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Neuropsychological components of intellectual disability: the contributions of immediate, working, and associative memory

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Abstract

Background Efficient memory functions are important to the development of cognitive and functional skills, allowing individuals to manipulate and store information. Theories of memory have suggested the presence of domain-specific (i.e. verbal and spatial) and general processing mechanisms across memory domains, including memory functions dependent on the prefrontal cortex (PFC) and the hippocampus. Comparison of individuals who have syndromes associated with striking contrasts in skills on verbal and spatial tasks [e.g. Down syndrome (DS) and Williams syndrome (WS)] allows us to test whether or not these dissociations may extend across cognitive domains, including PFC and hippocampal memory processes.

Methods The profile of memory function, including immediate memory (IM), working memory (WM) and associative memory (AM), was examined in a sample of adolescents and young adults with DS ($n = 27$) or WS ($n = 28$), from which closely CA- and IQ-matched samples of individuals with DS ($n = 18$) or WS ($n = 18$) were generated. Relations between memory functions and IQ and adaptive behaviour were also assessed in the larger sample.

Results Comparisons of the two matched groups indicated significant differences in verbal IM (DS < WS), spatial IM (DS > WS) and spatial and verbal AM (DS > WS), but no between-syndrome differences in WM. For individuals with DS, verbal IM was the most related to variation in IQ, and spatial AM related to adaptive behaviour. The pattern was clearly different for individuals with WS. Verbal and spatial AM were the most related to variation in IQ, and verbal WM related to adaptive behaviour.

Conclusions These results suggest that individuals with these two syndromes have very different patterns of relative strengths and weaknesses on memory measures, which do not fully mirror verbal and spatial dissociations. Furthermore, different patterns of memory dysfunction relate to outcome in individuals with each syndrome.

Keywords adaptive behaviour, cognition, Down syndrome, intellectual disability, Williams syndrome, working memory

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Efficient memory processes allow individuals to keep incoming information on-line, perform mental computations on it and either act on it or store it for future use. Since the work of Daneman & Carpenter (1980), there has been a wide body of literature highlighting the importance of memory skills in cognitive attainment across a range of tasks, including language and fluid intelligence. The importance of memory for individuals with Williams syndrome (WS), a syndrome associated with intellectual disability (ID), has been emphasised by Robinson *et al.*'s (2003) finding that verbal working memory (WM) was more highly correlated with variation in language development in children with WS than in typically developing (TD) children. In individuals with ID syndromes, we expect that multiple memory systems may be impaired, resulting in decreases in the ability to learn broader cognitive skills (and therefore, lower IQ).

Neural evidence points to specialised but interactive subsystems underlying immediate memory (IM), WM and associative memory (AM). IM is based on the time-limited representational capacity of the brain. The left hemisphere, especially posterior left hemisphere, has been found to be important for verbal IM, while spatial IM is linked with the right hemisphere, including right prefrontal cortex (PFC) and right posterior parietal areas (Martin 2005). However, there is also some evidence for variability in the neural correlates of IM across individuals (Feredoes *et al.* 2007). WM allows us to briefly store and manipulate incoming information. WM has been found to have separable components of executive control and item maintenance, with executive control reliant on the PFC (Postle *et al.* 1999). Finally, AM, reliant on the hippocampus, includes the consolidation of memory over a longer time course, often through the formation of associations.

The literature has suggested dissociations based on the representational content of memory (i.e. verbal vs. spatial) in each of these memory systems. For example, Baddeley and Hitch (Baddeley & Hitch, 1974; Baddeley 1986) proposed a WM model with separate systems devoted to processing verbal and spatial information (i.e. the phonological loop and visual-spatial sketchpad). Evidence from behavioural dual-task paradigms and neuroimaging suggests that processing in these domains is dissociable. However, Baddeley's (2000) theory also includes systems which process information across domains (e.g. the central executive and the episodic buffer). The central executive controls information flow across the devoted verbal and spatial subsystems and the episodic buffer forms integrated representations of information across domains, much like the piecing together of an episodic memory. Similarly, in reference to AM, Cognitive map theory (O'Keefe & Nadel 1978) has emphasised that the hippocampus is specialised to process spatial information. However, other theories of hippocampal function [e.g. Relational theory (Cohen & Eichenbaum 1993) and Declarative theory (Squire 1986)] posit that the hippocampus may have more general processing mechanisms and is crucial for the acquisition of both spatial and semantic memories and the formation of arbitrary associations between types of information.

