

# Memory and neuropsychology in Down syndrome

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This paper outlines the strengths and weaknesses in both short-term and long-term memory in Down syndrome, and the implications of these patterns for both other aspects of cognitive development and underlying neural pathology. There is clear evidence that Down syndrome is associated with particularly poor verbal short-term memory performance, and a deficit in verbal short-term memory would be expected to negatively affect aspects of language acquisition, particularly vocabulary development. Individuals with Down syndrome also show impaired explicit long-term memory for verbal information, and may also have particular problems in explicit long-term memory for visual-object associations. However, implicit memory appears to be less affected in Down syndrome, and may therefore provide an important basis for intervention approaches. These findings are consistent with the suggestion of dysfunction within the hippocampal system in Down syndrome, and problems in verbal memory may be linked to impaired functioning of pre-frontal brain regions.

## Introduction

The human memory system can be divided into a number of sub-components. Evidence from experimental studies of memory, and from adult patients with acquired brain damage, suggests that one key distinction in memory function is between the active, ongoing maintenance of information in a 'short-term' or 'working' memory system, and the storage of material that is not kept active, but which can be retrieved from, long-term memory<sup>[1,2]</sup> (see REF 3; though see REF 4). In addition, the short-term and long-term memory systems can also themselves be fractionated. Again, both experimental and neuropsychological evidence suggests that there may be separate verbal and visuo-spatial short-term memory systems, with potentially domain-general control of these storage systems in working memory<sup>[2]</sup>. Similarly, long-term memory can be sub-divided along a number of lines. One common distinction is between 'explicit' (conscious) memory for facts and events and 'implicit' (non-conscious) knowledge and learning (see REF 50). A related distinction can be drawn between the learning of 'declarative' knowledge about facts and 'procedural' knowledge about how to perform particular tasks<sup>[6]</sup>. The former represents an aspect of explicit memory, while the latter is often (though not necessarily) implicit. This review of strengths

and weaknesses in memory in Down syndrome follows these distinctions in the human memory system, before turning to the neuropsychological implications of memory impairments observed in the condition.

## Short-term memory in Down syndrome

A long-standing finding in the Down syndrome literature is that verbal short-term memory performance is impaired relative to visuo-spatial short-term memory performance (see REF 7). Verbal short-term memory is typically assessed by asking individuals to repeat, in correct serial order, a list of words that they have just heard. In contrast visuo-spatial short-term memory tasks typically require participants to recreate a visually presented sequence of spatial locations by manually selecting the appropriate locations in serial order. In the clear majority of studies that have given these two types of task to individuals with Down syndrome and appropriate comparison samples (e.g., control groups matched for mental age), individuals with Down syndrome have shown impaired verbal, but not visuo-spatial short-term memory performance (see REF 8).

One obvious explanation for such a finding is that individuals with Down syndrome struggle on verbal short-term

memory tasks because these tasks require them to perceive auditorily presented information, and then respond verbally. Given that speech perception and production problems are relatively common in Down syndrome, these difficulties might affect performance on such tasks, regardless of the quality of the underlying short-term memory system. Studies that have examined this issue, either by measuring speech and hearing problems or by trying to remove their influence on performance, have suggested that these 'peripheral' effects are not the fundamental cause of poor verbal short-term memory in Down syndrome (e.g. REFS 9-12).

Two studies illustrate this point particularly well. Laws presented individuals with Down syndrome and typically developing children of a comparable vocabulary level with two versions of a test of short-term memory for colours<sup>[13]</sup>. In one condition 'focal' colours, such as red, blue, and green, were presented visually, and participants had to recall the presented sequence by touching the appropriate colours in the correct order on a response board. In a second condition, hard to name 'non-focal' colours were presented for recall in the same manner. Precisely because these colours are very difficult to generate a verbal label for, participants are forced to maintain them in visuo-spatial short-term memory, and indeed the two

groups showed comparable performance on the non-focal condition. However, in the focal condition individuals with Down syndrome were impaired because they failed to recode the visual image of each colour into a verbal label for maintenance in verbal short-term memory. In other words, this study shows a selective deficit in verbal short-term memory ability, even though no words were presented auditorily and responses were made manually rather than verbally.

