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The cognitive profile of Sotos syndrome

Chloe Lane*, Elizabeth Milne and Megan Freeth

Department of Psychology, University of Sheffield, UK

Sotos syndrome is a congenital overgrowth disorder, associated with intellectual disability. Previous research suggests that Sotos syndrome may be associated with relative strength in verbal ability and relative weakness in non-verbal reasoning ability but this has not been explicitly assessed. To date, the cognitive profile of Sotos syndrome is unknown. Cognitive abilities of a large and representative sample of individuals with Sotos syndrome ($N = 52$) were assessed using the British Ability Scales (BAS3). The majority of participants had intellectual disability or borderline intellectual functioning. The cluster score profile analysis revealed a consistent verbal ability > non-verbal reasoning ability profile. Four specific criteria were proposed as the Sotos syndrome cognitive profile (SSCP): verbal ability > non-verbal reasoning ability; quantitative reasoning T-score or matrices T-score <20th percentile; quantitative reasoning T-score < mean T-score; recognition of designs T-score or recognition of pictures T-score > mean T-score. Of the 35 participants included in the profile analysis, 28 met all four SSCP criteria, yielding a sensitivity of 0.8. The sensitivity of each of the SSCP criteria was >0.9. Individuals with Sotos syndrome display a clear and consistent cognitive profile, characterized by relative strength in verbal ability and visuospatial memory but relative weakness in non-verbal reasoning ability and quantitative reasoning. This has important implications for the education of individuals with Sotos syndrome.

Sotos syndrome is a congenital overgrowth disorder with an incidence of approximately 1 in 14,000 (Tatton-Brown & Rahman, 2004). The cardinal features of the syndrome are overgrowth, characteristic facial appearance and intellectual disability (Tatton-Brown *et al.*, 2005). Individuals with Sotos syndrome typically display distinctive neurological abnormalities, including abnormality of the corpus callosum, ventricular abnormalities, midline abnormalities and delayed or disturbed maturation of the brain (Schaefer, Bodensteiner, Buehler, Lin, & Cole, 1997). Sotos syndrome is caused by intragenic mutations or microdeletions of the NSD1 (nuclear receptor binding SET domain protein 1) gene (Kurotaki *et al.*, 2002).

Distinct cognitive profiles have been identified in a number of congenital syndromes such as Williams syndrome (Mervis *et al.*, 2000; Udwin & Yule, 1991), Fragile X syndrome (Borghgraef, Fryns, Dlelkens, Pyck, & Berghe, 1987; Van der Molen *et al.*, 2010) and Down syndrome (Silverman, 2007; Wang, 1996). These syndromes are typically associated with intellectual disability, as well as varied cognitive profiles. The presence of such variability has important implications when considering the most effective educational strategies for individuals with neurodevelopmental disorders and for designing interventions and support to improve the outcomes of these populations.

*Correspondence should be addressed to Chloe Lane, Department of Psychology, The University of Sheffield, Sheffield S1 2LT, UK (email: clane2@sheffield.ac.uk).

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Sotos syndrome is associated with intellectual disability but the cognitive profile is unknown. It is therefore an important population in which to investigate cognition.

In the largest study to date to investigate the clinical features of Sotos syndrome, Tatton-Brown *et al.* (2005) found that intellectual disability was present in 97% of 266 individuals with Sotos syndrome. However, intellectual ability was determined via clinical assessment in this study, rather than using a standardized cognitive assessment. Therefore, it is not possible to identify the associated cognitive profile from this study.

A recent systematic review of cognition and behaviour in Sotos syndrome (Lane, Milne, & Freeth, 2016) identified that only 34 studies relating to cognition and/or behaviour have been published since the initial recognition of Sotos syndrome in 1964 (Sotos, Dodge, Muirhead, Crawford, & Talbot, 1964). In general, the findings from the systematic review identified that the majority of individuals with Sotos syndrome have intellectual disability (IQ < 70) or borderline intellectual functioning (IQ 70–84), although there was a significant range of reported IQ scores from 21 to 113. An additional finding was that individuals with Sotos syndrome appear to display relative strength in verbal IQ (VIQ), compared with performance IQ (PIQ) (Lane *et al.*, 2016). However, the discrepancy between VIQ and PIQ was not explicitly assessed in any of the studies that reported these scores.

