Short Report: Relationships between Sensory Processing, Repetitive Behaviours, Anxiety, and Intolerance of Uncertainty in Autism Spectrum Disorder and Williams Syndrome

Running title: Sensory and Repetitive Behaviours in ASD and WS

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Abstract

Autism spectrum disorder (ASD) and Williams syndrome (WS) share psychopathology relating to sensory processing and repetitive behaviours. The relationships between the sensory features and repetitive behaviours in both disorders, and the mechanisms underlying these relationships, are not well understood. The aim of this study was to examine the relationships between sensory processing, repetitive behaviours, anxiety, and intolerance of uncertainty in children with ASD and those with WS to better understand the complexity of psychopathology in these disorders. Parents of 19 children with ASD and 16 children with WS, aged between 4 and 9 years, were asked to complete questionnaires assessing their children's sensory experiences, anxiety symptoms, severity and frequency of repetitive behaviours, and level of intolerance of uncertainty. Serial mediation analysis was performed. Direct significant relationships between sensory features and repetitive behaviours were found only for the ASD group. The relationship between sensory processing difficulties and repetitive behaviours was mediated via intolerance of uncertainty in WS. The findings support the value of considering the complexity of the mechanisms underlying the relationship between sensory processing and repetitive behaviours across neurodevelopmental disorders and the mechanisms underlying these aspects of psychopathology in these groups. Understanding these relationships will shed light on some

of the most challenging and intractable characteristics of both conditions and inform suitable interventions to improve quality of life for individuals with either ASD or WS.

Lay Summary

In autism spectrum disorder (ASD) and Williams syndrome (WS) difficulties processing the sensory aspects of the environment, repetitive behaviours and high levels of anxiety co-occur, but the relationships between these features is not well understood. This study found that sensory difficulties were directly associated with repetitive behaviours in children with ASD, but not WS, and in WS this relationship was mediated by intolerance of uncertainty. The findings support the value of considering the complexity of the mechanisms underlying the relationship between sensory processing and repetitive behaviours across neurodevelopmental disorders.

Key words

Sensory; Restricted/Repetitive Behaviours; Anxiety

Introduction

Sensory processing difficulties, restricted and repetitive behaviours, and significant levels of anxiety are behavioural atypicalities that have been reported in numerous developmental disorders (e.g. Downs syndrome, Fragile X syndrome, ADHD; Leekam et al., 2011; John & Mervis, 2010), and both autism spectrum disorder (ASD) and Williams syndrome (WS; Riby et al., 2013; Rodgers et al., 2012). ASD is characterized by deficits in communication and social interaction, as well as the presence of stereotyped behaviours and restricted interests (APA, 2013). WS is a genetically diagnosed developmental disorder caused by the deletion of approximately 25-28 genes on one copy of chromosome 7 (Donnai & Karmiloff-Smith, 2000), and associated with mild to moderate intellectual difficulty, relatively better language skills alongside weaker spatial processing, and behavioural issues such as hypersociability (Jones et al., 2000). In both disorders, however, the aetiology, course, correlates and impact of the presence of sensory difficulties, RRB and anxiety may vary. There are only two studies to date investigating the relationships between sensory processing, repetitive behaviours and anxiety in individuals with ASD (Lidstone et al., 2014; Wigham et al., 2015). Lidstone and colleagues (2014) reported both low registration and sensation seeking were related to insistence on sameness behaviours and anxiety, and sensation avoiding was a mediating factor between anxiety and insistence on sameness behaviours. Wigham et al. (2015) explored the role of intolerance of uncertainty in understanding the relationship between sensory atypicalities, repetitive behaviours and anxiety. Intolerance of uncertainty (IU) is a way of perceiving information in uncertain situations and responding to it in a cognitive, emotional and behavioural way (Freeston et al., 1994). Individuals who are intolerant of uncertainty are more likely to perceive everyday uncertain events as unacceptable and disturbing (Dugas et al., 2001). It has been shown that children with ASD not only have significantly higher levels of intolerance of uncertainty than

typically developing children, but also that intolerance of uncertainty accounted for the increased levels of anxiety in those individuals with ASD (Boulter et al., 2014). Using mediational analyses Wigham and colleagues (2015), reported evidence of direct relationships between sensory hyporesponsiveness and repetitive motor behaviours and insistence on sameness, and between sensory hyperresponsiveness and insistence on sameness. Most importantly, anxiety combined with IU mediated the relationships between sensory atypicalities and repetitive behaviours in ASD. In the only study exploring the interrelationship between intolerance of uncertainty, sensory hyper-sensitivity and anxiety in adults with WS (Uljarevic et al., 2018), intolerance of uncertainty and sensory hyper-sensitivity were found to be unique independent predictors of anxiety. Also, sensory hyper-sensitivity mediated the relationship between intolerance of uncertainty and anxiety, reflecting the pattern seen in ASD.