In a similar vein, Brock and Jarrold presented individuals with and without Down syndrome with two short-term memory tasks, one verbal, one visuo-spatial, which each required participants to remember the presented sequence of items by manually selecting positions on a touchscreen<sup>[14]</sup>. Individuals with Down syndrome were selectively impaired when their re-ordering of the presented sequence had to be done on the basis of verbal short-term memory. In addition, Brock and Jarrold showed that these individuals with Down syndrome were unimpaired in their ability to identify single verbal items, suggesting that speech perception problems were not the cause of poor performance on the verbal memory task.

It therefore appears that people with Down syndrome have a real problem in representing verbal, or 'phonological' information in short-term memory. This has potentially important implications for the condition, as other evidence suggests that children's verbal short-term memory capabilities are closely linked to aspects of their language development (see REFS 15,16). This could be because individuals with generally poor language skills are less familiar with the verbal material employed in typical tests of verbal short-term memory, or have generally poorer phonological skills as a result of their language problems<sup>[17,18]</sup>. However, the above studies have shown that, in Down syndrome at least, verbal short-term memory deficits can be observed even relative to comparison individuals of the same level of language knowledge (see also REF 19). An alternative hypothesis put forward by Baddeley, Gathercole, and colleagues is that verbal short-term memory plays a causal role in aspects of language development, particularly vocabulary, because individuals have to maintain in short-term memory an accurate phonological

representation of any new word that they hear in order to create a more stable, long-term representation of it. If this account were correct, then one would expect the poor verbal short-term memory skills of individuals with Down syndrome to compromise their subsequent vocabulary development.

The problem for this suggestion is that, while language abilities are often particularly delayed in Down syndrome, vocabulary is by no means the weakest of the various aspects of language function in Down syndrome; indeed, vocabulary is typically in advance of syntactic skill for example<sup>[20,21]</sup>. Furthermore, studies of 'fast mapping' - the ability to learn that a novel sound must apply to a novel object - have shown generally good word learning skills among individuals with Down syndrome<sup>[22]</sup>. Reconciling the apparent conflict between impaired verbal short-term memory performance and relatively good vocabulary knowledge in Down syndrome is a key area for future research. Recent work by the first author and colleagues has suggested that individuals with Down syndrome are unimpaired on word learning tasks in which the experimenter provides the novel word and the participant selects the object that it has been paired with<sup>[23]</sup>. This task is arguably analogous to tests of receptive vocabulary in which individuals select the object named by the tester, and on which individuals with Down syndrome do relatively well. In contrast, participants with Down syndrome were impaired on a word-learning task that was more analogous to a measure of expressive vocabulary, in which they were required to select the appropriate non-word name that had been previously paired with a particular object. It may well be that the latter task requires the participant to have a 'finer-grained' and more accurate phonological representation of the non word in question, and therefore is more closely related to verbal short-term memory abilities.

## Long-term memory in Down syndrome

People with intellectual disabilities learn and successively retain new information less efficiently than age-matched typically developing individuals. Although this statement may seem trivial, awareness of the central role of long-term memory

impairment in the emergence of learning difficulties and adaptation problems of people with intellectual disability has prompted a large body of experimental literature aimed at clarifying the qualitative characteristics and basic mechanisms of this deficit.

Down syndrome is the aetiologic group whose long-term memory impairment has been investigated most extensively. However, memory effects vary as a function of the type of memory being assessed. Explicit memory involves things like facts and events that participants consciously recollect, whereas implicit memory can be demonstrated indirectly, without conscious recollection. For example, one common kind of implicit memory test looks at skills or procedures, such as mirror-tracing; another common implicit memory test involves "priming", where prior exposure to a word or picture can influence subsequent performance on word-stem or partial-picture completion tasks even though the participants might not recall having seen the relevant items before. This distinction has been shown to be important in understanding organic amnesia, since most individuals with amnesia are profoundly impaired on explicit memory tasks but show relatively intact performance on implicit tasks. This distinction turns out to also be important in Down syndrome.