Similarly, study of the cognitive profiles of individuals with ID syndromes includes competition between theories proposing the importance of memory systems with modality-specific versus general processing mechanisms. A large body of research has examined the cognitive profiles of individuals with two genetic syndromes, Down syndrome (DS) and WS. Broadly, the cognitive profile of individuals with WS is characterised by relative strengths in concrete language and a severe weakness in visuospatial construction (Mervis *et al.* 2000). In contrast, individuals with DS typically display the opposite pattern, with relative strengths on visuospatial tasks and severe language difficulties (Chapman & Hesketh 2000). Consistent with these cognitive profiles is the robust finding of a crossover interaction between verbal and spatial IM in individuals with DS and individuals with WS (Wang & Bellugi 1994; Jarrold *et al.* 1999), often measured by the digit and Corsi forward span tasks (Milner, 1971). The striking contrast in the profiles of individuals with these two ID syndromes emphasises the dissociation of processing in these domains.

However, the presence of isolated, domain-specific deficits cannot fully explain data regarding the cognitive profiles of individuals with ID. For instance, correlations among various cognitive tasks are higher in individuals with IDs than in individuals who have intelligence in the normal range (Detterman & Daniel 1989). Additionally, Mervis (1999)

found that spatial and verbal abilities were highly correlated in individuals with WS despite the uneven profile of these skills in this syndrome. Previous theories have suggested sets of functions that could limit cognitive development across domains in individuals with different IDs, including deficits in WM or high levels of cognitive control (Pennington 1994; Pennington & Bennetto 1998; Cornoldi & Vecchi 2003).

While WM is a candidate for a key process underlying cognitive limitations across IDs, previous research on the factor structure of intelligence has found that AM may also be important for general intellectual development (Carroll, 1993). Similarly, the data of Pennington *et al.* (2003) suggested a role for both WM and AM in intellectual development in individuals with DS given that each of these processes made an independent contribution to variation in IQ scores. However, the relation between AM and global cognitive delay, or decreased IQ, has not been examined fully across individuals with syndromes resulting in ID. Therefore, in the present study we examine the importance of both WM and AM in the cognitive profile of individuals with DS and WS to determine whether or not deficits on in the domains may be present in both syndromes and may be a factor limiting cognitive and everyday skills attainment.

Indeed, some previous evidence does suggest that individuals with DS or WS may display deficits in WM and AM regardless of domain. For instance, Pennington *et al.* (2003) found that individuals with DS had deficits in comparison with mental age controls on both verbal and spatial measures of AM. Other studies have found verbal and spatial WM deficits in individuals with DS as compared with matched TD controls and individuals with ID of mixed aetiologies (Visu-Petra *et al.* 2007).

Similar findings have been reported for individuals with WS, with studies showing deficits in both spatial and verbal long-term recall (Vicari *et al.* 1996; Nichols *et al.* 2004). Wang & Bellugi (1994) and Devenny *et al.* (2004) found that the verbal WM ability of individuals with WS (as measured by backward digit span) did not differ significantly from that of CA- and IQ-matched groups with DS or mixed aetiologies. A recent study of individuals with WS found that implementing a 5-s delay resulted in WM impairment in relation to MA controls across a variety of stimuli, including memory for faces and location (O'Hearn *et al.* 2009). The authors concluded that impairments in frontal-parietal circuits may lead to impairments across differing types of stimuli when memory load is high (i.e. due to delay). However, Jarrold *et al.* (2007) argued that the absence of domain-specific dissociations in past research may reflect study-matching procedures with much younger TD controls. Therefore, more work using groups closely matched for both CA and IQ, is needed to better understand if performance on WM and AM tasks may mirror the dissociation in verbal and spatial IM often observed in these groups.