Previous research with other neurodevelopmental disorders has explored discrepancies between verbal ability and non-verbal reasoning ability. In Williams syndrome, this is a striking component of the cognitive profile, with individuals typically displaying relative strength in verbal ability and relative weakness in non-verbal reasoning ability (Udwin & Yule, 1991). In contrast, Down syndrome is typically associated with relative weakness in verbal ability (Wang, 1996). Both of these syndromes are associated with intellectual disability, yet the cognitive profiles are distinct (Klein & Mervis, 1999). As Sotos syndrome is a neurodevelopmental disorder associated with a similar range of intellectual ability to that reported for Williams syndrome and Down syndrome, it is important to investigate the relationship between verbal ability and non-verbal reasoning ability within the Sotos syndrome population. This will inform understanding of the cognitive profile associated with Sotos syndrome.

The identification of syndrome-specific cognitive profiles enables differentiation between individuals with distinct congenital syndromes. Specific criteria extend the broad phenotype established by research investigating discrepancies in verbal ability and non-verbal reasoning ability. For example, Mervis *et al.* (2000) operationalized the cognitive profile of Williams syndrome with four specific criteria. An example criterion from this study is 'pattern construction T-score < digit recall T-score' (Mervis *et al.*, 2000). This provides a specific quantitative measure of the cognitive profile associated with Williams syndrome. As there is currently very limited knowledge available in relation to the cognitive profile associated with Sotos syndrome, it is important to establish the relative cognitive strengths and weaknesses of individuals within this population in order to ensure that appropriate educational strategies are utilized.

The primary aim of this study was to investigate the prevalence of intellectual disability within the Sotos syndrome population, using a standardized cognitive assessment and to identify the associated cognitive profile. Cognitive abilities were assessed using the British Ability Scales, third edition (BAS3) (Elliott & Smith, 2011) in a large and representative sample of adults and children with Sotos syndrome. The BAS3 is a standardized battery of cognitive tasks, appropriate for use with individuals of a wide age range, as well as individuals of varying intellectual ability. The American equivalent of the BAS3 (The Differential Ability Scales; DAS) (Elliott, Murray, & Pearson, 1990) has been used to

quantify the cognitive profile associated with Williams syndrome and is therefore an appropriate and established methodology for identifying cognitive profiles associated with neurodevelopmental disorders.

Method

Participants

The sample comprised 52 participants (31 males) with a clinical diagnosis of Sotos syndrome, ranging in age from 3 years 8 months to 50 years 3 months (M = 14.62 years, SD = 9.61 years). Families were recruited via the Child Growth Foundation (CGF; a UK charity that supports families of individuals affected by growth disorders) and advertisements on a Sotos syndrome support group on social media (the 'Sotos Syndrome – UK' group on Facebook). In order to assess eligibility for the study, families were asked to complete a screening form and to indicate whether their child or partner had been diagnosed with any developmental disorders. If Sotos syndrome was stated on the screening form, families were invited to participate and were sent further information about the study.

Procedure

The majority of participants were visited at their home (n = 24) or their school (n = 23). One participant took part in the study at the University, and a small number of participants completed the study at the annual CGF Conventions, in either 2015 or 2016 (n = 4). Participants were administered the BAS3; a standardized battery of cognitive tasks, designed to assess a range of cognitive abilities. The BAS3 consists of two batteries: an early years (EY) battery, which has norms for children aged 3:0–7:11 years and a school age (SA) battery, which has norms for children aged 5:0–17:11 years of age. Each battery comprises six core scales which are used to determine a General Conceptual Ability (GCA) score (equivalent to an IQ score). GCA scores are calculated as standard scores (M = 100, SD = 15) on the basis of the distribution of T-scores (M = 50, SD = 10) for the six core scales.

The BAS3 core scales form three distinct clusters: verbal (V) ability, non-verbal reasoning (NVR) ability and spatial (S) ability. These clusters were derived by the authors of the BAS3 using confirmatory factor analysis of scores from the BAS3 normative sample (1,480 UK children). The cluster scores are also calculated as standard scores (M = 100, SD = 15). Completion of all core scales is required for profile analysis. A description of the abilities measured by each task and the corresponding clusters, as stated in the BAS3 administration and scoring manual (Elliott & Smith, 2011), is presented in Table 1.