Evidence suggests that the explicit long-term memory abilities of individuals with Down syndrome are impaired. In a study comparing individuals with Down syndrome, individuals with intellectual disability of unspecified aetiology and a group of mental age-matched typically-developing children, the Down syndrome group scored significantly lower than both of the other groups on tests of free recall of word lists and a short story, and in the reproduction of Rey's figure from memory<sup>[24-26]</sup>.

Explicit long-term memory for visual-spatial information has been much less investigated than memory for verbal material. In a recent study, Vicari, Bellucci, and Carlesimo investigated the performance of a group of 15 participants with Down syndrome compared to a control group of mental age-matched typically developing children<sup>[27]</sup>. A further group of people with intellectual disability was also included in that study, namely 15 adolescents with Williams syndrome.

A visual-object and a visual-spatial learning test were developed on the assumption that visual-object long-term memory (i.e., for the physical characteristics of objects) and visual-spatial long-term memory (i.e., for position or motion in space) are mediated by different neural systems and, therefore, constitute two distinct aspects of the organisation of explicit long-term memory<sup>[28]</sup>. During the study phase of the visual-object test, fifteen figures of common objects (e.g., a tree) were shown to the participants. During the test phase immediately following the study phase, four different versions of the same object (e.g., 4 trees) were depicted on each page; only one of the four was the same as the target object in the study phase and the other three were physically different distracters. Study and test phases were presented three consecutive times. In the visual-spatial learning test, the pages were divided into four quadrants and each figure was positioned in one of the quadrants. During the test phase, the target stimuli were presented and the participant was asked to indicate the position of the figure on an empty page divided into four quadrants. The entire test was administered three times. The results of this study showed analogous learning of visual-spatial sequences and poorer learning of visual-object patterns in the individuals with Down syndrome compared to their own control group of mental age matched typically developing children. Interestingly, individuals with Williams syndrome showed the opposite profile, with poorer visual-spatial learning but analogous visual-object learning.

The performance profile observed in people with Down syndrome highlights a dissociation between more preserved visual-spatial memory and greater impairment of visual-object learning ability. There is general agreement in the literature that the neuropsychological profile of people with Down syndrome is characterised by strength in nonverbal abilities, as revealed by their performance on graphic, constructive and spatial tests, which are generally less impaired than linguistic abilities<sup>[29]</sup>. However, few studies have made a detailed analysis of the visual-spatial domain. In the only study that compared visual-object and visual-spatial learning abilities in people with Down syndrome, a relative sparing of

visual-spatial memory was found with respect to visual-object memory<sup>[30]</sup>. These authors argued that memory for the spatial position of objects is characterised by greater automaticity than memory for visual and/or verbal content of information and, for this reason, is less impaired in persons with mental retardation<sup>[30]</sup>. In the Vicari et al. study, the comparison of the two groups of subjects with known genetic syndromes suggests a different type of interpretation<sup>[27]</sup>. In fact, individuals with Down syndrome have greater difficulty in learning visual-object material with a substantial saving of visual-spatial learning, and participants with Williams syndrome show the opposite pattern. This suggests that not all persons with intellectual disability present a preserved visual-spatial memory (as Ellis seems to suggest (see REF 30)). Accordingly, this finding also gives greater validity to the performance pattern exhibited by the persons with Down syndrome and Williams syndrome. It indicates that the impairment exhibited by the two groups cannot be attributed simply to the presence of intellectual disabilities but that it is a peculiar characteristic of each syndrome.