Although there are syndrome-specific patterns of social functioning between ASD and WS, elevated levels of sensory processing abnormalities, repetitive behaviours and anxiety are common across disorders. Investigating the relationships between sensory features, repetitive behaviours, anxiety and IU, and undertaking a cross-syndrome approach will shed light on some of the most challenging and intractable characteristics of both conditions and inform suitable intervention programmes to improve quality of life for individuals living with either ASD or WS.

Study aims and objectives

The aim was to examine the relationship between sensory processing, repetitive behaviours, anxiety and IU in children with ASD and WS. It was hypothesized that sensory processing abnormalities would predict repetitive behaviours directly in ASD and WS groups. IU and anxiety would mediate these relationships in the ASD group and the

relationships between sensory hyperresponsiveness and repetitive behaviours in the WS group.

Method

Participants

The parents of nineteen children with ASD and sixteen children with WS, between 4 and 9 years of age and without other co-morbid diagnoses of neurodevelopmental disorders or visual, hearing or motor impairments, were recruited to the study. Parents of children with ASD were recruited through mainstream and special needs primary schools from the North East of England and a local branch of a national charity (Contact). All children with ASD had previously been diagnosed with ASD based on a multidisciplinary team assessment following the guidelines of the UK National Autism Plan for Children (Le Couteur, 2003). Children with WS were recruited via the Williams Syndrome Foundation and had previously had their WS diagnosis confirmed by positive fluorescent in situ hybridization testing. Favourable ethical opinion was granted by the local ethics committee.

Measures

1. Sensory Profile (SP; Dunn, 1999) - a caregiver questionnaire assessing a child's sensory processing abilities. Children can be classified into one of the four general sensory processing patterns: low registration, sensory sensitivity, sensation seeking and sensation avoiding. The first two patterns represent a sensory hyporesponsiveness pattern, the latter two represent sensory hyperresponsiveness.

2a. Spence Children's Anxiety Scale-Parent Version (SCAS-P; Spence, 1998) - a questionnaire rating the frequency of occurrence of anxiety symptoms.

2b. Preschool Anxiety Scale (PAS, Spence et al., 2001) - a version of SCAS-P adapted for use with very young children.

3. Anxiety Scale for Children-ASD, parent-version (ASC-ASD©, Rodgers et al., 2016b) – a questionnaire assessing anxiety symptoms specific to the ASD population. The measure has four sub-scales: Separation Anxiety, Uncertainty, Performance Anxiety and Anxious Arousal.

4. Repetitive Behaviour Questionnaire (RBQ; Turner, 1995) – a questionnaire on which parents rate the severity or frequency of repetitive behaviours that their child engaged in over the last month. Behaviours reported include repetitive movements (sensory/motor behaviours; SM), insistence on sameness behaviours (IS), circumscribed interests and repetitive use of language.

5. Social Responsiveness Scale – Second Edition (SRS-2; Constantino & Gruber, 2012) - a parent-report of autistic symptoms that covers unusual interpersonal behaviours, communication or repetitive/stereotyped behaviours.

Sensory hyporesponsiveness and sensory hyperresponsiveness were calculated as sums of items marked as either low or high neurological threshold as indicated by the Sensory Profile (Dunn, 1999). T-scores from the SCAS-P/PAS were entered as an anxiety scores and the Uncertainty subscale of ASC-ASD was used as a measure of IU.

Results

Descriptive statistics are presented in Table 1 and Table 2.

