Title: Profiles of atypical sensory processing in Angelman, Cornelia de Lange and Fragile X syndromes

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Abstract

Background: There is growing evidence to suggest that children with neurodevelopmental disorders may evidence differences in their sensory processing. The aim of this study was to compare sensory processing patterns in three genetic syndromes associated with sensory difference.

Method: Sensory processing in Angelman syndrome (AS; *n* = 91), Cornelia de Lange syndrome (CdLS; *n* = 28) and Fragile X syndrome (FXS; *n* = 40) was examined using the informant report measure the Sensory Experiences Questionnaire (SEQ).

Results: All three groups were associated with a heightened prevalence of unusual sensory processing in comparison to normative data, evidenced in over 80% of all participants. Cross-syndrome comparisons highlighted syndrome-specific sensory processing profiles, with heightened hypo responsivity in CdLS and sensory seeking in AS.

Conclusions: The results have important implications for the understanding of sensory processing in genetic syndromes and the development of tailored behavioural interventions.

Keywords: Angelman syndrome, Cornelia de Lange syndrome, Fragile X syndrome, Sensory processing

Profiles of atypical sensory processing in Angelman, Cornelia de Lange and Fragile X syndromes

BACKGROUND

There is growing evidence that some children and adults with neurodevelopmental disorders evidence unusual responses to sensory stimuli. The main focus of research has been within Autism Spectrum Disorder (ASD), in which it is estimated that over 60–70% of children display unusual behavioural responses to sensory stimuli (Baranek *et al.* 2007; Baranek *et al.* 2006). Processing differences in ASD are described across sensory modalities including auditory, visual and tactile domains (Tomchek & Dunn 2007) and across both social and non-social contexts (Baranek *et al.* 2013). The identification of atypical sensory processing has led to the inclusion of sensory sensitivity within *The Diagnostic and Statistical Manual of Mental Disorders* criteria (5th ed.; DSM–5; American Psychiatric Association 2013). With this increasing focus on sensory processing, there is emerging interest within the wider intellectual disability (ID) population, particularly in the association with other characteristics of ASD (Baranek *et al.* 2006; Kientz & Dunn 1997; Simpson *et al.* 2019).

Children who display unusual responses towards sensory stimuli are often described as having 'sensory processing difficulties', although the presentation is variable. Sensory responses can be categorised as *hyper*-responsive ('over' responsive/sensitive to sensory experiences), or *hypo*-responsive (under-responsive/low sensitivity). These contrasting responses to sensory input are not necessarily mutually exclusive; individuals may be hypo- and hyper-responsive to different modalities of sensory input (Baranek *et al.* 2006). In Dunn and Brown (1997)'s theory of sensory processing, behaviours indicative of sensory responsiveness can be further categorised as *passive* or *active*, depending on the behavioural response. For example, behaviour in children who have a low sensitivity to sensory events may present with a lowered response to external events (passive; e.g. ignoring/not responding

to loud noises) and/or sensory seeking (active; e.g. seeking out auditory stimuli). In order to describe the nature of sensory processing within an individual adequately, sensory processing is often described in terms of the *type* of responsiveness and the *modality* for which the response occurs. Whilst this process may be less revealing in neurodevelopmental disorders in which sensory sensitivity is found across all modalities, emerging literature suggests that certain genetic syndromes may be associated with specific sensory processing patterns in the absence of a diagnosis of ASD. Examples include hypo-responsivity across sensory modalities in Down syndrome (Bruni *et al.* 2010) and hyper-responsivity towards auditory stimuli in Williams syndrome (Nigam & Samuel 1994). Delineating the specific sensory profiles associated with a syndrome can contribute to tailoring behavioural management programmes (Baranek, 2002) and has the potential to inform the delineation of different pathways to observable characteristics of ASD.

Angelman syndrome (AS), Cornelia de Lange syndrome (CdLS) and Fragile X syndrome (FXS) are three genetic syndromes associated with unusual responses to sensory stimuli in the literature. AS, prevalent in approximately 1 in 10,000 live births, is caused by disrupted information on the maternal chromosome 15q11-13 region (Buckley *et al.* 1998; Williams 1995). AS is associated with a range of clinical characteristics, including seizures, ataxic gate and a severe to profound ID (Horsler & Oliver 2006a; Pelc *et al.* 2008; Peters *et al.* 2004). The behavioural phenotype of AS is characterised by frequent laughing and smiling (Adams *et al.* 2011, 2015; Horsler & Olive, 2006b), sleep difficulties (Pelc *et al.* 2008) and a high prevalence of ASD (34.0%; Richards *et al.* 2015). AS is also associated with behaviours indicative of unusual sensory processing; children and adults are often described as having ‘fascination’ with water and shiny/reflective objects (Didden *et al.* 2008). Broad sensory processing difficulties are reported (Walz & Baranek 2006), although the

precise nature of the response and modality in which this is evident has been relatively unexplored.

CdLS is prevalent in approximately 1 in 30,000 live births (Beck 1976). A number of genetic pathways to CdLS have been identified, with phenotypic variability noted across variants (Kline *et al.* 2018). Clinical characteristics noted include limb abnormalities, distinctive facial characteristics and gastrointestinal disorders, with the degree of ID ranging from mild to profound (Kline *et al.* 2007; Oliver *et al.* 2008). The behavioural phenotype of CdLS is characterised by a high prevalence of ASD (43%; Moss *et al.* 2009; Richards *et al.* 2015), social anxiety (Richards *et al.* 2009) and an increased likelihood of self-injurious behaviour (Arron *et al.* 2011). Unusual responses to sensory stimuli are suggested in the literature, with particular reference to lowered sensory sensitivity and heightened pain threshold (Berney *et al.* 1999).