In the last few years, some experimental data have been reported regarding the possible extension to individuals with intellectual disability of the dissociation noted above between explicit and implicit memory processes so frequently described in brain damaged adults with memory disorders. Regarding *repetition priming*, studies investigating facilitation in identifying perceptually degraded pictures, induced by previous exposure to the same pictures, have consistently reported a comparable priming effect in individuals with intellectual disability and in typically-developing subjects matched for chronological age<sup>[31, 32]</sup> or mental age<sup>[33]</sup>. Similar findings were found using verbal material. Most of these studies were based on the Stem Completion procedure in which subjects are requested to complete a list of stems (i.e., the first three letters) with the first word that comes to mind. In this test, the priming effect is revealed by a bias in completing the stems with previously studied rather than unstudied words. Carlesimo et al.<sup>[24]</sup> and Vicari, Bellucci, and Carlesimo<sup>[34, 35]</sup> reported a priming effect with this procedure in various groups of individuals with intellectual disability (aetiologi-

cally unspecified, Down syndrome and Williams syndrome) comparable to that of mental age matched typically developing subjects.

Less experimental work has been devoted to investigating the ability of individuals with intellectual disability to learn *visuo-motor* or *cognitive skills*. In a first study, Vakil, Shelef-Reshef, and Levy-Shiff compared the improvement in accuracy displayed by groups of individuals with intellectual disability and mental age-matched children on successive trials of the Tower of Hanoi and the Proteus Maze tests<sup>[36]</sup>. On both tests, the individuals with intellectual disability performed significantly less accurately than the controls. However, on the first test (which requires completing a spatial pattern according to a series of predetermined rules) the rate of trial-to-trial improvement was higher in the typically-developing than in the intellectual disability group, and on the Proteus Maze test (which requires solving a series of mazes with the least number of errors possible) the two groups improved at the same rate. Recently, Vicari and co-workers pointed out an intriguing difference in the skill learning abilities of two genetically distinct groups of individuals with intellectual disability. In the first study<sup>[34]</sup>, a group of individuals with Down syndrome showed the same rate of improvement as a group of mental-age matched typically-developing children across successive trials of the Tower of London test (analogous to the Tower of Hanoi) and in the comparison of the repeated versus random blocks of a facilitated version of the Serial Reaction Time test<sup>[37]</sup>, which requires implicit learning of the sequential order of a series of visual events. In a second study, a group of children with Williams syndrome showed significantly less procedural learning than typically developing children on both of these tests<sup>[35]</sup>. Certainly, the relative sparing of implicit memory function may help explain why infants with Down syndrome show unimpaired performance on a memory task that requires acquisition of a motor response (i.e., procedural learning<sup>[38]</sup>) and why 20-43-month old children with Down syndrome are able to succeed at a deferred imitation task<sup>[39]</sup>.

## The neuropsychology of memory in Down syndrome

The different cognitive profiles exhibited by the various aetiological groups of people with intellectual disability presumably result from some specific characteristics of their anomalous brain development. In a recent study, Pennington, Moon, Edgin, Stedron and Nadel tested adolescents with Down syndrome on a range of tasks designed to directly assess the function of specific brain systems. This 'cognitive neuropsychological' approach often uses tasks first developed in animal models, where the critical underlying brain circuits can be identified and carefully studied in invasive experiments. The team started with a focus on three brain systems identified by the neuropathological data: the hippocampal system, the prefrontal cortex, and the cerebellum. They developed a set of tasks that could, collectively, tell us something about how these brain systems are faring. In the first set of studies, they found evidence of specific hippocampal dysfunction in a sample of 28 adolescents, using mental age matched controls<sup>[40]</sup>. This impairment in hippocampal function could in principle reflect problems in any of the structures of the hippocampal region; a recent study of two neuropsychological paradigms dependent on parahippocampal and perirhinal regions (delayed nonmatching to sample and visual paired comparison), however, suggests that these areas are functioning appropriately, and that the impairment is more likely to reflect improper development of the hippocampus itself<sup>[41]</sup>.

Little evidence of prefrontal dysfunction was observed in a battery of nonverbal tasks in the Pennington et al. study<sup>[40]</sup>. Subsequent pilot work from that group, however, suggested that verbal tasks might yield a different result, and indeed that is what is being observed<sup>[42]</sup>. Using verbal tasks to explore the prefrontal cortex, these researchers found in the young (aged 5-11) and old (aged 30-41) groups strong signs of dysfunction in both the hippocampal and prefrontal systems. Deficits were observed in a range of tasks although verbal mediation was necessary to bring out the prefrontal effect.