To address these questions, we examined the memory profile of groups with DS and WS using measures with verbal and spatial variants. To replicate the verbal and spatial dissociation in IM, we used forward digit and Corsi span tasks. To study WM, we utilised the backward digit and Corsi span tasks to keep the task demands similar to IM tasks, only varying the executive demands. Recent neuroimaging findings in typical adults suggest that forward and backward digit span tasks may share a common network including the dorsolateral PFC, but that the activation of this network is far greater during the backward manipulation, thereby reflecting the increased executive demands (Gerton *et al.* 2004). The AM tasks included supraspan list learning and the Cambridge Neuropsychological Test Automated Battery (CANTAB) spatial paired associates learning (PAL). Patients with hippocampal damage are impaired in supraspan list learning tasks, and imaging studies show that these tasks activate the posterior hippocampus, particularly after a delay (Fernandez *et al.* 1998; Kohler *et al.* 1998). Furthermore, individuals with hippocampal damage showed significantly impaired performance on a similar measure to the CANTAB PAL, and this measure has been shown to be 98% accurate in discriminating between individuals with Alzheimer's disease and the general population (Miller *et al.* 1993; Swainson *et al.* 2001).

Using these carefully chosen assessments, we aimed to answer the following questions:

1. Will individuals with syndromes displaying striking domain-specific strengths and weaknesses, such as DS and WS, have deficits on prefrontal and hippocampal neuropsychological measures which

mirror these strengths and weaknesses? To answer this question, we examined the profile of verbal and spatial memory functions (IM, WM and AM) in closely matched samples of individuals with DS and WS. By including verbal and spatial tasks with varying processing demands, we were able to test whether any measured group differences on WM and AM measures resulted from already present differences in verbal and spatial IM.

2. Which memory types may be most related to variation in intellectual and adaptive abilities in individuals with DS and WS? Answers to this question are important, because beyond understanding which memory processes may show specific impairments in relation to IQ, it is crucial to pinpoint the memory systems that may be driving ID in individuals with these syndromes. Currently, interventions are being developed to modify function in these syndromes (Fernandez *et al*. 2007; Salehi *et al*. 2009), often with the goal of modifying function in the hippocampus and the PFC. Understanding which of these processes may be the most related to overall intellectual ability may help further target those interventions.

3. Are there correlations among verbal and spatial memory measures within each syndrome? Significant correlations across domains would suggest the presence of domain-general processes.

Based on past research, we expected that memory processes would be correlated across domains and that domain-specific associations in IM would not extend to tests of WM or AM. Based on previous findings (Pennington *et al*. 2003) and theories regarding the components of intelligence, we also expected that measures of WM and AM would be related to measures of IQ and adaptive behaviour even after controlling for differences in IM span.

Methods

Participants

Twenty-seven individuals with DS (10 males, 17 females; mean CA = 17.81 years, SD = 2.90, range: 13–23 years) and 28 individuals with WS (17 males, 11 females; mean CA = 18.63 years, SD = 3.98, range: 12–26 years) participated in this study. Participants with DS were recruited from a Denver, CO DS organisation ($n = 26$) and in Louisville, KY ($n = 1$). Individuals with WS were recruited in the Denver, CO area ($n = 3$), Louisville, KY ($n = 11$), at a Williams Syndrome Association (WSA) family convention in Long Beach, CA ($n = 10$), and in the Pittsburgh, PA area ($n = 4$). All of the individuals with DS had trisomy 21 based on parent report, and all of the individuals with WS had a positive FISH (fluorescence in situ hybridization) test for the WS microdeletion.

Between-syndrome comparisons were based on subsamples of 18 participants with DS (7 males, 11 females) and 18 participants with WS (13 males, 5 females) for which the group means were closely matched for both CA and full scale IQ (Table 1, $P > 0.65$). The groups were selected to be matched on full-scale IQ. However, they also ended up being matched for both verbal IQ and performance IQ. As noted by Jarrold *et al*. (2007), previous studies have often been based on group comparisons to TD MA control groups. Comparisons between individuals with IDs with much younger TD children are often inaccurate due to differences in the developmental trajectories of various measures, a problem which may be especially relevant for memory tasks (Mervis & Robinson 2005). Therefore, in the present study, we examined the memory abilities of individuals with DS and WS closely matched for both CA and IQ. Demographics for the matched sample are reported in the Results section.

Procedure

All study procedures were approved by the human subjects review board of the University of Denver and the University of Louisville. Participants completed the measures described below during a 3-hour session in a university lab, comparable home setting, or in a quiet testing location at the WSA convention. Each participant worked individually with a trained examiner and was given breaks as needed.