FXS syndrome (FXS), prevalent in approximately 1 in 4,000 males and 1 in 8,000 females (Crawford et al., 2002), is caused by expansions of CGG trinucleotide repetitions in the *FMR1* gene. FXS is associated with a mild to moderate ID (Kemper *et al.* 1988; Merenstein *et al.* 1996), executive function deficits (Hooper *et al.* 2008) and a high prevalence of ASD (22.0%; Moss & Howlin 2009; Moss *et al.* 2012; Richards *et al.* 2015). Behavioural differences between genders are described, with a milder phenotype reported in females (Cornish *et al.* 2008). Unusual responses to sensory stimuli are noted both within informant report (Baranek *et al.* 2002; Rogers *et al.* 2003) and direct observations (Baranek *et al.* 2008).

Although sensory processing difficulties have been described in all three syndromes, there is evidence to suggest that there may be syndrome-related profiles of behaviours towards sensory stimuli. AS is associated with a range of atypical behavioural responses towards both social (Mount *et al.* 2011) and non-social stimuli (Didden *et al.* 2006) indicative

of Dunn's description of 'sensory seeking' within the sensory processing model (Dunn & Bennett 2002), but with few descriptions of hyper-responsivity. This contrasts with FXS, in which children and adults are reported to show hyper-responsivity to sensory stimuli (Miller *et al.* 1999), and CdLS, where there are anecdotal reports of hypo-responsivity (Berney *et al.* 1999). Despite evidence suggesting differences in sensory profiles, to date there have been no direct cross-syndrome comparisons. Research examining sensory processing in genetic syndromes typically compares individual groups to children with ASD and typically developing children, highlighting broad sensory processing difficulties rather than delineating sensory profiles.

In addition to the *profile* of behaviours towards sensory stimuli in AS, CdLS and FXS, the association between this and person characteristics, including age, gender and adaptive behaviour, has been neglected. An association between age/adaptive behaviour and sensory processing is often described in the ID literature, with studies suggesting higher levels of sensory processing difficulties with lower adaptive functioning (Jasmin *et al.* 2009; Lane *et al.* 2010; Rogers *et al.* 2003), although this is not reported consistently (O'Donnell *et al.* 2012). Given the low levels of adaptive behaviour in AS and CdLS (Peters *et al.* 2004), there is a rationale to examine whether the observed sensory processing difficulties frequently reported within these syndromes are independent of these skills.

The current study was designed to describe the sensory processing profiles of AS, CdLS and FXS using the Sensory Experiences Questionnaire (Baranek 1999), an informant report questionnaire measuring responses to everyday sensory events. Whilst AS, CdLS and FXS are not comparable across some characteristics including adaptive behaviour (Oliver *et al.* 2008, 2013; Peters *et al.* 2004) and ASD (Oliver *et al.* 2011), all three syndromes are associated with unusual sensory processing. Comparing sensory processing in AS, CdLS and

FXS may identify how these behaviours may present across different syndromes in which broadly similar levels of sensory processing difficulties are reported.

This study had three main aims:

i) To examine the proportion of individuals with FXS, CdLS and AS exhibiting 'unusual' responses to sensory stimuli compared to typically developing children (TD), children with ASD and children with a developmental delay (DD).
ii) To compare sensory processing across FXS, AS and CdLS.
iii) To examine the association between sensory processing and age, gender and self-help skills across AS, FXS and CdLS.

METHOD

Recruitment

Parents/carers of children aged between 2 and 15 years inclusive with AS, CdLS and FXS were invited to take part in an online questionnaire study. Families were invited to take part following their participation in a large-scale questionnaire study exploring behaviour in neurodevelopmental disorders, conducted at (anonymised for blind review) and through syndrome support groups.

Participants

One hundred and sixty-two parents/carers completed the survey. Inclusion criteria were: a diagnosis of the genetic syndrome from a relevant professional (e.g. clinical geneticist), aged between 2 and 15 years and no additional chromosomal abnormalities. Children with FXS were only recruited if they were male, as behavioural differences across gender are often

reported (Dykens *et al.* 2000). Three participants did not meet the inclusion criteria and were excluded from the analysis. Table 1 displays the participant demographics for the final sample of 159 parents/carers of children with AS (N = 91), CdLS (N = 28) and FXS (N = 40).

+++Insert Table 1 about here+++

As expected, analysis of the demographic characteristics showed a significant gender difference across groups, as all participants with FXS were male. AS and CdLS were associated with significantly lower self-help scores than FXS, and a greater degree of impaired mobility. FXS and CdLS showed significantly higher levels of ASD characteristics than individuals with AS.

Although comparisons across demographic characteristics revealed differences across measures of self-help and ASD characteristics, there is already a well-established literature on the comparatively low levels of adaptive abilities in AS and CdLS (Oliver *et al.* 2008) and ASD characteristics in FXS and CdLS (Oliver *et al.* 2011).

Procedure

Parents/carers were invited to complete the survey online, with six parents (3.8%) requesting a paper copy of the survey.

Measures

Demographic questionnaire

Parents/carers provided information on demographic characteristics including date of birth, gender, mobility, speech and genetic diagnosis.