Taken as a whole, these neuropsychological studies show that particular problems

emerge in the memory domains served by the hippocampal system and the prefrontal system. The latter impairment appears to be linked to the use of verbal test materials. There is not yet sufficient evidence to evaluate the role of presumed cerebellar impairments. There is at present little consensus on the role of the cerebellum in learning and memory. Latash discussed some abnormalities in motor coordination in children with Down syndrome, but future research will need to look more carefully at any cognitive sequelae of improper development of the cerebellum<sup>[43]</sup>.

Given the neuropsychological evidence of a developmental trend toward hippocampal neuropathology and the fact that older individuals with Down syndrome show many features consistent with Alzheimer's neuropathology, there has been particular focus on hippocampal functions in neurophysiological studies of Down syndrome. Evidence for hippocampal deficits has been observed in mouse models. Hyde and Crnic reported that Ts65Dn mice show hippocampal-dependent learning deficits as a function of age, and they propose that these deficits may be related to reduced cholinergic innervation of the hippocampus<sup>[44]</sup>. A very recent study demonstrates decreased neurogenesis in the dentate gyrus of the hippocampus in both foetuses with Down syndrome and Ts65Dn mice, suggesting a possible mechanism for at least some of the memory related difficulties in Down syndrome<sup>[45]</sup>. The dentate gyrus plays a particularly important role in contextual aspects of long-term memory, and it has recently been shown that the neurons formed by post-natal neurogenesis are incorporated into learning circuits and may even be critical in fostering normal learning capacity. This is clearly an area ripe for future research.

Recent neuro-imaging studies have also attempted to document the presence of particular morphological cerebral characteristics to explain the distinct cognitive and behavioural profiles observed in persons with intellectual disability, especially of known genetic syndromes<sup>[46,47]</sup>. Magnetic resonance imaging studies have shown reductions in hippocampal volume in Down syndrome prior to the onset of dementia, and these reductions were found to relate to memory deficits<sup>[48]</sup>.

Based on a morpho-volumetric analysis of the brains of individuals with Down syndrome and Williams syndrome, Jernigan, Bellugi, Sowell, Doherty, and Hesselink described important differences that explain, at least in part, the peculiarities of the neuropsychological processes associated with these syndromes<sup>[49]</sup>. Specifically, people with Down syndrome have a hypofrontality associated with cerebellar hypoplasia and with substantial saving of the trunk and the posterior cortical structures. Therefore, Down syndrome may be associated with relatively preserved maturation of the dorsal compared to the ventral component of the visual system, leading to relatively better performance on visual-object than on visual-spatial memory tests. The particularly impaired visual-object learning found in individuals with Down syndrome is also at variance with the hypothesis that, irrespective of the aetiology of the cerebral insult, during development the dorsal stream is more vulnerable to brain damage than the ventral stream<sup>[50,51]</sup>. Further studies are obviously needed to investigate in more detail the presently postulated dissociation of the long-term memory abilities underlying the functions of the dorsal and ventral visual systems in individuals with Down syndrome.

Concerning implicit memory, both neuropsychological<sup>[52]</sup> and functional neuroimaging<sup>[53]</sup> data assign a critical role to basal ganglia and cerebellum in the implicit learning of visuo-motor skills. The brains of individuals with Down syndrome, instead, exhibit severe cerebellar hypoplasia with normal morphology of basal ganglia<sup>[49]</sup>. In the light of these data, we can tentatively conclude that the deficient maturation of visuo-motor skill learning in people with Williams syndrome is related to the deficient maturation of striatal circuits known to be critical for this ability.

## Directions for future research

The above review has highlighted a number of potential directions for future research. While it seems clear that individuals with Down syndrome perform particularly poorly on tests of verbal short-term memory, the consequences of this impairment for more general language development in the condition need to be determined.

In addition, the role of impaired language knowledge, and phonological awareness in particular (see REF 54), in mediating potential links between verbal short-term memory and vocabulary development needs to be more precisely specified.