Although both the EY and SA batteries have norms for children 5:0–7:11 years of age, the EY battery was used with participants from the ages of 3:8–7:11 years, as it was anticipated that the majority of participants would have intellectual disability. All participants who were 8 years or older were administered the SA battery. Of the 52 participants, 15 were tested on the EY battery and 37 were tested on the SA battery. The BAS3 was administered in accordance with the administration manual.

All families provided informed consent. Participants aged 18 years and over provided informed consent, and for children under the age of 18 years, the parent/caregiver of the participant was required to give informed consent. The study received ethical approval from the departmental ethics committee.

Table 1. Early years battery and school age battery core scales

Core scales	Abilities measured
EY Battery	
Verbal cluster	
Verbal comprehension	Receptive language: understanding of oral instructions involving basic language concepts
Naming vocabulary	Expressive language; knowledge of names
Non-verbal reasoning cluster	
Picture similarities	Non-verbal reasoning shown by matching pictures that have a common element or concept
Matrices[a]	Inductive reasoning: identification and application of rules governing relationships among pictures and abstract figures
Spatial cluster	
Pattern construction[a]	Non-verbal reasoning and spatial visualization in reproducing designs
Copying	Visual-perceptual matching and fine-motor co-ordination in copying line drawings
SA Battery	
Verbal cluster	
Word definitions	Expressive language; explanation of word meanings
Verbal similarities	Verbal reasoning and verbal knowledge
Non-verbal reasoning cluster	
Matrices[a]	Inductive reasoning: identification and application of rules governing relationships among pictures and abstract figures
Quantitative reasoning	Inductive reasoning: detection and application of rules concerning sequential patterns in dominoes and relationships between pairs of numbers
Spatial cluster	
Recognition of designs	Short-term memory for geometric forms
Pattern construction[a]	Non-verbal reasoning and spatial visualization in reproducing designs

[a]Task included in both the EY and SA batteries.

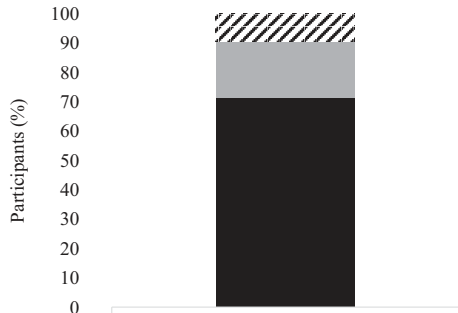
Results

General conceptual ability

The mean GCA of the 52 participants was 60.75 (SD = 16.68) and GCA scores ranged from 37 to 101. Intellectual disability was considered as GCA < 70, borderline intellectual ability was considered as GCA of 70–89 and average intellectual ability was considered as GCA of 90–109. See Figure 1 for percentage of participants in each of these categories. There was no significant difference between GCA scores for participants who completed the EY battery (M = 59.93, SD = 16.96) and participants who completed the SA battery, (M = 61.08, SD = 16.80), $t(50) = -0.223$, p = .825. Pearson's bivariate correlation did not find a significant increase or decrease in GCA with age r = .036, N = 52, p = .802.

Gender differences

Gender differences in relation to intellectual disability and the associated cognitive profile of Sotos syndrome were explored. GCA scores for male participants were not normally distributed so non-parametric analyses were carried out. A Mann-Whitney



	Participants (n = 52)
Average	9.62%
Borderline	19.23%
ID	71.15%

Figure 1. Percentage of participants with ID (GCA <70), borderline intellectual functioning (GCA 70–89) and average intellectual functioning (GCA 90–109).

U-test identified a significant difference in GCA between genders (U = 218.5, p = .046), indicating that female participants (M = 66.52, SD = 17.35) typically achieved higher GCA scores than male participants (M = 56.84, SD = 15.27). In total, 14.29% (n = 3) of female participants had average intellectual ability, 28.57% (n = 6) had borderline intellectual ability and 57.14% (n = 12) had intellectual disability. For male participants, 6.45% (n = 2) had average intellectual ability, 12.9% (n = 4) had borderline intellectual ability and 80.65% (n = 25) had intellectual disability. This suggests that males with Sotos syndrome may be more severely affected by intellectual disability than females. No significant differences in relation to gender were observed in any of the other analyses.