The Wessex Behaviour Scale (Kushlick et al. 1973)

The Wessex Behaviour Scale is a 15-item informant report questionnaire which gives an estimate of self-help skills.. Whilst not a comprehensive measure of adaptive behaviour, the Wessex is a brief reliable measure for use in large scale surveys which provides an indication of ability including reading, writing, mobility, vision and continence within individuals with ID. The Wessex produces a self-help score out of 9, with higher scores indicating a greater degree of self-help skills. The measure has good inter-rater reliability (Kushlick *et al.* 1973) and has previously been used with both children and adults with ID (for example, Moss, Richards, Nelson & Oliver, 2012; Oliver, Petty, Ruddick & Bacarese-Hamilton, 2012)

Sensory Experiences Questionnaire (SEQ; Baranek 1999)

The Sensory Experiences Questionnaire (SEQ version 2.1) is an informant report questionnaire which measures sensory experiences in children aged 6 months to 6 years. Three subscales relate to the response to sensory input: *hypo-responsivity*, *hyper-responsivity* and *sensory seeking*. The SEQ has additional subscales measuring responses in different environmental contexts: *social* and *non-social*, and across modalities: *tactile*, *visual*, *auditory*, *vestibular* and *gustatory*. Higher scores indicate a greater degree of sensory processing difficulties. The SEQ has a good reliability and validity, with an internal consistency of 0.8 and test-retest reliability of 0.92 (Version 1.0; Little *et al.* 2011)[1]. The SEQ version 2.1 has been used with children with autism and ID (Watson *et al., 2011*). Concurrent validity has been established with direct measures of sensory processing (Baranek & Costello 2003). Although predominantly designed for children aged six months to six years of age, the SEQ has previously been used with individuals with Angelman syndrome aged two to 22 years old (Walz & Baranek, 2006).

[1] Version 2.1 contains the same questions as 1.0, with the addition of the 'sensory seeking' subscale to capture sensory behaviours which do not fall into the category of hyper- or hypo-responsive

Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003)

The SCQ is a 40 item informant report questionnaire which assesses the presence of Autism Spectrum Disorder (ASD) characteristics. It is comprised of three subscales: *social interaction*, *communication* and *stereotyped patterns of behaviours*. The SCQ is an Autism screening questionnaire, with higher scores indicating a greater presence of Autism Spectrum characteristics. The SCQ has good internal consistency (Berument, Rutter, Lord, Pickles, & Bailey, 1999).

Data analysis

In order to establish the prevalence of 'unusual' sensory responses, data for each group were compared to normative data for typically developing children (TD), children with Autism and children with a developmental delay (DD) from the SEQ manual (Baranek 1999). Two cut-offs for 'clinically significant' differences in behaviour are included in the SEQ manual based on data from TD children: 'at risk' (-1 SD from the mean) and 'deficient' (-2 SD). The proportion of participants in each group exceeding cut-offs was calculated in order to estimate the presence of sensory processing differences in this sample.

Data from each syndrome group were also compared to data (mean and SD) provided in the manual for TD, DD and ASD using one sample t-tests. The data from the SEQ subscales relating to 'context' should be interpreted with caution, as only the data from the responsiveness subscales were normally distributed. There are no normative data for the modality subscales.

In order to compare sensory processing profiles *across* groups, comparisons of SEQ total and subscale scores were conducted across AS, CdLS and FXS. To allow for comparisons across subscale scores, mean item subscale scores were calculated. Where the

distribution of data did not differ from normality, established using the Kolmogorov–Smirnov test ($p > 0.05$), parametric statistics were employed. As two of the 'responsiveness' subscales (*hypo-* and *hyper-responsivity*) were normally distributed, a syndrome group by responsiveness mixed ANOVA was conducted. Although *sensory seeking* scores were not normally distributed, ANOVAs are considered to be robust even when dealing with statistics which violate the assumption of normality (Maxwell & Delaney 2004). In order to check the validity of these findings, non-parametric post hoc analyses were conducted. Where the data were not normally distributed, Kruskal-Wallis analyses were employed with Mann-Whitney post hocs, as data could not be transformed. All post hoc analyses were fixed at $p<0.01$ to allow for multiple comparisons.

Within each group, the association between SEQ subscale scores and age, gender and adaptive ability was examined. Differences across gender were examined using Mann-Whitney tests, as the data were not normally distributed. The association between SEQ scores, age and self-help skills were assessed using Spearman Rho correlation coefficients.

RESULTS

Sensory processing

Clinical cut-offs

Using the SEQ manual cut-offs, 87.9% of children with AS exceeded the 'at risk' cut-off, as did 92.9% of children with CdLS and 80.0% of children with FXS ($\chi^2=2.61$, $p=0.27$). Figure 1 displays the percentage of participants exceeding clinical cut-offs. As shown, the results highlight within syndrome variability in the proportion of children exceeding individual subscales, with between 3.6% and 55% of participants within 1 SD of the typical range (see Figure 1).

+++Insert Figure 1 about here+++

Chi Square tests across syndrome groups using the proportion of children exceeding the 'at risk' cut-off revealed no significant difference for *sensory seeking* (χ^2=4.17, p=0.12), *hyper-responsivity* (χ^2=4.29, p=0.12) and *non-social* (χ^2=0.68, p=0.71). There was a significant difference in the proportion of participants exceeding the cut-off for the subscales across syndrome groups for *hypo-responsivity* (χ^2=11.33, p<0.01) and *social* (χ^2=7.93, p<0.05), driven by a higher proportion of children with CdLS exceeding the cut-off than children with AS (*hypo responsivity*: χ^2=10.13, p<0.01; *social*: χ^2=4.83, p=0.03).

Sensory processing in AS, FXS and CdLS

Table 2 shows the mean SEQ subscale scores across AS, CdLS and FXS, alongside TD, DD and ASD normative data.