(Insert Table 1 about here)

(Insert Table 2 about here)

Mediation analysis

The model was based on previous computational work (Wigham et al., 2015). Total, direct and indirect effects were calculated (Kenny, 2016) and single (via IU or via anxiety)

and double mediator paths (via IU and anxiety) estimated. The bootstrapping technique with 1000 resamples and generated accelerated 95% confidence intervals was implemented to adjust for measurement error when interpreting indirect effects (Shrout & Bolger, 2002). Non-significant paths in the models are indicated by confidence intervals which include zero; effect sizes are indicated by R^2 values. Age was entered as covariate for WS sample as it correlated with IU (r=-.642, p=.007), SM (r=-.591, p=.016) and IS (r=-.520, p=.039). Inter correlations between the covariates for both the ASD and WS samples are presented in Table 3 and Table 4. Due to the scoring of the SP, negative direction of correlations suggest that high levels of repetitive behaviours, anxiety and IU were associated with more sensory processing atypicalities in both ASD and WS samples.

(Insert Table 3 about here)

(Insert Table 4 about here)

In the ASD sample, significant total and direct effects were found: from sensory hyporesponsiveness to SM (β=-.12, p=.003; β=-.14, p=.018) and IS (β=-.17, p<001; β=-.19, p=.007); and from sensory hyperresponsiveness to SM (β=-.13, p=.002; β=-.11, p=.031) and IS (β=-.17, p=.001; β=-.13, p=.040). Significant indirect effects through anxiety (β=-.09, LL=-.21, UL=-.00) and IU and anxiety (β=.19, LL=.02, UL=.46) from sensory hyporesponsiveness to IS were found (see Table 5 for the summary).

(Insert Table 5 about here)

In the WS sample, significant total and non-significant direct effects were found: from sensory hyporesponsiveness to SM (β=-.09, p<.001; β=-.01, p=.80) and IS (β=-.11, p<.001; β=-.01, p=.81); and from sensory hyperresponsiveness to SM (β=-.07, p=.01; β=-.04, p=.24) and IS (β=-.09, p=.01; β=-.01, p=.84). Significant indirect total effects and indirect effect through IU were found from sensory hyporesponsiveness to IS (β=-.10, LL=-.28, UL=-.04;

β=-.08, LL=-.22, UL=-.01) and from sensory hyperresponsiveness to IS (β=-.08, LL=-.18, UL=-.03; β=-.06, LL=-.18, UL=-.02). The summary of the analysis can be found in Table 6. (Insert Table 6 about here)

Discussion

The examination of the direct relationships between sensory processing abnormalities (hypo- and hyperresponsiveness) and repetitive behaviours and the indirect paths through IU and/or anxiety showed syndrome-specific associations. In the ASD group significant relationships between sensory processing abnormalities and repetitive behaviours were found, similar to Wigham et al. (2015) (including a direct relationship between sensory hyperresponsiveness and SM that was found only significant in this study, but not in Wigham et al. 2015). This pattern was not found in the WS sample, suggesting that sensory processing difficulties and heightened levels of repetitive behaviours were significantly associated only in the ASD group, but not in the WS sample. It is important to highlight that in this study the children were younger (4-9 years) than those in Wigham et al. (2015) (8-16 years) and it is possible that SM were more prevalent in our younger sample as repetitive behaviours may decrease with age in individuals with ASD (Bishop et al., 2006; Esbensen et al., 2009).

Significant total indirect effects in the ASD group suggest that all the paths between sensory hypo- and hyperresponsiveness and SM and IS were partially mediated by at least one of the mediation variables (IU or anxiety). However, in the WS group the relationships between sensory processing abnormalities and repetitive behaviours were completely mediated via IU and/or anxiety, showing for the first time a potential role for IU and/or anxiety in the presentation of repetitive behaviours in WS, even evidenced in the relatively small sample studied here.

Significant indirect effects from sensory hyporesponsiveness to IS through anxiety, and IU and anxiety were found in the ASD group, supporting Wigham et al. (2015). In

contrast to Wigham et al. (2015), we did not find a significant indirect path from hyperresponsiveness through IU and anxiety to IS, possibly due to lower power.

Interestingly, a significant relationship between sensory hyporesponsiveness and IS mediated via IU only was found in the WS group. The relationship between sensory hyperresponsiveness and IS was also mediated via IU. Such an important mediating role of IU between sensory processing and repetitive behaviours in WS was not predicted. This novel finding suggests that those children with WS who find the sensory environment unpredictable, can display more repetitive behaviours perhaps in order to regain predictability in their world. The results support the value of considering the complexity of the mechanisms underlying the relationship between sensory processing abnormalities and repetitive behaviours across neurodevelopmental disorders. Although the role of IU has already been taken into account as part of anxiety treatments in the typically developing population (McEvoy & Mahoney, 2012) and in one treatment programme for young people with ASD (Rodgers et al., 2016a), it has not been targeted in any interventions designed for children with WS, although IU and sensory hyper-sensitivity were recently found to be unique predictors of the severity of anxiety in adults with WS (Uljarevic et al., 2018).