Cluster score profile

In order to establish whether participants displayed a distinct profile of performance on the clusters, a repeated-measures ANOVA was used to compare scores for the verbal (V) ability, non-verbal reasoning (NVR) ability and spatial (S) ability clusters. Six of the participants (all male) found the tasks too challenging so were unable to complete all or some of the core scales and were therefore removed from the subsequent analyses regarding the cognitive profile of Sotos syndrome (4 from the EY battery and 2 from the SA battery). In total, 46 participants completed all six core scales of either the SA battery (n = 35) or the EY battery (n = 11) so were included in the cluster score profile analyses.

A repeated-measures ANOVA identified a significant difference in performance on the three clusters, $F(2, 90) = 31.50$, $p < .001$, $\eta\rho^2 = .41$, and this was a large effect. After correcting for multiple comparisons (using a Bonferroni correction, $p < .017$ required for significance), paired samples t-tests revealed that performance on the V ability (M = 76.80, SD = 15.33) cluster was significantly better than performance on the NVR ability (M = 63.80, SD = 12.96) cluster, $t(45) = 8.41$, $p < .001$. This was a large effect (d = 1.24). Performance on the V ability cluster was significantly better than performance on the S ability (M = 69.48, SD = 15.19) cluster, $t(45) = 4.26$, $p < .001$, and this was a

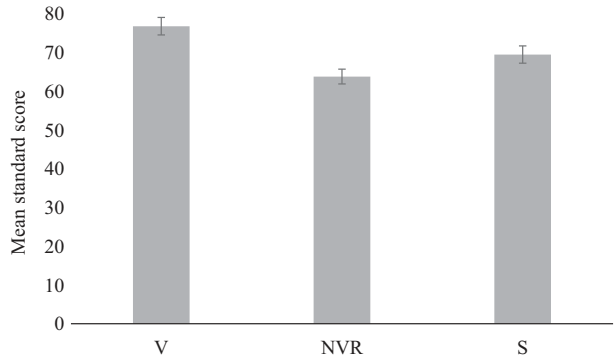


Figure 2. Mean standard scores for the verbal ability (V) cluster, non-verbal reasoning ability (NVR) cluster and spatial ability (S) cluster. Error bars show ± standard error.

medium effect (d = 0.63). In addition, performance on the S ability cluster was significantly better than performance on the NVR ability cluster, $t(45) = -3.43$, p = .001, and this was a medium effect (d = 0.51). Overall, the findings indicate that participants displayed relative strength in V ability and relative weakness in NVR ability (see Figure 2).

Verbal–non-verbal reasoning discrepancies

The cluster score analyses revealed relative strength in V ability and relative weakness in NVR ability for the combined EY and SA cluster scores. For each battery, the cluster scores are calculated on the basis of performance on the core scales of either the EY or the SA battery and most of the core scales tasks are unique to each of the batteries. In order to ensure that the V–NVR discrepancy was consistently observed for participants in both the EY and SA batteries, a 2 × 2 (V/NVR × EY/SA) mixed-measures ANOVA was conducted. The analysis revealed a main effect of cluster, $F(1,44) = 45.73$, $p < .001$, $\eta\rho^2 = .51$, as V ability was significantly better than NVR ability. This was a large effect. There was no significant cluster × battery interaction, $F(1,44) = 0.52$, $p = .47$, $\eta\rho^2 = .01$.

To establish the consistency of a V > NVR profile for individuals with Sotos syndrome, the consistency of discrepancies between V ability and NVR ability between individuals within the sample was explored. Of the 46 participants who completed all of the core scales of either the EY battery or the SA battery, 43 (10 from the EY battery and 33 from the SA battery) exhibited a V > NVR profile of performance on the cluster scores, demonstrating a consistent relative strength in V ability and relative weakness in NVR ability within the Sotos syndrome population.