Tasks were presented in one of two fixed orders, with order counterbalanced across groups. The order of the IM and WM tasks varied in the two testing orders, but the presentation of the other measures remained relatively fixed. Families were given $25 or an equivalent gift for their participation.

The IQ was assessed using the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler 1999).

Table 1 Descriptive statistics for the matched Down syndrome and Williams syndrome samples

Measure	Down syndrome ($n = 18$)	Williams syndrome ($n = 18$)	t/χ^2	P
Mean (SD) age	17.42 (2.92)	17.40 (3.20)	–0.07	0.95
% Male	38.9	72.2	4.05	0.05
% Caucasian	89.9	94.4	3.03	0.39
Mean (SD) WASI Full-4 IQ	59.33 (6.05)	59.56 (6.20)	0.45	0.66
Mean (SD) WASI Verbal IQ	64.89 (8.91)	65.94 (7.31)	0.73	0.48
Mean (SD) WASI Vocabulary Raw Score	22.78 (9.15)	26.33 (7.84)	–1.25	0.22
Mean (SD) WASI Similarities Raw Score	19.61 (7.34)	20.17 (5.80)	–0.25	0.80
Mean (SD) WASI Performance IQ	59.78 (3.54)	58.72 (5.83)	–0.71	0.49
Mean (SD) WASI Block Design Raw Score	8.39 (5.83)	4.00 (4.33)	2.56	0.02
Mean (SD) WASI Matrix Reasoning Raw Score	5.83 (2.85)	7.72 (5.57)	–1.28	0.21
Mean (SD) SIB-R broad independence standard score*,†	51.27 (14.80)	43.33 (18.13)	–1.87	0.08

* $n = 15$ for the WS group, † An ANCOVA with the full samples controlling for IQ showed a significant difference between adaptive behaviour standard scores, with the group with WS more impaired than the group with DS ($F_{1,47} = 4.09$, $P = 0.05$). SIB-R, Scales of Independent Behavior – Revised; WASI, Wechsler Abbreviated Scale of Intelligence.

This measure was chosen because it is a full-scale IQ test normed for the entire age range of participants (12–26 years). The WASI includes four subtests (Vocabulary, Similarities, Matrices and Block Design), which are used to generate Verbal IQ, Performance IQ and full-4 IQ (mean = 100, SD = 15).

Adaptive functioning was assessed by the Scales of Independent Behavior – Revised (SIB-R; Bruininks *et al.* 1996), which was administered in interview format with a parent. The SIB-R has four clusters: Motor, Social Interaction and Communication, Personal Living, and Community Living Skills. It yields standard scores (SS; mean = 100, SD = 15) for each cluster and also an overall SS, the Broad Independence SS.

Immediate memory

The Forward Corsi Block Span Task and a Forward Digit Span task [Test of Auditory Perceptual Skills – Revised (TAPS-R) auditory number memory test; Gardener 1996] were used as measures of IM span. In the spatial variant, the Corsi span test, participants were shown a board with a random distribution of blocks painted the same colour. The examiner tapped a sequence of blocks; the participant's task was to repeat the examiner's sequence. Sequences ranged from two to eight blocks, and two trials were administered at each sequence length. The forward digit span task measured verbal IM, and required participants to repeat a sequence of numbers ranging from 2 to 8 in length. Administration rate for both tasks was one item per second. For each task, span was calculated as the length of the longest string that the participant repeated correctly.

Working memory

The WM measures included the backward Corsi span task and the TAPS-R backward auditory number memory test. These tasks were administered in the same manner as the IM tasks. However, the participant was required to repeat the items in the reverse order of that presented by the examiner. Backward span was calculated as the number of items in the longest sequence that the participant correctly repeated in reverse order. The backward digit and Corsi span tasks are very similar to the forward digit and Corsi span tasks, except for the addition of the processing demands required to reverse the recall of the stimuli.

Associative memory

The AM tasks had memory demands tapping hippocampal function, including storing representations of associated information over a longer time

course. The verbal AM measure was a test of supraspan word list learning, the NEPSY List Learning Test (Korkman *et al.* 1998). Individuals were orally presented with a list of 15 words by the examiner. After the presentation of the entire word list, the participant was instructed to recall as many words as possible. The target list was presented five times in succession, followed by immediate list recall each time. After five repetitions the examiner orally presented an interference list and then there was a 10-min delay after which the participant was asked to recall the first list. The dependent variables included the total number of words recalled across the five presentations (out of 75 possible) and the number of words recalled after the delay. Evidence supports a dissociation in the neural processes underlying immediate versus delayed recall on this task, with delayed recall relying more on the hippocampus (Kohler *et al.* 1998). Therefore, we analysed both variables.