+++Insert Table 2 about here+++

Responsiveness

Comparison to normative data

The responsiveness subscale scores for AS, FXS and CdLS were compared to normative data provided in the SEQ manual using one sample t-tests (see Table 2). AS, CdLS and FXS scored significantly higher than TD and DD groups on *hypo-responsivity* and *sensory seeking* subscales. CdLS and FXS scored higher than TD and DD on *hyper-responsivity*, with AS scoring higher only than the TD group. Scores from the SEQ ASD comparison sample scored lower only on *hypo-responsivity* in comparison to CdLS and lower on *sensory seeking* compared to AS.

Comparison across syndrome groups

Figure 2 displays the mean item scores for subscales relating to responsiveness to sensory stimuli. SEQ manual normative data are shown in Figure 2 for reference. A responsiveness by syndrome group mixed ANOVA showed a significant syndrome x responsiveness interaction ($F(4,312)=10.95$, $p<0.001$, partial $\eta^2=0.12$). There was also a significant effect of syndrome group ($F(2,150)=9.51$, $p<0.001$, partial $\eta^2=0.11$) and subscale ($F(2,312)=45.00$, $p<0.001$, partial $\eta^2=0.22$), largely driven by the interaction. Post hoc analyses across syndrome groups revealed a significant difference in scores for the *hypo-responsivity* subscale ($F(2,158)=18.54$, $p<0.001$, partial $\eta^2=0.19$), driven by significantly higher levels of scores in CdLS compared to FXS and AS (FXS: $t(66)=3.39$, $p<0.01$, $d=.81$; AS: $t(117)=6.20$, $p<0.001$, $d=1.22$). There was also a significant difference across groups for *hyper-responsivity* scores ($F(2,158)=9.05$, $p<0.001$, partial $\eta^2=0.10$), driven by significantly higher scores in CdLS than AS ($t(117)=3.48$, $p<0.01$, $d=.69$). The difference across groups for the sensory seeking subscale approached significance ($\chi^2=5.59$, $p=0.06$).

++++ Insert Figure 2 about here +++

Analyses *across* responsiveness subscales within syndromes revealed significant differences across subscales in AS ($F(2,180)=100.91$, $p<0.001$, partial $\eta^2=0.53$), CdLS ($F(2,54)=4.21$, $p<0.05$, partial $\eta^2=0.26$) and FXS ($F(2,78)=10.13$, $p<0.001$, partial $\eta^2=0.14$). Post hoc analyses revealed that in AS these differences were driven by significantly higher *sensory seeking* scores than *hypo-responsivity* ($t(90)=12.92$, $p<0.001$, $d=.81$) and *hyper-responsivity* ($t(90)=10.38$, $p<0.001$, $d=.74$). In FXS *sensory seeking scores* were higher than *hypo-responsivity* only ($t(39)=4.87$, $p<0.001$, $d=.61$). In CdLS *sensory seeking* scores were higher than *hyper-responsivity* ($t(27)=2.87$, $p<0.01$, $d=.48$).

To summarise, CdLS was associated with a greater level of hypo-responsivity towards sensory stimuli compared to AS and FXS. AS was associated with higher levels of seeking behaviours towards sensory experiences, compared to the likelihood of displaying hyper- and hypo-responsive behaviours. Seeking behaviours in AS were more prevalent relative to FXS and CdLS, but this did not reach significance. FXS was associated with heightened hyper-responsivity towards sensory experiences relative to children with AS.

Context

Comparison to normative data

Figure 3 shows SEQ subscale mean item scores relating to the context for sensory responsiveness: *social* and *non-social*. Single sample t-tests revealed that individuals with AS, CdLS and FXS scored significantly higher on both *social* and *non-social* subscales than the TD and DD groups. Additionally, CdLS scored higher than those in the ASD group on both context subscales.

+++Insert Figure 3 about here+++

Comparison across syndrome groups

Significant differences across syndrome groups were found for the subscale *social* (χ^2=24.08, p<0.001), driven by lower scores in AS than CdLS (Z=-3.78, p<0.001, r=0.37) and FXS (Z=-4.03, p<0.001, r=0.35). No significant effect for *non-social* was found (χ^2=5.39, p=0.07).

Sensory modality

Figure 4 shows the mean item scores for SEQ subscales relating to sensory modality. No comparisons to TD, DD and ASD groups were made as there are no normative data for modality scores. There were significant syndrome group differences for the subscales *visual*

(χ^2=13.65, p<0.01), *tactile* (χ^2=20.44, p<0.001) and *auditory* (χ^2=13.74, p<0.01). Post hoc analyses revealed that these differences were driven by significantly higher scores in CdLS compared to FXS and AS for the *visual* subscale (AS: Z=-3.64, p<0.001, r=0.34; FXS: Z= -2.89, p<0.01, r=0.35) and for the *tactile* subscale (AS: Z=-4.53, p<0.001, r=0.42; FXS: Z=-2.47, p=0.01, r=0.30). Differences in the *auditory* subscale were driven by higher scores in FXS compared to AS (Z=-3.78, p<0.001, r=0.33).

+++Insert Figure 4 about here+++

To summarise, both AS and FXS were associated with fewer 'unusual' responses to visual and tactile stimuli than CdLS. In addition, children with FXS showed a higher frequency of unusual responses to auditory sensory stimuli in comparison to children with AS.

Factors relating to sensory processing

Gender

As the data were not normally distributed, gender differences in CdLS and AS were analysed using Mann Whitney comparisons. As previously acknowledged, no female participants with FXS were recruited, thus no analyses could be conducted. For CdLS and AS, there were no differences across gender for any of the SEQ subscales (p's>0.05).