Similar issues are relevant for work on long-term memory in Down syndrome, where evidence suggests that the modality of information to be recalled moderates the degree of any deficit seen on certain tasks; particularly in the case of verbal tests of frontally-mediated memory systems. The relation between the degree of any impairment on such tasks, and individuals' gen-

erally delayed language abilities, needs to be clarified in future work. At the same time, while visual memory skills may be less impaired, there is evidence of a particular difficulty in visual-object memory, and the causes and consequences of such an impairment need to be outlined.

A final point to note is that the learning and memory problems that begin to emerge in late infancy in Down syndrome become considerably more noticeable as the infant grows to childhood and adolescence. While much of our knowledge for this period comes from the learning of language, there is information available

about other kinds of learning and memory. One major point to be stressed from these language learning data has less to do with the inability of children with Down syndrome to acquire words, or linguistic constructions, or other non-verbal material, and more to do with their inability to 'stabilise' the information that they do manage to acquire. Wishart<sup>[55]</sup> and Fowler<sup>[56]</sup> stress this point, which might reflect, among other factors, impairments in memory consolidation, another function of the hippocampal system.

1. Atkinson RC, Shiffrin RM. Human memory: A proposed system and its control processes. In Spence KW, editor. *The psychology of learning and motivation*. New York: Academic Press; 1968. p. 89-195.
2. Baddeley AD. *Working memory*. Oxford: Oxford University Press; 1986.
3. Unsworth N, Engle RW. The nature of individual differences in working memory capacity: Active maintenance in primary memory and controlled search in secondary memory. *Psychological Review*. 2007;114:104-132.
4. Nairne JS. Remembering over the short-term: The case against the standard model. *Annual Review of Psychology*. 2002;53:53-81.
5. Schacter, DL. Implicit memory: history and current status. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. 1987;13:501-518.
6. Cohen NJ, Squire LR. Preserved learning and retention of pattern-analyzing skills in amnesia: dissociation of knowing how from knowing that. *Science*. 1980;210:207-210.
7. Marcell MM, Armstrong V. Auditory and visual sequential memory of Down syndrome and nonretarded children. *American Journal of Mental Deficiency*. 1982;87:86-95.
8. Jarrold C, Purser HRM, Brock J. Short-term memory in Down syndrome. In: Alloway TP, Gathercole SE, editors. *Working memory and neurodevelopmental disorders*. Hove, UK: Psychology Press; 2006. p.239-266.
9. Jarrold C, Baddeley AD. Short-term memory for verbal and visuo-spatial information in Down's syndrome. *Cognitive Neuropsychiatry*. 1997;2:101-122.
10. Jarrold C, Baddeley AD, Phillips CE. Verbal short-term memory in Down syndrome: A problem of memory, audition, or speech? *Journal of Speech, Language, and Hearing Research*. 2002;45:531-544.
11. Marcell MM, Cohen S. Hearing abilities of Down syndrome and other mentally handicapped adolescents. *Research in Developmental Disabilities*. 1992;15:533-551.
12. Marcell MM, Weeks SL. Short-term memory difficulties and Down's syndrome. *Journal of Mental Deficiency Research*. 1988;32:153-162.
13. Laws G. Working memory in children and adolescents with Down syndrome: Evidence from a colour memory experiment. *Journal of Child Psychology and Psychiatry*. 2002;43:353-364.
14. Brock J, Jarrold C. Serial order reconstruction in Down syndrome: Evidence for a selective deficit in verbal short-term memory. *Journal of Child Psychology and Psychiatry*. 2005;46:304-316.
15. Baddeley A, Gathercole S, Papagno C. The phonological loop as a language learning device. *Psychological Review*. 1998;105:158-173.
16. Gathercole, SE. Nonword repetition and word learning: The nature of the relationship. *Applied Psycholinguistics*. 2006;27:513-543.