For each participant, a discrepancy score was calculated by subtracting the NVR ability score from the V ability score. V–NVR discrepancies ranged from −7 to 46 (M = 13, SD = 10.48). A one sample t-test was used to determine whether V–NVR discrepancies were significantly >0. The analysis revealed a significant difference, $t(45) = 8.41$, $p < .001$, indicating that the discrepancy between V ability and NVR ability was significantly >0. This was a large effect (d = 1.24). This demonstrates that participants displayed a consistent V > NVR profile, indicating that relative strength in V ability is a defining characteristic of the cognitive profile of Sotos syndrome.

Early years core scales profile

Eleven participants (four males) completed all six of the EY core scales and participants ranged in age from 3 years 8 months to 7 years 10 months ($M = 6.53$, $SD = 1.39$). As this was a small sample size, statistical differences in performance on the core scales were not assessed due to a lack of power. However, the means and standard error of the EY core scales are reported in Table 2. Inspection of the mean scores for the EY core scales indicates that participants achieved better scores on the naming vocabulary task and lower scores on the copying task.

Table 2. Mean T-scores for the core scales of the EY battery

Core scale	*M*	*SD*
Verbal comprehension	36.09	9.13
Naming vocabulary	44.36	10.73
Picture similarities	33.82	8.84
Matrices	34.00	6.16
Pattern construction	33.55	8.03
Copying	30.45	7.03

Sotos syndrome cognitive profile (SSCP)

In order to investigate the specific cognitive profile in more detail, a repeated-measures ANOVA was used to compare performance on the six core scales of the SA battery (see Figure 3 for means and standard error of the SA core scales). The cognitive profile associated with Sotos syndrome was established on the basis of performance on the core scales of the SA battery as the majority of participants completed this battery and only 11 participants completed the EY battery. Thirty-five participants were included in the profile analyses (21 males) and participants ranged in age from 8 years 3 months to 50 years 3 months ($M = 18.17$, $SD = 9.69$). All analyses were conducted using T-scores ($M = 50$, $SD = 10$). Mean T-score was calculated on the basis of scores on the six core scales of the SA battery.

The analysis identified a significant difference between scores on the core scales of the SA battery, $F(5,170) = 23.97$, $p < .001$, $\eta\rho^2 = .41$, indicating that individuals with Sotos syndrome display specific strengths and weaknesses, as evidenced by relative differences in performance on the core scales of the SA battery. Pairwise comparisons using a Bonferroni correction ($p < .003$ required for statistical significance) were used to compare performance on all of the core scales of the SA battery. The comparisons revealed that the recognition of designs mean T-score was significantly higher than the mean T-scores of three of the other scales: the quantitative reasoning mean T-score ($p < .001$), the matrices mean T-score ($p < .001$) and the pattern construction mean T-score ($p < .001$). The verbal similarities mean T-score was significantly higher than the mean T-scores of two of the other scales: the quantitative reasoning mean T-score ($p < .001$) and the matrices mean T-score ($p < .001$). The word definitions mean T-score was significantly higher than the mean T-scores of two of the other scales: the quantitative reasoning mean T-score ($p < .001$) and the matrices mean T-score ($p = .001$). Therefore, the findings from these analyses provide insight into the cognitive profile of Sotos syndrome. Overall, participants displayed enhanced performance on a task assessing visuospatial memory (recognition of designs), as well as tasks assessing verbal ability (verbal similarities

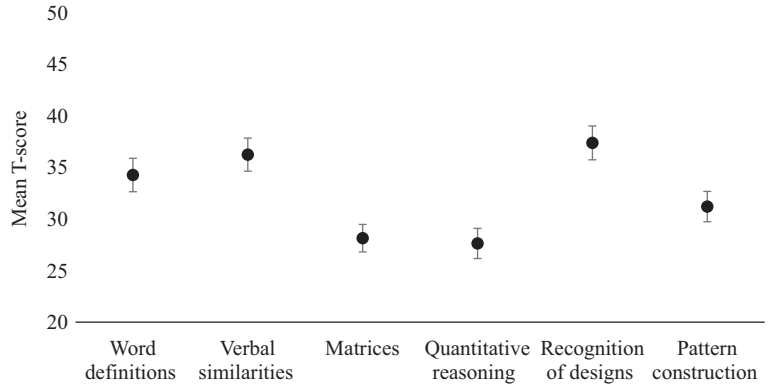


Figure 3. Mean T-scores for the core scales of the SA battery. Error bars show ± standard error.

and word definitions) but relative weakness in performance on tasks designed to assess non-verbal reasoning ability (quantitative reasoning and matrices).