Age

In order to assess the relationship between age and SEQ scores, Spearman Rho correlations were conducted between age and SEQ subscale scores (see Table 3). There were no significance associations between age and SEQ subscale scores for AS and CdLS. In FXS, there was a significant negative relationship between age and *sensory seeking* scores (*R*=-0.48, *p*<0.01) and *vestibular* scores (*R*=-0.49, *p*<0.01), suggesting that older children

displayed fewer unusual responses towards sensory stimuli, including seeking behaviours, and behaviours towards vestibular sensory experiences.

+++Insert Table 3 about here+++

Self-help skills

In order to assess the association between self-help skills and SEQ scores, Spearman Rho correlations were conducted between total self-help scores and each responsiveness subscale on the SEQ. In FXS and AS, higher levels of sensory processing difficulties were associated with lower levels of self-help skills for several subscales: *hypo-responsivity* (FXS: R=-.50, p<.01), *sensory-seeking* (AS: R=-.33, p<.01; FXS: R=-.55, p<.01), *non-social* (FXS: R=-.50, p<.01) and *visual* (AS: R=-.30, p<.01; FXS: R=-.48, p<.01). There were no significant relationships between sensory processing subscales and self-help skills in CdLS.

As 65.0% of the sample of children with CdLS had hearing difficulties, differences across those rated as having 'normal' hearing compared to 'poor' were analysed using Mann Whitney comparisons. No significant differences were obtained for any of the SEQ subscales (p's>0.05).

DISCUSSION

The main aim of this study was to examine profiles of sensory processing across AS, CdLS and FXS. Whilst sensory processing in AS and FXS has been examined previously, this is the first study to delineate the profile of behaviours towards sensory stimuli across AS, CdLS and FXS in terms of responsivity, context and association to participant characteristics. The results suggest that all three syndrome groups evidence different responses to sensory stimuli when compared to typically developing children and children with ID. Cross-syndrome comparisons suggest syndrome-related sensory processing profiles, with sensory seeking behaviours evident in AS, hypo-responsivity in CdLS and hyper-responsivity in FXS. Associations between self-help skills and sensory processing were not consistent, suggesting that sensory processing differences observed may not be due to the level of intellectual ability alone.

Children with AS, FXS and CdLS displayed higher levels of unusual responses to sensory stimuli across all dimensions of responsiveness and context subscales compared to TD and DD groups: 87.9% of the total sample of children with AS exceeded the total score cut-off for unusual sensory processing, as did 80.0% of children with FXS and 92.9% of children with CdLS. This supports previous literature reporting unusual responses to sensory stimuli in each of these syndromes (Baranek *et al.* 2002; Baranek *et al.* 2006). Whilst broad sensory processing differences were described across groups, it is important to note the within syndrome variability observed, with between 3.6% and 55% of participants within 1 SD of the 'typical' range. This has important implications for clinical intervention, and highlights the need for comprehensive assessment within these populations.

Cross-syndrome comparisons suggest syndrome-related sensory processing profiles. In AS, although children showed fewer hypo- and hyper-responsive behaviours towards sensory stimuli than children with CdLS and FXS, higher levels of sensory seeking

behaviours were evident. Comparisons *across* responsiveness subscales in AS suggest that the level of sensory seeking behaviours may be higher relative to both hypo- and hyper-responsivity. This suggests that the broad sensory processing differences reported in AS may be driven largely by an 'active' response to lowered sensory sensitivity in Dunn's sensory processing model (Dunn 2007). This is supported by research highlighting a 'fascination' with sensory stimuli relative to individuals without AS (Didden *et al.* 2006; Didden *et al.* 2008). This contrasts with the sensory processing profile commonly reported in ASD, in which the prevalence of sensory seeking behaviours is relative to hyper- and hypo-responsivity (Dunn 2007). This may have important implications for tailoring the learning environment with children with AS and alludes to a differing profile of ASD characteristics.

In FXS, unusual responses to sensory stimuli were evident across all contexts and modalities of sensory stimuli/experiences, supporting existing literature (Baranek *et al.* 2002). There were no significant differences between FXS and ASD for any of the responsiveness or context subscales, consistent with similar investigations across these groups (Rogers *et al.* 2003), and further strengthening the link between ASD and FXS for some characteristics. Although not heightened in comparison to other responsiveness subscale in FXS, hyper-responsivity was heightened compared to AS and the ID and TD data samples. This supports the wider literature on FXS, with behaviours indicative of heightened response to both social and non-social stimuli reported consistently (Cohen *et al.* 1988).

In CdLS, cross-syndrome comparisons highlighted a difference in the frequency of hypo-responsive behaviours with 96.4% of children exceeding the clinical cut-off. Hypo-responsivity in CdLS was higher compared to syndrome groups and the normative data samples, supporting anecdotal report in the literature (Berney *et al.* 1999). Whilst hypo-responsivity and sensory seeking are proposed as indicating lowered sensory sensitivity (Dunn 2007), the difference in the presentation of behaviours is thought to be due to a passive

(hypo-responsivity) or active (sensory seeking) response. The results suggest that although CdLS and AS may both be associated with lowered sensory sensitivity, the striking difference in sensory processing across these syndromes may reflect contrasting behavioural responses to a heightened threshold for sensory input. The results warrant direct investigations in order to delineate the precise nature of behavioural response to sensory stimuli and experiences in these groups. An examination of demographic characteristics yielded no significant associations between age, gender and SEQ scores in AS and CdLS. This supports previous literature examining longitudinal changes in sensory sensitivity in AS which found no significant difference in scores across a 12-month time period (Peters *et al.* 2012). In FXS, older age was associated with lower levels of sensory seeking behaviour and unusual responses to vestibular stimuli. This contrasts with previous examinations of sensory processing in FXS, finding the opposite relationship: *higher* levels of sensory processing difficulties associated with increasing age (Baranek *et al.* 2008). Although it could be argued that this may reflect a discrepancy in the use of measures, it is important to note that the age range of children in Baranek *et al.* (2008) was from 9 months to 5 years in comparison with the wider age range in the current study. Given the age-related differences observed, there is a rationale for examining sensory processing in a larger sample of children with FXS across a broad age range.