17. Hulme C, Roodenrys S. Practitioner review: Verbal working memory development and its disorders. *Journal of Child Psychology and Psychiatry*. 1995;36:373-398.
18. Snowling M, Chiat S, Hulme C. Words, non-words, and phonological processes: Some comments on Gathercole, Willis, Emslie, and Baddeley. *Applied Psycholinguistics*. 1991;12:369-373.
19. Brock J, Jarrold, C. Language influences on verbal short-term memory performance in Down syndrome: Item and order recognition. *Journal of Speech, Language, and Hearing Research*. 2004;47:1334-1346.
20. Laws G, Bishop DVM. A comparison of language abilities in adolescents with Down syndrome and children with specific language impairment. *Journal of Speech, Language and Hearing Research*. 2003;46:1324-1339.
21. Vicari S, Caselli MC, Gagliardi C, Tonucci F, Volterra, V. Language acquisition in special populations: a comparison between Down and Williams syndromes. *Neuropsychologia*. 2002;40:2461-2470.
22. Chapman RS, Kay-Raining Bird E, Schwartz SE. Fast mapping of words in event contexts by children with Down syndrome. *Journal of Speech and Hearing Disorders*.1990;55:761-770.
23. Jarrold C, Thorn ASC, Stephens E. New word learning in Down syndrome. *Paper presented at the British Psychological Society, Developmental Section Annual Conference, Portsmouth, August; 2007*.
24. Carlesimo GA, Marotta L, Vicari S. Long-term memory in mental retardation: Evidence for a specific impairment in subjects with Down's syndrome. *Neuropsychologia*. 1997;35:71-79.
25. Jarrold C, Baddeley AD, Phillips C. Long-term memory for verbal and visual information in Down syndrome and Williams syndrome: Performance on the doors and people test. *Cortex*. 2007;43:233-247.
26. Mattson SN, Riley EP. Implicit and explicit memory functioning in children with heavy prenatal alcohol exposure. *Journal of International Neuropsychology Society*. 1999;5:462-471.
27. Vicari S, Bellucci S, Carlesimo GA. Visual and spatial long-term memory: Differential pattern of impairments in Williams and Down syndromes. *Developmental Medicine and Child Neurology*. 2005;47:305-311.
28. Moscovitch C, Kapur S, Kohler S, Houle S. Distinct neural correlates of visual long-term memory for spatial location and object identity: a positron emission tomography study in humans. *Proceedings of the National Academy of Science*. 1995;92:3721-3725.
29. Wang PP, Bellugi U. Evidence from Two Genetic Syndromes for a Dissociation between Verbal and Visual-Spatial Short-Term Memory. *Journal of Clinical and Experimental Neuropsychology*. 1994;16:317-322.
30. Ellis NR, Woodley-Zanthos P, Dulaney CL. Memory for spatial location in children, adults, and mentally retarded persons. *American Journal on Mental Retardation*. 1989;93:521-527.
31. Takegata R, Furutuka T. Perceptual priming effect in mentally retarded persons: Implicit and explicit remembering. *Japanese Journal of Educational Psychology*. 1993;41:176-182.
32. Wyatt BS, Conners FA. Implicit and explicit memory in individuals with mental retardation. *American Journal on Mental Retardation*. 1998;102:511-526.
33. Perrig P, Perrig WJ. Implicit and explicit memory in mentally retarded, learning disabled, and normal children. *Swiss Journal of Psychology*. 1995;54:77-86.
34. Vicari S, Bellucci S, Carlesimo GA. Implicit and explicit memory: A functional dissociation in persons with Down syndrome. *Neuropsychologia*. 2000;38:240-251.
35. Vicari S, Bellucci S, Carlesimo GA. Procedural learning deficit in children with Williams syndrome. *Neuropsychologia*. 2001;39:665-677.
36. Vakil E, Shelef-Reshef E, Levy-Shiff R. Procedural and declarative memory processes: Individuals with and without mental retardation. *American Journal on Mental Retardation*. 1997;102:147-160.
37. Nissen MJ, Bullemer P. Attentional requirements of learning: Evidence from performance measures. *Cognitive Psychology*. 1987;19:1-32.
38. Ohr PS, Fagen JW. Conditioning and long-term memory in three-month-old infants with Down syndrome. *American Journal on Mental Retardation*. 1991;96:151-162.
39. Rast M, Meltzoff AM. Memory and representation in young children with Down syndrome: Exploring deferred imitation and object permanence. *Development and Psychopathology*. 1995;7:393-407.