Based on the previous analyses, specific criteria were devised to operationalize the cognitive profile associated with Sotos syndrome. These criteria were chosen due to the significant V–NVR cluster score discrepancy identified in the previous analyses, as well as the relative strengths and weaknesses that were identified in the analysis of performance on the core scales of the SA battery (see Figure 3). The following criteria were proposed as the Sotos Syndrome Cognitive Profile (SSCP):

SSCP1: Verbal ability > Non-verbal reasoning ability

SSCP2: Quantitative reasoning T-score or Matrices T-score < 20th percentile

SSCP3: Quantitative reasoning T-score < Mean T-score

SSCP4: Recognition of designs T-score or Recognition of pictures T-score > Mean T-score

A visualization of SSCP3 and SSCP4 is presented in Figure 4. This presents the 'quantitative reasoning' task T-score, 'recognition of designs' task T-score and mean T-score of each participant and demonstrates the consistency of relative strength in

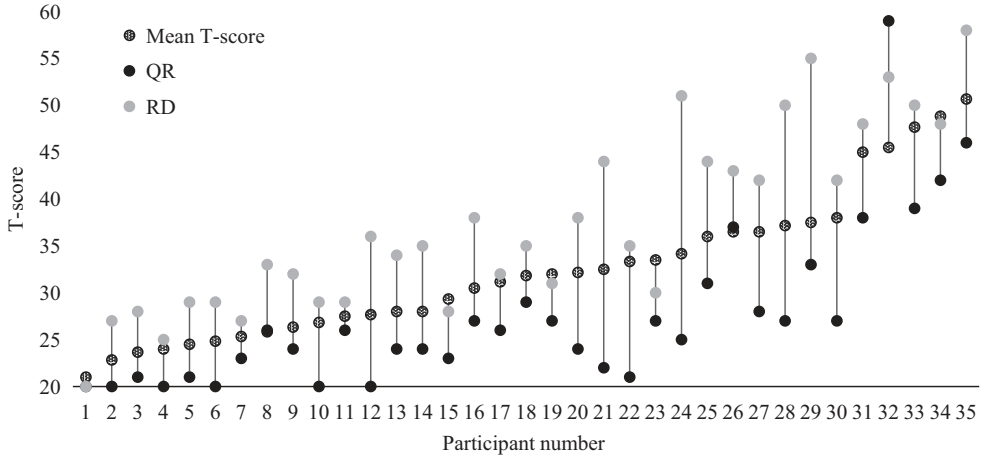


Figure 4. Mean T-score, quantitative reasoning (QR) T-score and recognition of designs (RD) T-score for each participant. Participants ordered by mean T-score.

visuospatial memory, as assessed by the recognition of designs task and relative weakness in quantitative reasoning between participants.

SSCP sensitivity

To establish the sensitivity of each of the SSCP criteria, the proportion of individuals meeting each criteria was calculated (see Table 3). The SSCP criteria were applied to all participants who completed all six core scales of the SA battery in order to determine the sensitivity of the SSCP. Of the 35 participants who completed the SA battery, 28 (80%) met all four criteria of the SSCP, yielding a sensitivity (Se) of 0.8. In total, 34 (97.14%) of the participants met at least three of the SSCP criteria and all participants met at least two of the SSCP criteria.

Table 3. Proportion of participants meeting SSCP criteria and sensitivity of each SSCP criteria

Criteria	*N*	Se
SSCP1: Verbal ability > Non-verbal reasoning ability	33	0.94
SSCP2: Quantitative reasoning T-score or Matrices T-score < 20th percentile	34	0.97
SSCP3: Quantitative reasoning T-score < Mean T-score	32	0.91
SSCP4: Recognition of designs T-score or Recognition of pictures T-score > Mean T-score	33	0.94

Discussion

The aim of the present study was to investigate the prevalence of intellectual disability within the Sotos syndrome population and to identify the associated cognitive profile. This was assessed using a standardized battery of cognitive tasks, in a large and representative sample of adults and children with Sotos syndrome.