Strengths and limitations

Despite the small sample size, the repetitive behaviours variance accounted for in the models was large, ranging from 51% to 67%. The IU subscale from the ASC-ASD was used as a measure of IU as it has good psychometric properties in ASD populations (Rodgers et al., 2016b; Keen et al., 2017); however, that ASD-specific anxiety measure has not been validated in the WS population. The motor behaviour subscale of the RBQ contains some sensory-related items. In future research measures should be chosen which provide a differentiation between sensory and motor repetitive behaviours to avoid potential overlap leading to high inter correlations. The data were obtained only from parental reports and use

of multiple informants and direct assessments would reduce the shared method variance bias in future research. Finally, the striking strength of the intercorrelations between the covariates in both samples raises some interesting questions. It could suggest a presence of a general severity effect that could have both conceptual and clinical implications.

This is the first study to explore the role of IU and anxiety in relation to sensory processing and repetitive behaviours in children with ASD and WS. These findings have potential clinical applications; yet the findings need to be replicated in larger samples.

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Table 1 Descriptive statistics (mean (SD)) of participant characteristics

	ASD (n=19)	WS (n=16)
Gender: male	16	8
Age in months	84.74 (21.81)	85.13 (22.56)
SRS-2 total score	111.13 (35.94)[a]	80.00 (25.54)
SRS-2 normal range	0	3
SRS-2 mild to moderate range	8	10
SRS-2 severe range	8	3

Note: [a]n=16

Abbreviations: ASD-autism spectrum disorder, WS-Williams syndrome, SRS-2-Social Responsiveness Scale – Second edition

Table 2 Mean scores on outcome variables

Outcome variable	ASD (n=19)	WS (n=16)
Sensory profile		
Registration	56.84 (12.88)	48.75 (14.32)
Seeking	87.63 (16.58)	87.06 (17.22)
Sensitivity	66.18 (14.83)[d]	62.25 (14.17)
Avoiding	89.73 (19.90)[b]	93.94 (17.22)
Hyporesponsiveness	140.13 (24.78)	135.81 (29.00)
Hyperresponsiveness	155.27 (33.87)[b]	156.19 (29.02)
RBQ		
Total score	23.00 (16.94)	12.00 (10.17)
Sensory/Motor	8.63 (5.52)	4.69 (4.25)
Insistence on Sameness	10.32 (7.30)	4.94 (4.85)
SCAS-P/PAS T-scores		
Total score	52.28 (17.67)[e], 30-90	48.63 (12.69), 30-74
Separation	56.94 (14.65)[e], 40-95	53.44 (11.67), 40-75
Physical injury fears	55.83 (13.39)[e], 40-83	55.19 (11.33), 40-83
Social Anxiety	51.06 (15.71)[e], 40-100	44.63 (6.51), 40-57
OCD	54.72 (20.16)[e], 40-100	47.87 (13.87), 40-92
GAD	53.94 (17.48)[e], 40-99	58.00 (17.78), 40-99
ASC-ASD		
Total score	19.94 (18.37)[d]	13.00 (10.08)[a]
Performance anxiety	3.47 (5.71)[d]	1.13 (1.87)[b]
Anxious arousal	3.22 (4.53)[e]	2.33 (2.97)[b]

Separation anxiety	4.56 (3.88)[e]	3.57 (2.93)[a]
Uncertainty	10.17 (7.88)[e]	7.19 (5.98)[c]

Note:[a] n=14, [b] n=15, [c] n=16, [d] n=17, [e] n=18; SCAS-P data were available for 11 WS and 11ASD participants, PAS data were available for 5 WS and 7 ASD participants

Abbreviations: WS-Williams Syndrome, ASD-autism spectrum disorder, RBQ-Repetitive Behaviour Questionnaire, SCAS-P-Spence Children's Anxiety Scale-Parent Version, PAS-Preschool Anxiety Scale, OCD-Obsessive Compulsive Disorder, GAD-Generalised Anxiety Disorder, ASC-ASD-Anxiety Scale for Children-ASD, parent-version