As low levels of adaptive behaviour are consistently noted in CdLS and AS (Oliver *et al.* 2008; Peters *et al.* 2004), and sensory processing is consistently associated with adaptive behaviour in ASD and other neurodevelopmental disorders (Lane *et al.* 2010; Olson *et al.* 2007), the association between these behaviours was examined within each group. Self-help skills were associated with two subscales in AS (sensory seeking, visual stimuli), with increasing levels of sensory processing difficulties associated with poorer self-help skills. This may suggest that adaptive behaviour may mediate some areas of sensory processing but,

importantly, it is not the sole factor relating to sensory processing difficulties in AS. There was no association between self-help skills and sensory processing in CdLS.

There are several implications of the results from the study. Understanding sensory processing difficulties can aid the development of behavioural interventions. Although the efficacy of interventions which address directly sensory processing has not been shown (e.g. sensory integration therapy; Hoehn & Baumeister 1994), knowledge about sensory processing, including preference, can be incorporated into behavioural interventions. In AS, the results suggest sensory stimuli may function as effective reinforcers; this is particularly pertinent considering the difficulties with learning noted within this population (Jiang *et al.* 1998). Given the robust association between sensory processing and anxiety identified within the wider literature on neurodevelopmental disorders (e.g. Williams syndrome; Uljarević *et al.* 2018), the identification of syndrome-related sensory processing profiles in FXS and CdLS may also have a role in understanding the heightened prevalence of anxiety reported within these groups (Crawford *et al.* 2017).

The main limitation of the study is the small sample size in CdLS (n = 28), compared to AS (n = 91) and FXS (n = 40), differentially impacting on both comparisons of sensory processing across syndrome groups, and correlations between sensory processing and behavioural characteristics in CdLS. As a consequence, the results presented may underestimate the differences in sensory processing across syndrome groups. Although significant differences were found for CdLS, even with a small sample size, there is a rationale to examine sensory processing in CdLS with a larger sample size. In addition, there is an absence of normative data obtained specifically for this study, with a reliance on historic data collected as part of the SEQ 1.0 reliability analysis. The data are also based upon proxy report, which are interpreted based on an individual's behavioural response to the sensory input (Simpson *et al.*, 2019). Although proxy-reporting is commonplace amongst individuals

with intellectual disabilities, its limitation must be acknowledged and the potential impact of elevated parent stress (Adams et al., 2018a,b) on reporting considered.

Overall, the results support previous literature suggesting that children with AS, FXS and CdLS may experience unusual responses to sensory stimuli in comparison to typically developing children. Cross-syndrome comparisons highlighted syndrome-specific sensory processing profiles with heightened sensory seeking in AS, lowered sensory sensitivity in CdLS and heightened sensitivity associated with FXS. In addition to clinical implications, the results warrant further investigation into sensory processing in these groups, using direct measures to observe children's response to sensory stimuli.

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Table 1. Mean age in years (standard deviation), gender, adaptive behaviour skills and Autism Spectrum characteristics across AS, CdLS and FXS groups

		AS	CdLS	FXS	F / X ^{2}	df	*p*	Post hoc analyses
N*		91	28	40				
Age (years)	Mean (SD)	7.68 (3.77)	8.39 (4.09)	9.24 (3.84)	2.32	2	0.10	-
	Range	2-15	2-15	2-15				
Gender[a]	% Male	49.5	60.7	100	31.05	2	<0.01	FXS > AS, CdLS
Self help[b]	% Partly able/able[c]	31.9	32.1	80.0	28.07	2	<0.01	FXS > AS, CdLS
Mobility[b]	% Mobile	44.4	39.3	85.0	10.66	2	<0.01	FXS > AS, CdLS
Vision[b]	% Normal	80.2	59.3	87.2	7.78	2	0.02	FXS > CdLS
Hearing[b]	% Normal	100.0	35.7	95.0	83.26	2	<0.01	FXS, AS > CdLS
Speech[b]	% Verbal	30.8	64.3	92.5	44.43	2	<0.01	FXS > CdLS > AS
SCQ	Mean score (SD)	16.52 (6.07)	20.88 (5.82)	20.48 (7.08)	7.99	2	<0.01	CdLS, FXS > AS

* N may vary due to missing data.
[a] Females with FXS were excluded from the study because the syndrome characteristics vary between males and females in the syndrome (Dykens et al., 2000).
[b] Information obtained from the Wessex Scale (Kushlick et al., 1973).
[c] Partly able/able if obtain a score of six or above on the self-help sub-scale of the Wessex.

Table 2. Mean subscale scores across AS, CdLS and FXS alongside normative data from the Sensory Experiences Questionnaire manual. Comparisons were made between individual syndrome groups and normative data using single sample t-tests. No normative data were collected for the modality subscales.