Results indicate that the majority of participants either had intellectual disability (GCA < 70) or fell in the borderline intellectual ability range (GCA 70–89). This finding supports previous research (Lane *et al.*, 2016; Tatton-Brown *et al.*, 2005), indicating that the majority of individuals with Sotos syndrome have impaired intellectual ability. However, in the present study, nearly 10% of participants had average intellectual ability (GCA 90–109). This highlights the variability of intellectual ability within this population and demonstrates that some individuals with Sotos syndrome do not have intellectual disability.

Differences in intellectual ability in relation to gender have not previously been explored within the Sotos syndrome population. The findings from the present study indicated that females with Sotos syndrome had significantly higher GCA scores, compared to males with Sotos syndrome. This suggests that, on average, males with Sotos syndrome may be more likely to have a greater degree of intellectual disability than females with Sotos syndrome. No significant relationship was identified between age and GCA scores, indicating that increase or decrease in intellectual ability is not associated with age within the Sotos syndrome population. However, as the present study used a cross-sectional design, it will be important for future research to utilize a longitudinal design to establish the rate and trajectory of cognitive development within this population.

A finding from a recent systematic review (Lane *et al.*, 2016) identified that individuals with Sotos syndrome may have higher VIQ compared to PIQ scores. However, this finding was based on just seven studies, the majority of which were case studies and none of

which explicitly assessed the discrepancy between VIQ and PIQ. In the present study, the cluster score analyses revealed that participants displayed a consistent relative strength in V ability and relative weakness in NVR ability. Thus, the finding of a consistent V > NVR profile in individuals with Sotos syndrome supports the suggestion from the systematic review (Lane *et al.*, 2016). As the present study included a large cohort of individuals with Sotos syndrome of a wide age range, this is a robust finding which has now been established in a large and representative sample.

To identify the cognitive profile associated with Sotos syndrome, performance on the core scales of the SA battery of the BAS3 was compared. This approach has not previously been used within the Sotos syndrome population. It is important to note that the focus of this approach was to establish relative, as opposed to absolute, cognitive strengths and weaknesses. The profile analysis revealed that participants displayed relative strength in visuospatial memory, as assessed by the recognition of designs task and relative weakness in quantitative reasoning. The finding of relative strength in visuospatial memory is a novel finding which has important implications for understanding how individuals with Sotos syndrome process and learn information. Furthermore, the finding of a relative weakness in quantitative reasoning supports a suggestion reported by Cole & Hughes, (1994) that individuals with Sotos syndrome display particular difficulty with numeracy. This finding indicates that individuals with Sotos syndrome may require additional support with numeracy.

To operationalize the cognitive profile, four specific criteria were proposed as the Sotos syndrome cognitive profile (SSCP). In total, 80% ($n = 28$) of participants met all four criteria of the SSCP and 97.14% ($n = 34$) met at least three of the criteria. This suggests that the SSCP has a good degree of sensitivity. In addition, each of the SSCP criteria had a sensitivity >0.9 ($M = 0.94$), indicating that reasons for not meeting all criteria for the SSCP were varied. Thus, the SSCP criteria provide a quantifiable and replicable characterization of the cognitive profile associated with Sotos syndrome which can be used to differentiate between individuals with and without a diagnosis of Sotos syndrome.

Performance on the core scales of the EY battery of the BAS3 was reported in order to explore cognitive abilities in young children with Sotos syndrome. It is important to note that only 11 participants completed all six core scales of the EY battery so statistical differences in performance on the EY core scales were not assessed. However, the mean scores for the core scales indicated that participants performed better on the naming vocabulary task, which is a measure of expressive language. In contrast, participants achieved particularly low scores on the copying task, which assesses visual-perceptual matching and fine-motor co-ordination. As the copying task involves fine motor control and children with Sotos syndrome often have delayed fine and gross motor skills (Tatton-Brown & Rahman, 2007), this could account for the weak performance on this task. Unfortunately, the EY core scales are not designed to assess visuospatial memory or quantitative reasoning so the findings from the EY battery cannot be used to determine whether the full SSCP can be generalized to young children with Sotos syndrome. However, relative strength in V ability and relative weakness in NVR ability were consistently observed for participants in both the EY and SA batteries.

