38.53) *57.00 – 184.00*	105.00 (35.33) *73.00-196.00*	.51	.72	.06
BPVS AE	43.45 (22.25) *28.00-101.00*	42.90 (23.03) *28.00-91.00*	-.08	.94	.01
BPVS raw	24.80 (29.27) *0.00-88.00*	25.00 (28.09) *0.00-78.00*	.02	.98	.004

CA = chronological age; AE= age equivalence; VABS = Vineland Adaptive Behavior Scale (Sparrow et al., 1984); ABC = Adaptive Behavior Composite; BPVS = British Picture Vocabulary Scale (Dunn et al., 1997).

Table 2: Maximum possible scores and cut off scores for modules 1-3 of the ADOS

		Communication	Social Interaction	Communication + Social Interaction	Play	Repetitive behaviour
Module 1	*Maximum score*	10	14	24	4	6
	ASD cut off	2	4	7	-	-
	Autism cut off	4	7	12	-	-
Module 2		10	14	24	2	6
		3	4	8	-	-
		5	6	12	-	-
Module 3		8	14	22	2	8
		2	4	7	-	-
		3	6	10	-	-

- cut off scores are not available for these domains

Table 3: proportion of participants scoring above clinical cut off scores (total N ₚₑᵣ ₉ᵣₒᵤₚ=20).

	ADOS Domain	ASD % above cut off (N)	CdLS % above cut off (N)	χ^2	*p* value
ASD cut off	*Communication*	100.0 (20)	90.0 (18)	**	.49
	Social Interaction	100.0 (20)	90.0 (18)	**	.49
	Total Social-Communication Score	100.0 (20)	85.0 (17)	**	.23
Autism cut off	*Communication*	90.0 (18)	60.0 (12)	4.80	**.07**
	Social Interaction	95.0 (19)	65.0 (13)	**	**.04**
	Total Social-Communication Score	95.0 (19)	65.0 (13)	**	**.04**