	Syndrome group			**SEQ normative data**			
	AS (n = 91)	**CdLS** (n = 28)	**FXS** (n = 40)	**TD** (n = 53)	**DD** (n = 44)	**Autism** (n = 75)	**Single sample t-tests comparisons (p < 0.01)**
Hyper-responsivity	31.02 (7.32)	37.07 (10.10)	36.63 (9.72)	24.08 (4.62)	28.50 (6.10)	35.28 (7.14)	CdLS, FXS, Autism > AS, DD > TD
Hypo-responsivity	12.37 (3.43)	17.32 (4.46)	13.83 (3.99)	8.68 (1.91)	10.45 (3.25)	13.51 (4.34)	CdLS > FXS, Autism, AS > DD > TD
Sensory seeking	41.08 (7.77)	39.93 (6.91)	37.33 (9.32)	29.74 (8.68)	30.59 (9.20)	36.21 (8.39)	AS > ASD, FXS > DD, TD CdLS > DD, TD
Social	20.44 (4.05)	25.43 (6.88)	25.13 (6.88)	15.92 (2.84)	17.82 (4.53)	23.24 (4.62)	CdLS, FXS, Autism > AS > DD, TD
Non-social	62.23 (8.22)	66.50 (10.88)	60.95 (11.55)	45.49 (10.15)	50.30 (10.67)	59.70 (11.02)	CdLS > Autism, AS, FXS > DD, TD
Auditory	15.15 (3.00)	16.00 (3.95)	17.63 (3.72)	-	-	-	
Visual	13.64 (3.60)	17.29 (4.80)	14.00 (3.88)	-	-	-	
Tactile	24.16 (4.29)	30.68 (7.15)	26.45 (6.64)	-	-	-	
Vestibular	12.98 (2.98)	12.50 (2.71)	13.03 (3.72)	-	-	-	
Gustatory	16.85 (3.07)	16.11 (3.98)	15.18 (4.37)	-	-	-	
Total score	84.47 (10.67)	94.32 (16.25)	87.78 (17.28)	-	-	-	

Table 3. Spearman Rho correlations between age/adaptive abilities as assessed by the Wessex scale and Sensory Experiences Questionnaire subscales. Correlations are shown for AS, CdLS and FXS.

	Age			Adaptive Behaviour		
	AS	**CdLS**	**FXS**	**AS**	**CdLS**	**FXS**
Hypo responsive	0.01	0.02	-0.13	-0.22*	-0.10	-0.50**
Hyper responsive	-0.07	-0.11	0.30	-0.05	-0.04	-0.07
Sensory seeking	-0.05	0.27	-0.48**	-0.33**	-0.14	-0.55**
Social	-0.01	0.02	0.06	0.02	0.04	-0.23
Non-social	-0.09	-0.02	-0.13	-0.28**	-0.24	-0.50**
Auditory	-0.10	-0.03	0.17	-0.14	0.20	-0.19
Visual	-0.19	0.09	-0.19	-0.30**	-0.15	-0.48**
Tactile	-0.03	0.05	0.10	-0.14	-0.16	-0.18
Vestibular	0.02	-0.05	-0.49**	-0.15	-0.21	-0.61**
Gustatory	-0.03	-0.20	-0.05	-0.11	-0.24	-0.28
Total score	-0.09	-0.00	-0.08	-0.24*	-0.22	-0.44**

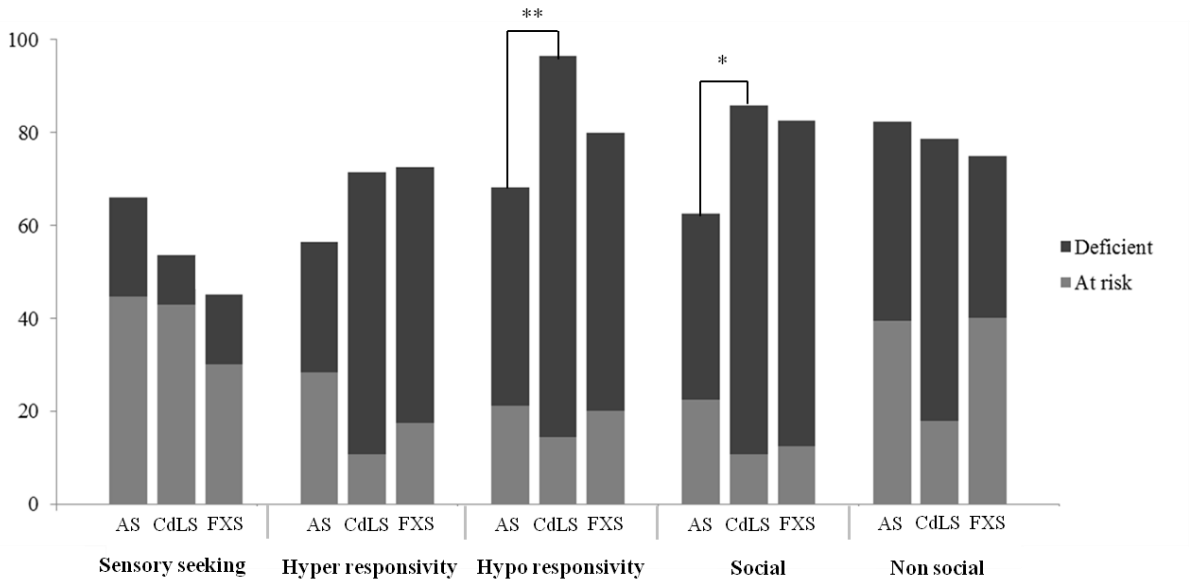

Figure 1. Percentage of participants with AS, CdLS and FXS exceeding the clinical cut-offs in the SEQ.