We assessed spatial AM using the Paired Associates Learning (PAL) task from the CANTAB (Sahakian & Owen 1992). This task requires the participant to learn associations between abstract visual patterns and locations. Participants viewed six to eight white boxes on a touch-screen computer monitor. On each trial, the boxes opened up to reveal patterns or empty boxes inside. The task increased in difficulty from one to eight pattern locations to be remembered at each stage with eight stages in total. After the presentation of all the hidden patterns, each pattern was presented one at a time and the participant had to touch the box to demonstrate where it is located. If the participant failed a trial, all the boxes opened up again to display the hidden patterns. If the participant completed eight consecutive trials incorrectly, the task was terminated. The main variable of interest was the total number of stages completed.

Results

For the full samples, mean IQ was 57.37 (SD = 5.70, range: 51–72) for the DS group and 62.93 for the WS group (SD = 9.24, range: 50–81). This difference was significant [$t(53) = -2.70$, $P = 0.01$], consistent with past findings (Klein & Mervis 1999).

Descriptive statistics for the matched groups with DS and WS are reported in Table 1. The two groups were closely matched at the group level for both CA ($P = 0.95$) and full scale IQ ($P = 0.66$). In addition, they turned out to be well-matched for both Verbal IQ and Performance IQ. However, despite being well-matched on Performance IQ, the groups differed significantly on the Block Design sub-scale raw score ($P = 0.02$), with the WS group displaying poorer performance. The groups were similar in ethnic background but differed significantly in gender distribution ($P = 0.05$). Therefore, in subsequent analyses, we controlled for gender differences. The between-group analyses reported below were based on these matched samples. Between-group results were also analysed for the whole sample with IQ as a covariate, with similar results.

Profile of memory skills for individuals with Down syndrome and Williams syndrome

Descriptive statistics and statistical comparisons for the measures of IM, WM and AM in the matched samples are presented in Table 2. To determine if the previously reported crossover interaction between verbal and spatial IM was replicated for the present samples, we conducted a 2 (Group: DS vs. WS) × 2 (Domain: verbal vs. spatial) mixed ANOVA with IM span as the dependent variable. As was found in previous studies, there was a significant group by domain interaction ($F_{1,34} = 23.91$, $P < 0.001$), with the group with WS outperforming the group with DS on the verbal IM task, and the group with DS outperforming the group with WS on the spatial IM task. *Post hoc* tests of simple effects indicated significant between-group differences with the group with DS performing better than the group with WS on the Corsi span task ($P = 0.05$) and the group with WS performing better than the group with DS on the digit span task ($P < 0.01$).

Consistent with our first hypothesis, this crossover interaction did not hold for WM. Neither the main effect of Group and Domain, nor the interaction term ($F_{1,34} = 2.39$, $P = 0.13$) was significant. No significant differences were found despite an adequate distribution of scores, with few individuals performing at floor. In the matched group with DS,

Table 2 Immediate, working and associative memory in the matched groups with Down syndrome and Williams syndrome

Measure mean (SD)	Down syndrome ($n = 18$)	Williams syndrome ($n = 18$)	*F*	*P*
Immediate memory				
TAPS-R digit span forward	3.83 (0.99)	4.94 (1.51)	6.81	0.01*
Corsi span forward	4.17 (0.86)	3.50 (1.04)	4.39	0.05*
Working memory				
TAPS-R digit span backward	2.39 (0.98)	2.61 (0.85)	0.53	0.47
Corsi span backward	2.78 (1.11)	2.56 (0.92)	0.43	0.52
Associative memory				
Verbal list learning, total words recalled on all trials	35.11 (10.01)	31.89 (8.52)	1.08	0.31
Verbal list learning, total words recalled at delay	8.05 (4.05)	6.11 (2.56)	4.47	0.05*
CANTAB Spatial Paired Associates, stages completed	7.78 (0.55)	6.50 (1.43)	12.61	0.001*

* Difference remained significant after control for gender and immediate memory in the same domain ($P < 0.05$). CANTAB, Cambridge Neuropsychological Test Automated Battery; Corsi; TAPS-R, Test of Auditory Perceptual Skills – Revised.