Clinical cut off scores are not available for imagination/play or repetitive behaviour domains.
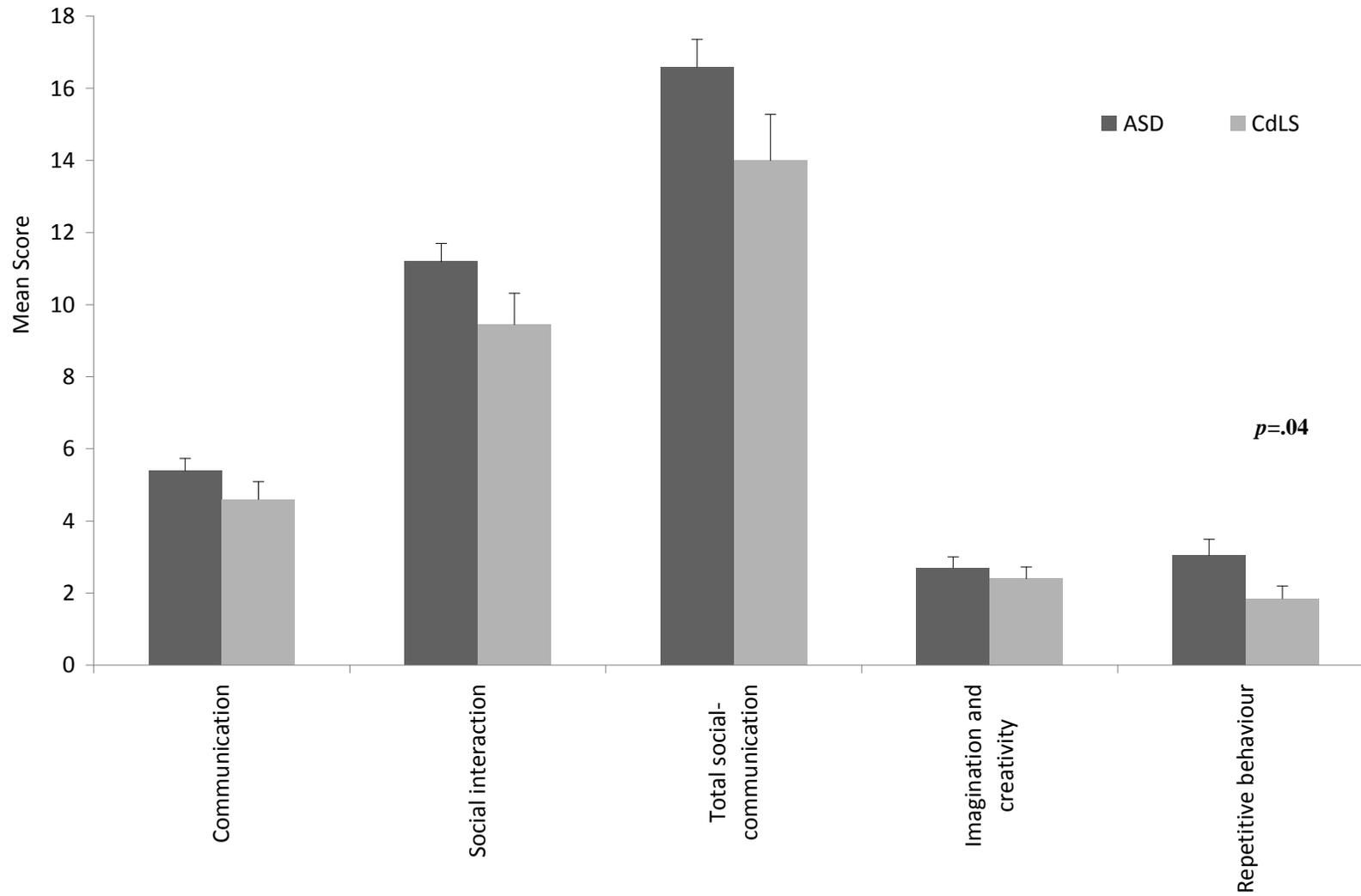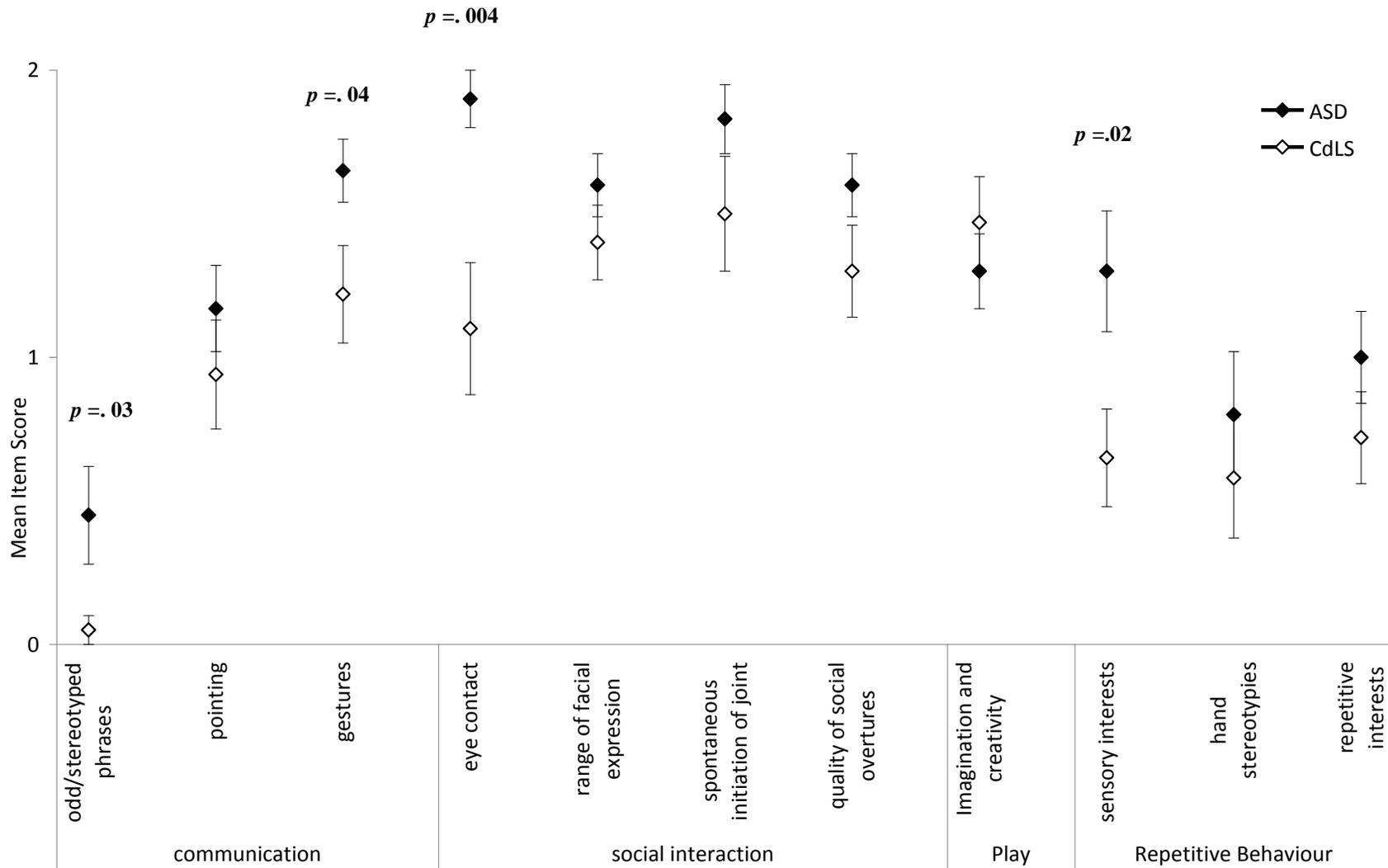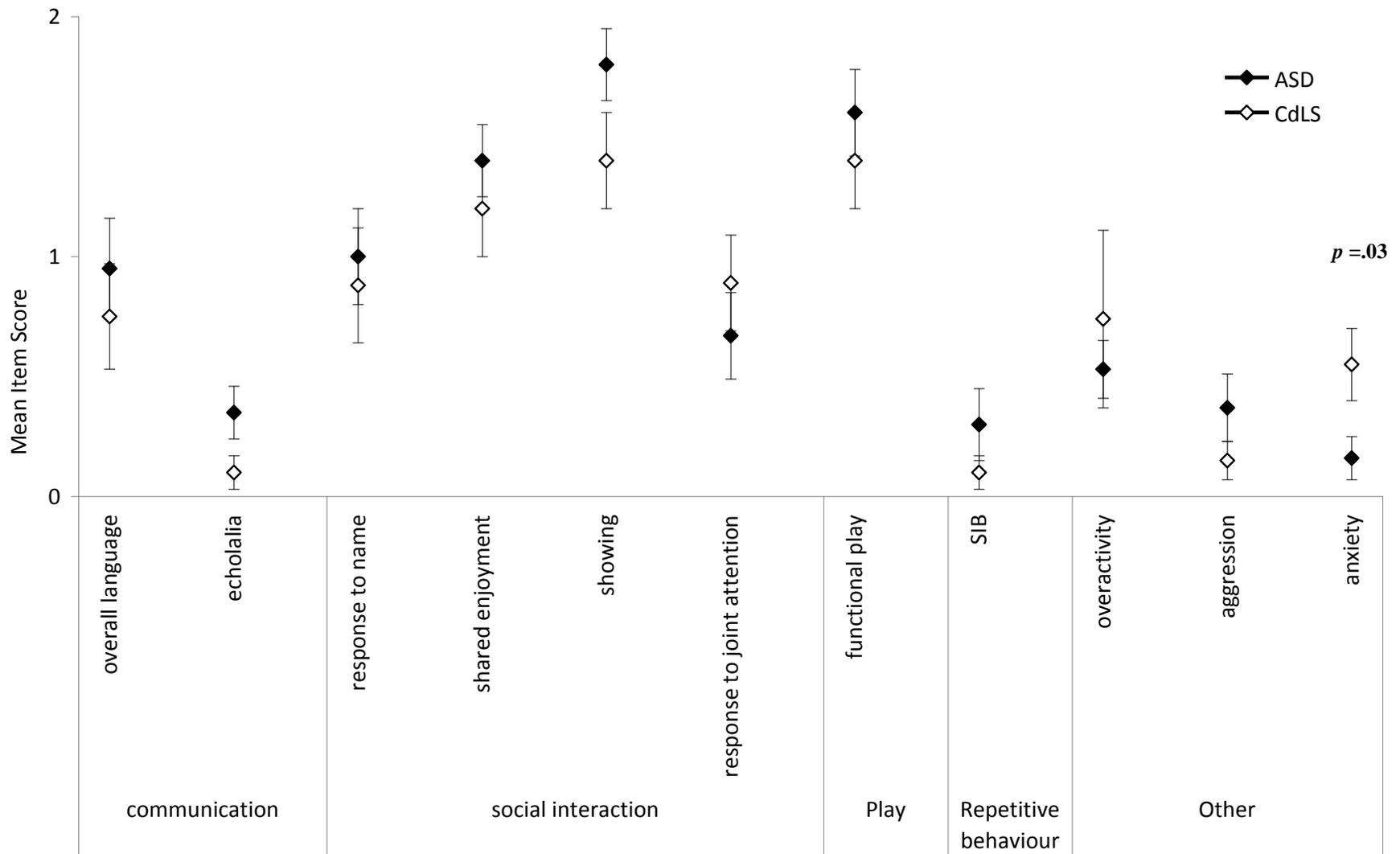** Fisher's exact (value not available in SPSS)