Establishing the cognitive profiles associated with congenital syndromes is valuable in discriminating between individuals with distinct syndromes (Mervis *et al.*, 2000). Previous research has identified that individuals with Williams syndrome typically display relative strength in verbal ability but relative weakness in non-verbal reasoning ability (Udwin & Yule, 1991), and the findings from the present study indicate that this is also characteristic of individuals with Sotos syndrome. However, by investigating differences

in the abilities underlying these domains, these populations can be distinguished. For example, individuals with Williams syndrome typically display relative strength in auditory memory and relative weakness in pattern construction (Mervis *et al.*, 2000) but individuals with Sotos syndrome display relative strength in visuospatial memory and relative weakness in quantitative reasoning. Although the focus of the present study was to conduct within-group comparisons, it will be important for future research to build on this initial work, using cross-syndrome comparisons. For example, this approach has been used to compare specific cognitive skills, such as face recognition, in individuals with autism, Williams syndrome and Down syndrome (Annaz, Karmiloff-Smith, Johnson, & Thomas, 2009) and to explore the dissociation between verbal and visuospatial short-term memory in individuals with Williams syndrome and Down syndrome (Jarrold, Baddeley, & Hewes, 1999; Wang & Bellugi, 1994). Thus, cross-syndrome comparisons will enable the specificity of the SSCP to be established and will contribute to understanding of the cognitive profiles associated with distinct congenital syndromes. In addition, this approach could inform understanding of the potential genetic mechanisms underlying performance in specific cognitive domains.

Previous studies investigating Williams syndrome have identified an association between verbal ability and the relative discrepancy between verbal ability and non-verbal reasoning ability, indicating that higher verbal ability is associated with a greater discrepancy (Jarrold, Baddeley, & Hewes, 1998; Jarrold, Baddeley, Hewes, & Phillips, 2001). This suggests that the rate of development of these abilities is distinct within the Williams syndrome population. As Sotos syndrome is also characterized by relative strength in V ability compared with NVR ability, it will be important for future research to use a longitudinal design to assess the relationship between these abilities within the Sotos syndrome population in order to explore the trajectory of these abilities.

The development of cognition is a complex process, and there is considerable value in establishing cognitive profiles in infancy (Paterson, Brown, Gsödl, Johnson, & Karmiloff-Smith, 1999). In the present study, as the SSCP was established in relation to the core scales of the SA battery, children with Sotos syndrome under the age of 8 years were not included in the profile analysis. It will therefore be valuable for future research to use tasks to assess skills such as visuospatial memory and quantitative reasoning in infants and young children with Sotos syndrome in order to determine whether the SSCP is consistent across age groups. This will inform understanding of the development of cognitive abilities within the Sotos syndrome population.

Previous research has established that the majority of individuals with Sotos syndrome display clinically significant behavioural symptomatology associated with ASD (Lane, Milne, & Freeth, 2017; Sheth *et al.*, 2015). Therefore, it will be valuable for future research to further understand the relationship between Sotos syndrome and ASD by investigating the association between cognition and autistic features within this population and whether the cognitive profiles are similar or distinct.

The study of cognition and behaviour in genetically identified disorders can provide insight into the interactions between genes, brain and behaviour (Scerif & Karmiloff-Smith, 2005). This informs understanding of the relationship between genotype and cognitive phenotype as congenital syndromes are often associated with genetic abnormalities and in most cases, intellectual disability. As Sotos syndrome is associated with abnormality of the NSD1 gene (Kurotaki *et al.*, 2002), as well as neurological abnormalities (Schaefer *et al.*, 1997), it will be important for future research to explicitly assess the relationship between these facets of the syndrome, in relation to the cognitive profile. This could inform understanding of the mechanism of the NSD1 gene and whether

the neurological abnormalities present in individuals with Sotos syndrome result in specific functional abnormalities.

Conclusion

In summary, this is the first study to identify the cognitive profile associated with Sotos syndrome. The findings from the present study indicate that the Sotos syndrome population is relatively homogeneous, with participants displaying a clear and consistent profile of distinct cognitive strengths and weaknesses. The Sotos syndrome cognitive profile is characterized by relative strength in verbal ability and visuospatial memory but relative weakness in non-verbal reasoning ability and quantitative reasoning. Thus, the findings from the present study provide important implications in relation to educational considerations for individuals with Sotos syndrome.

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