22% ($n = 4$) were at floor on the backward digit span task and 11% ($n = 2$) were at floor on backward Corsi span. In the group with WS, 11% ($n = 2$) were at floor on each measure. This level of floor performance is comparable with or better than many published neuropsychological measures in these populations. Moreover, when these analyses were performed excluding participants who displayed floor performance on backward span measures, the results were equivalent, with no effects found for Group, Domain or the interaction term ($F_{1,27} = 1.34$, $P = 0.26$).

We also tested Group by Domain interactions in AM. Z-scores (based on the matched groups' combined mean, $n = 18$ in each group) were constructed to allow for comparable scales across each measure. The interaction term for the analysis of AM was not significant for total score ($F_{1,34} = 2.43$, $P = 0.13$). There was a main effect of Group, with the group with DS outperforming the group with WS on both verbal and spatial AM total scores ($F_{1,34} = 9.48$, $P = 0.004$). Examining each task individually, number of PAL stages completed differed between the groups ($P = 0.001$), with more stages completed by the group with DS. On the verbal list-learning measure, there was no group difference in the total number of words recalled across trials. However, the number of words remembered after delay did differ significantly ($P < 0.05$), with the group with DS outperforming the group with WS. After control for gender and IM span for each task's domain (e.g. verbal or spatial), the between-group differences in CANTAB PAL and verbal list learning long-term delay remained significant.

Relations among memory skills, intellectual ability and adaptive behaviour

The correlations among memory type (verbal vs. spatial), intellectual ability and adaptive behaviour are shown in Table 3. The full samples were used to allow for the most representative results. Corsi forward span and digit forward span were related to IQ in both the group with WS and the group with DS and to adaptive behaviour SS in the group with DS. Univariate relations were evident between many of the memory measures and IQ and adaptive behaviour. However, after control for IM in the same domain, none of the correlations with IQ remained significant for the group with DS and the only correlation that remained significant with adaptive behaviour SS was Spatial AM. For the group with WS, verbal WM and both verbal and spatial AM remained significantly correlated with IQ and verbal WM and spatial AM remained significantly correlated with adaptive behaviour SS.

In a final set of analyses, we included verbal and spatial IM as well as the measures that retained significance with outcomes (IQ and adaptive behaviour SS) after control for IM in regressions to

Table 3 Relations among memory measures and IQ and adaptive behaviour (AB) standard scores: simple correlations and partial correlations controlling for IM in the same domain

	IQ: Down syndrome		IQ: Williams syndrome		AB: Down syndrome		AB: Williams syndrome	
	r	*r* adjusted*	*r*	*r* adjusted*	*r*	*r* adjusted*	*r*	*r* adjusted*
Verbal								
Digit span forward	0.84†	–	0.41‡	–	0.39‡	–	0.24	–
Digit span backward	0.69†	0.33§	0.55†	0.50†	0.41‡	0.22	0.51‡	0.48‡
List learning total words	0.46‡	0.11	0.49†	0.45‡	0.33§	0.17	0.08	0.03
List learning delay total	0.52†	0.03	0.67†	0.45‡	0.28	0.17	–0.03	–0.09
Spatial								
Corsi span forward	0.43‡	–	0.41‡	–	0.40‡	–	0.003	–
Corsi span backward	0.41	0.21	0.49†	0.31	0.26	0.02	0.29	0.39§
CANTAB PAL stages completed	0.31	0.21	0.51†	0.47‡	0.52‡	0.46‡	0.48‡	0.47‡

* Correlations were adjusted for IM in the same domain, † $P < 0.01$, ‡ $P < 0.05$, § $P < 0.10$. CANTAB PAL, Cambridge Neuropsychological Test Automated Battery Paired Associates Learning; Corsi; IM, immediate memory.