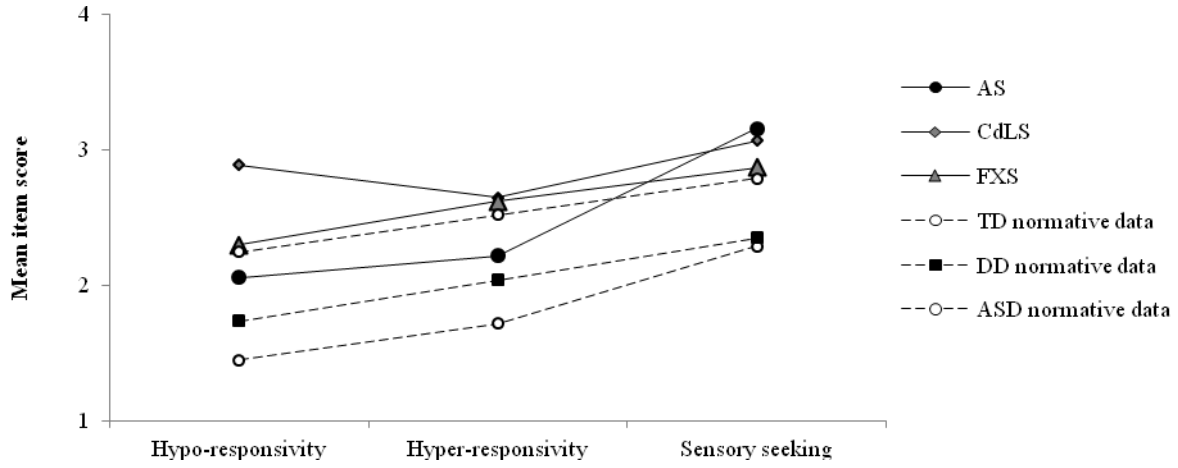

Figure 2. Mean item score on the Sensory Experiences Questionnaire responsiveness subscales. Data are shown for AS, CdLS, FXS and the SEQ manual data for typically developing children (TD), children with a developmental disorder (DD) and children with Autism Spectrum Disorder (ASD).[2]

[2] Error bars are omitted in order to see pattern across syndrome groups.

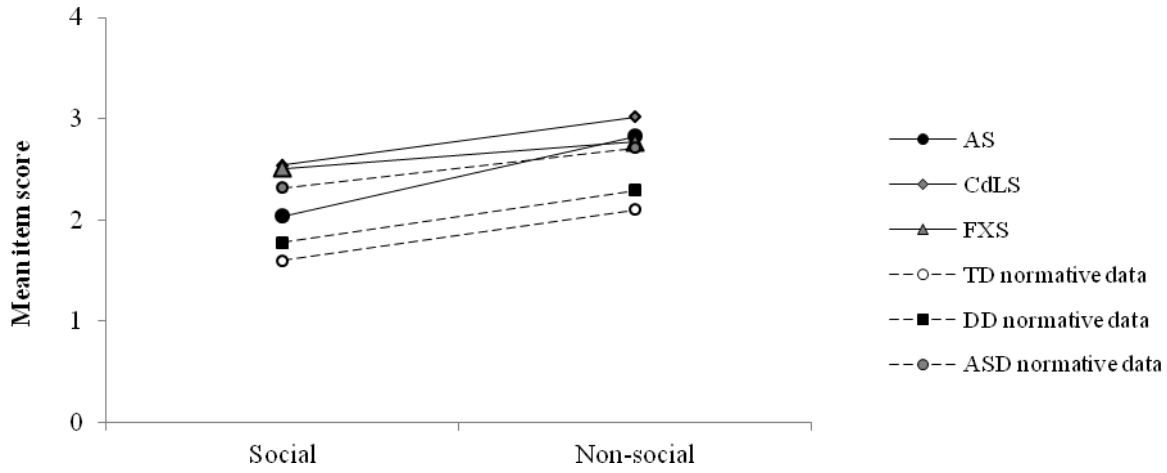

Figure 3. Mean item score on the Sensory Experiences Questionnaire context subscales. Data are shown for AS, CdLS, FXS and the SEQ manual data for typically developing children (TD), children with a developmental disorder (DD) and children with Autism Spectrum Disorder (ASD).

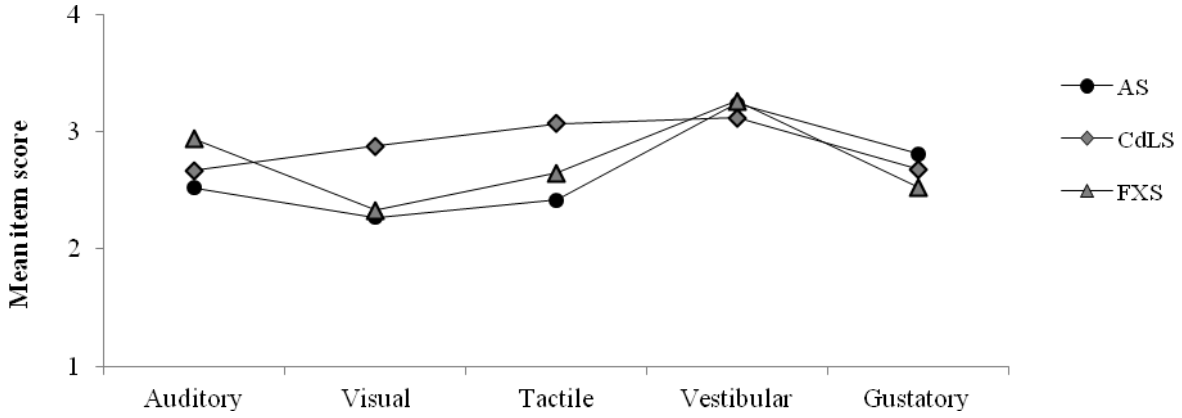

Figure 4. Mean item score on the Sensory Experiences Questionnaire modality subscales. Data are shown for AS, CdLS, FXS.