Figure 1: Mean ADOS domain scores and standard error bars. * *p* <.05

Figure 2: Mean ADOS algorithm item level scores. Only items which are shared across modules 1 to 3 are included. A higher score = greater severity of impairment.

Figure 3: Mean ADOS non-algorithm item level scores. Only items which are shared across modules 1 to 3 are included. A higher score = greater severity of impairment.

Key points:

- The prevalence of ASD is reported to be comparatively high in individuals with CdLS.

- As has been identified in many genetic syndromes, the presentation of ASD characteristics is considered to be atypical relative to individuals with ASD, although no previous studies have directly made this comparison.

- The findings in this study indicate that there may be shared characteristics of ASD phenomenology between individuals with CdLS and those with idiopathic ASD at a broad domain level. However, subtle differences in the manifestation of these characteristics are identifiable at a more refined level of investigation. Specifically, fewer repetitive behaviours, more eye contact, more gestures, less stereotyped speech and higher levels of anxiety were identified in CdLS compared to the ASD group.

- These subtle differences in the presentation of ASD characteristics may have important implications for clinical assessment and intervention in individuals with CdLS, and the wider genetic syndrome population.

- The findings also contribute to an expanding evidence base identifying atypicalities in ASD related characteristics among individuals with genetic syndromes which may have important implications regarding understanding and conceptualisation of ASD within this population.