Table 3 Inter correlations between the covariates for the ASD sample

	SRS-2	Hypo responsiveness	Hyper responsiveness	IU	Anxiety	RBQ SM
Hyporesponsiveness	-.776**					
Hyperresponsiveness	-.784**	.791**				
IU	.724**	-.780**	-.561*			
Anxiety	.666**	-.685**	-.629*	.826**		
RBQ SM	.695**	-.713**	-.739**	.465	.577*	
RBQ IS	.745**	-.776**	-.748**	.536*	.663**	.866**

Note: ** correlation is significant at the .01 level, * correlation is significant at the .05 level

Abbreviations: SRS-2 - Social Responsiveness Scale – Second edition, IU-Intolerance of uncertainty, RBQ SM-Repetitive Behaviour Questionnaire sensory/motor behaviours, RBQ IS-Repetitive Behaviour Questionnaire insistence on sameness behaviours

Table 4 Inter correlations between the covariates for the WS sample

	SRS-2	Hypo responsiveness	Hyper responsiveness	IU	Anxiety	RBQ SM
Hyporesponsiveness	-.865**					
Hyperresponsiveness	-.889**	.866**				
IU	.875**	-.775**	-.778**			
Anxiety	.743**	-.845**	-.683**	.792**		
RBQ SM	.800**	-.706**	-.751**	.797**	.786**	
RBQ IS	.849**	-.757**	-.723**	.888**	.785**	.800**

Note: ** correlation is significant at the .01 level, * correlation is significant at the .05 level

Abbreviations: SRS-2 - Social Responsiveness Scale – Second edition, IU-Intolerance of uncertainty, RBQ SM-Repetitive Behaviour Questionnaire sensory/motor behaviours, RBQ IS-Repetitive Behaviour Questionnaire insistence on sameness behaviours

Table 5 Mediation analysis summary for the ASD group

Variables		Total, direct and indirect effects																	
Dependent	Predictor	Total effect						Direct effect					Total indirect effects				Indirect effects (β)		
		R^2	β	se	LL	UL	p	β	se	LL	UL	p	β	se	LL	UL	IU	Anx	IU → Anx
Sensory hyporesponsiveness	SM	.51	-.12	.03	-.19	-.05	.003	-.14	.05	-.25	-.03	.018	.02	.06	-.08	.13	.08	-.06	.14
Sensory hyporesponsiveness	IS	.60	-.17	.04	-.25	-.09	<.001	-.19	.06	-.31	-.06	.007	.02	.05	-.06	.18	.11	-.09*	.19*
Sensory hyperresponsiveness	SM	.55	-.13	.03	-.20	-.06	.002	-.11	.04	-.21	-.01	.031	-.02	.04	-.11	.06	.01	-.03	.04
Sensory hyperresponsiveness	IS	.56	-.17	.04	-.26	-.08	.001	-.13	.06	-.25	-.01	.040	-.04	.05	-.13	.03	.01	-.06	.07

Abbreviations: Anx-Anxiety, IS-insistence on sameness behaviours, IU-intolerance of uncertainty, SM-sensory/motor behaviours

Table 6 Mediation analysis summary for the WS group with age entered as covariates

Variables		Total, direct and indirect effects																	
Dependent	Predictor	Total effect						Direct effect					Total indirect effects				Indirect effects (β)		
		R^2	β	se	LL	UL	p	β	se	LL	UL	p	β	se	LL	UL	IU	Anx	IU → Anx
Sensory hyporesponsiveness	SM	.65	-.09	.03	-.14	-.03	<.001	-.01	.05	-.12	.09	.80	-.08	.05	-.18	.02	-.01	-.06	.05
Sensory hyporesponsiveness	IS	.67	-.11	.03	-.18	-.05	<.001	-.01	.05	-.11	.09	.81	-.10*	.05	-.28	-.04	-.08*	-.02	-.05
Sensory hyperresponsiveness	SM	.65	-.07	.02	-.12	-.03	.01	-.04	.03	-.10	.03	.24	-.04	.03	-.10	.01	.00	-.04	.04
Sensory hyperresponsiveness	IS	.57	-.09	.03	-.15	-.02	.01	-.01	.03	-.07	.06	.84	-.08*	.03	-.18	-.03	-.06*	-.02	-.04

Abbreviations: Anx – Anxiety, IS-insistence on sameness behaviours, IU-intolerance of uncertainty, SM-sensory/motor behaviours