Table 4 Correlations among verbal and spatial memory measures

	Down syndrome	Williams syndrome
	r	*R*
Corsi span forward and digit span forward	0.33*	0.52†
Corsi span forward and digit span backward	0.49†	0.61†
List learning total score and PAL number of stages	0.24	–0.01
List learning # words after delay and PAL number of stages	0.21	0.20

* $P < 0.10$, † $P < 0.01$, Corsi; PAL, Paired Associates Learning.

determine the factors most related to outcome. For the group with DS, the only significant factor relating to IQ was forward digit span ($\beta = 0.84$; $P < 0.001$), with the model explaining 71% of the variance. For the group with WS, both list learning delay total and CANTAB PAL number of stages were significant (list delay: $\beta = 0.56$; $P < 0.001$; PAL: $\beta = 0.40$; $P < 0.01$), explaining 57% of the variance. For the group with DS only CANTAB PAL number of stages completed was significantly related to adaptive behaviour SS ($\beta = 0.52$; $P < 0.01$), explaining 27% of the variance. For the group with WS, the only variable significantly related to adaptive behaviour SS was backward digit span ($\beta = 0.51$; $P < 0.05$), explaining 26% of the variance.

Correlations between verbal and spatial memory measures

To determine the extent that verbal and spatial variants of memory tasks may share processing demands, we examined the correlation between the paired tasks in each task domain within individuals with each syndrome (Table 4). Correlations were examined in the full sample (DS $n = 27$, WS $n = 28$) to allow for the most representative results. For the group with WS, forward digit span and forward Corsi span significantly correlated, while in individuals with DS there was a trend toward a correlation between these measures. Backward digit span and backward Corsi span were significantly related for both groups. Interestingly, there were no signifi-

cant correlations between number of words remembered (either across the learning trials or at delay) and CANTAB PAL number of stages completed for either the group with DS or the group with WS.

Discussion

Down syndrome and WS are syndromes associated with ID in which there is a dissociation in verbal and spatial ability. This dissociation is evidenced by opposing profiles of performance on measures of visuospatial construction and language tasks, including measures of grammar (syntax and morphology) and verbal IM. A hallmark finding highlighting this dissociation is the presence of a crossover interaction between verbal and spatial IM in these groups. In the current study, we replicated this finding and tested the extent to which this crossover interaction may extend to other areas of neuropsychological function, including memory measures related to prefrontal and hippocampal function. We also examined the impact of these memory functions on the broader cognitive profile in individuals with these syndromes, including the relation between verbal and spatial memory and variation in IQ and adaptive behaviour.

Using groups of individuals with DS and WS closely matched for full-scale IQ and CA, we replicated the crossover interaction between verbal and spatial IM previously reported for individuals with these two syndromes. Verbal IM was more impaired in individuals with DS than in those with WS, and spatial IM was more impaired in individuals with WS than in those with DS. We then tested whether domain-specific dissociations extended to measures of AM and WM. As predicted from the past literature, we did not find these dissociations. Instead, verbal WM and spatial WM were comparable in both groups. Based on past studies this finding likely reflects equal levels of impairment relative to TD controls (Visu-Petra *et al.* 2007). We also found that the group with WS was more impaired than the group with DS on AM tasks, regardless of domain. Performance on AM measures also related to variation in IQ in individuals with WS.

The finding of considerable relative impairments on AM tasks for the group with WS is consistent with several recent reports (Vicari *et al.* 1996; Nichols *et al.* 2004; Lakusta *et al.* 2010) and highlighted by the comparison with individuals with DS, a population with a wide body of literature suggesting hippocampal dysfunction. Meyer-lindenberg *et al.* (2005) reported that even individuals with WS who have IQs in the average range for the general population evidenced marked abnormalities in function and metabolism in the hippocampus. These findings also are consistent with studies of knock-out mice deleted for *Cyln2*, *Limk1* or *frizzled 9* (three genes included in the WS deletion). These mice had difficulties with spatial navigation, suggesting that the WS deletion may contain several genes important for the development and function of the hippocampal formation (Hoogenraad *et al.* 2002; Meng *et al.* 2002; Zhao *et al.* 2005). In summary, individuals with WS have relative deficits in AM in comparison with a matched group of individuals with DS; these deficits in AM are above and beyond the influence of IM deficits; and these difficulties were apparent in both verbal and spatial domains.