40. Pennington BF, Moon J, Edgin J, Stedron J, Nadel L. The neuropsychology of Down syndrome: Evidence for hippocampal dysfunction. *Child Development*. 2003;74:75-93.
41. Dawson G, Osterling J, Rinaldi J, Carver L, McPartland J. Brief Report: Recognition memory and stimulus-reward associations: Indirect support for the role of ventromedial prefrontal dysfunction in autism. *Journal of Autism and Developmental Disorders*. 2001;31:337-341.
42. Edgin JO, Moon J, Nadel L, Hutaff C, Pennington, BF. *Neuropsychological development across the lifespan in Down syndrome: What's the shape of change?* Manuscript submitted for publication.
43. Latash M. Motor coordination in Down syndrome: The role of adaptive changes. In: Weeks DJ, Elliot D, Chua R, editors. *Perceptual-Motor Behavior in Down Syndrome*. Human Kinetics Publishers, Champaign, Illinois; 2000. p.199-224.
44. Hyde LA, Crnic LS. Age-related deficits in context discrimination learning in Ts65Dn mice that model Down syndrome and Alzheimer's disease. *Behavioral Neuroscience*. 2001;115:1239-1246.
45. Contestabile A, Fila T, Ceccarelli C, Bonasoni P, Bonapace L, Santini D, Bartesaghi R, Ciani E. Cell cycle alteration and decreased cell proliferation in the hippocampal dentate gyrus and in the neocortical germinal matrix of fetuses with Down syndrome and in Ts65Dn mice. *Hippocampus*. 2007;17:665-678.
46. Galaburda AM, Bellugi U. Multi-level analysis of cortical neuroanatomy in Williams syndrome. *Cognitive Neuroscience*. 2000;12:74-88.
47. Schmitt JE, Eliez S, Warsofsky IS, Bellugi U, Reiss AL. Corpus callosum morphology of Williams syndrome: relation to genetics and behavior. *Developmental Medicine and Child Neurology*. 2001;43:155-159.
48. Krasuski JS, Alexander GE, Horwitz B, Rapoport SI, Schapiro MB. Relation of medial temporal lobe volumes to age and memory function in non-demented Down syndrome adults: Implications for the prodromal phase of Alzheimer's disease. *American Journal of Psychiatry*. 2002;159:74-81.
49. Jernigan TL, Bellugi U, Sowell E, Doherty S, Hesselink R. Cerebral morphologic distinctions between WS and DS. *Archives of Neurology*. 1993;50:186-191.
50. Atkinson J, King J, Braddick O, Nokes L, Anker S, Braddick F. A specific deficit of dorsal stream function in Williams Syndrome. *NeuroReport*. 1997; 8:1919-1922.
51. Braddick O, Atkinson J, Wattam-Bell J. Normal and anomalous development of visual motion processing: motion coherence and "dorsal-stream vulnerability". *Neuropsychologia*. 2003;41:1769-1784.
52. Molinari M, Leggio MG, Solida A, Ciorra R, Misciagna S, Silveri MC, Petrosini L. Cerebellum and procedural learning: evidence from focal cerebellar lesions. *Brain*. 1997;120:1753-1762.
53. Van Der Graaf FH, De Jong BM, Maguire RP, Meiners LC, Leenders KL. Cerebral activation related to skills practice in a double serial reaction time task: striatal involvement in random-order sequence learning. *Brain Research and Cognitive Brain Research*. 2004;20:120-131.
54. Snowling MJ, Hulme C, Mercer RC. A deficit in rhyme awareness in children with Down syndrome. *Reading and Writing*. 2002;15:471-495.
55. Wishart J. The development of learning difficulties in children with Down's syndrome. *Journal of Intellectual Disability Research*. 1993;37:389-403.
56. Fowler AE. Determinants of rate of language growth in children with Down syndrome. In Nadel L, editor. *The psychobiology of Down syndrome*. Cambridge, MA: Bradford Books/MIT Press; 1988. p. 217-245.

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