The pattern of relative deficits was clearly different in individuals with DS. In comparison with individuals with WS, those with DS only showed specific difficulty on verbal IM. When we examined the relation of memory with IQ, verbal IM was clearly the most important predictor of outcome, accounting for 71% of the variance. When we examined the relations of AM and WM to IQ, none of the correlations remained beyond the influence of verbal IM. This finding suggests that IM is a bottleneck for the development of other cognitive functions in individuals with DS. Results of several studies suggest that verbal IM difficulties are due to memory problems, particularly in the processing of phonological representations, rather than to difficulties with audition or speech (Jarrold *et al.*, 2002; Lee *et al.*, 2010). However, given evidence for differing neural substrates underlying IM in the general population (Feredoes *et al.* 2007), more work is needed regarding the specific cognitive and neural underpinnings of the verbal IM deficit in individuals with DS.

The patterns of memory dysfunction relating to adaptive behaviour are somewhat different. First, the correlations between memory and adaptive behaviour were less strong, reflecting the multicomponent nature of this set of skills. Interestingly,

when IQ was controlled, adaptive behaviour was significantly better for the group with DS than for the group with WS. In those with DS, spatial AM related most strongly to variation in adaptive behaviour whereas in individuals with WS both verbal WM and spatial AM were most related. The relative absence of associations between adaptive behaviour and IM in these syndromes suggests that everyday skills may be easier to acquire than general cognitive skills (e.g. IQ) when faced with substantial IM deficits. However, more studies are needed to better understand why individuals with WS have more limited adaptive skills than individuals with DS (after controlling for IQ), and to piece apart the cognitive and behavioural characteristics that may lead to success in everyday skill development. One possible contributor to the relative impairment in adaptive skills shown by individuals with WS is reduced mastery motivation relative to CA-matched individuals with DS (Mervis & John, in press; Rowe 2007).

In summary, individuals with DS and individuals with WS evidence very different profiles of memory difficulties that are not entirely predictable based on the broader cognitive profiles associated with these two syndromes. These findings also suggest that there is no one set of shared deficits that may explain cognitive impairment across these syndromes. While at the group level both syndromes had comparable levels of WM impairment, these deficits were not primary correlates of outcome for the group with DS. Therefore, the mechanisms underlying IQ depressions across ID syndromes may be unique. These findings are consistent with a growing body of evidence suggesting that the cognitive profiles in individuals with different ID are non-homogeneous, displaying discrepant patterns of relative deficits across groups. For instance, Vicari and colleagues (Vicari & Carlesimo, 2006; Vicari *et al*. 2006) found that individuals with DS displayed differing patterns of visual-spatial and visual-object WM difficulties from individuals with WS. In particular, individuals with DS showed impairments in both types of visual WM, while individuals with WS were only impaired in visual-spatial WM.

Theories of hippocampal and prefrontal function have competing perspectives regarding the presence of domain-general vs. domain-specific mechanisms. In this study, we examined whether or not a correlation was present between verbal and spatial memory measures, a finding that would suggest some shared mechanisms across domains. IM and WM measures were significantly correlated across verbal and spatial variants, whereas AM was not. These findings suggest that prefrontal memory functions may tap common resources across domains, while the mechanisms underlying verbal and spatial AM may be quite different. Recent evidence has suggested that the PFC may be involved in recruiting resources to enhance representations in other parts of the cortex (Edin *et al*. 2009), while the hippocampus consolidates networks for long-term retrieval of information. In this sense, the enhancement role could operate across domains, whereas information consolidation may be best processed by uniquely operating systems (e.g. place cells). Along these lines, AM dysfunction in individuals with WS may result from deficient processing in two separate systems in the hippocampus. However, these findings could be specific to the measurements in the current study and need to be replicated.

There are certain limitations to the current study that should be mentioned. First, our assessments of memory, overall intellectual ability and adaptive behaviour were concurrent so we cannot definitively state that relative deficits in verbal IM and AM 'cause' depressions in IQ in individuals with these syndromes. Furthermore, the current study focused only on the relations between components of memory and either IQ or adaptive behaviour; other cognitive functions such as processing speed or cerebellar functions also could play a role in developmental outcomes across syndromes.

Despite these difficulties, we believe that the findings of this study have added to evidence suggesting memory problems are a robust factor influencing depressions in intellectual and adaptive function in both individuals with DS and WS. Thus, an important avenue for future research will be the development of effective interventions targeting syndrome-specific memory profiles in those with ID.

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