WILLIAMS SYNDROME: AN UNUSUAL NEUROPSYCHOLOGICAL PROFILE

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As a genetic experiment of nature, Williams syndrome (WMS) is expressed on multiple biological levels. Ultimately, WMS presents an unusual neurobehavioral profile, affording the opportunity to study both neurobiology and neuropsychology within a single, genetically-defined paradigm. The Salk Institute's Laboratory for Cognitive Neuroscience (LCN) has been engaged in a comprehensive program of study which spans multiple biological levels in WMS. These levels include the linguistic, the neuropsychological, the neuroanatomic, the neurophysiologic, and the genetic. The fundamental goal of these combined investigations is to help elucidate the brain bases of behavior.

In this chapter, we present first the unusual neuropsychological profile of WMS, a profile of peaks and valleys of abilities within and across domains of higher cognitive functioning. We then review the results of recent studies on the neuroanatomic basis of WMS and its neurophysiological characteristics, and the implications of this research program for an understanding of the neural systems that subserve language and cognitive functioning. A more complete discussion of the neuroanatomic and neurophysiologic investigations in WMS is presented in the chapters which follow. Importantly, these cross-disciplinary studies all are carried out on the same subjects, and thus give us the unusual opportunity to relate findings from cognitive, neuroanatomical and neurophysiological levels.

Overview of Williams Syndrome

Williams syndrome is a rare genetic disorder, first identified in 1961 by the cardiologist Williams et al. (Williams, Barratt-Boyes, & Lowe, 1961). They described four children with supravalvar aortic stenosis in association with mental retardation and a characteristic facial appearance. It is now recognized that the syndrome also commonly includes other abnormalities of the cardiovascular system, as well as of the renal, musculoskeletal, endocrine, and other organ systems (Jones & Smith, 1975; Martin, Snodgrass & Cohen, 1984; Morris, Demsey, Leonard, Dilts, & Blackburn, 1988). The overall incidence of WMS has been estimated at a rare 1 in 50,000 live births. Early medical observers remarked anecdotally on the ``friendly and loquacious'' personality of WMS subjects, and their ``unusual command of language'' (Von Arnim & Engel, 1964), but no systematic investigation of specific cognitive domains had been undertaken until recently.

A psychophysical feature of this genetic disorder is an unusual sensitivity to certain environmental sounds, manifested in specific ways: an <u>awareness</u> of sounds before others in the environment, and an <u>aversion</u> to sounds not usually considered aversive in normal populations (Bellugi, Bihrle, Doherty, Neville, & Damasio, 1989; Udwin, Yule & Martin, 1987). The implications of WMS subjects' sensitivity to sounds is considered in the chapter which follows (Neville, et al., this volume).

The genetic basis of WMS has been established recently by Morris' identification of a father-son pair, both with Williams syndrome (Morris, 1991). The mode of transmission is therefore likely to be autosomal dominant, with most cases representing new mutations. According to McKusick (1988), WMS is an autosomal dominant disorder characterized by supravalvar aortic stenosis, peripheral pulmonary stenosis, elfin facies, mental retardation, statural deficiencies, characteristic dental malformations and hypercalcemia. The hypercalcemia of Williams syndrome is associated with abnormal regulation of serum calcitonin (Culler, Jones, & Deftos, 1985), and, we have hypothesized, possible abnormalities related to the neuropeptide CGRP (calcitonin-gene related peptide) (Bellugi, et al., 1990). Molecular studies are underway to determine the specific location and nature of the gene responsible for WMS.

Previous Studies. Mental retardation is probably the most common feature of WMS, next to the defining facies. Large surveys have shown a prevalence of 95%, with full-scale IQs usually falling in the range of mild to moderate retardation (Jones & Smith, 1975; Morris, et al., 1988; Arnold, Yule, & Martin, 1985; Udwin, et al., 1987). This retardation is evident also in the adaptive behavior of WMS subjects. They uniformly require special educational placements, and their academic accomplishment lags far behind that of age- matched peers. Even in adulthood, the vast majority of WMS subjects have only rudimentary skills in reading, writing, and arithmetic (Udwin, 1990). As a consequence, WMS adults generally reside with their parents or in supervised group homes.

To date, most published research on WMS children's neuropsychological functioning has been based primarily on standard achievement tests and IQ measures with little attempt to probe specific domains of cognitive functions, with uneven or no controls, and across different age groups. Those behavioral studies that have appeared show conflicting outcomes and report inconsistent findings. For example, although some studies report that verbal abilities surpass nonverbal performance abilities, others report the opposite, concluding that linguistic abilities are not superior to nonlinguistic abilities (Crisco & Dobbs, 1988; Kataria, Goldstein, & Kushnick, 1984; Arnold et al., 1985). One limitation of these studies is that verbal abilities are assessed by instruments which confound linguistic with other cognitive processing, and thus do not permit differential assessment of specific domains of functioning.

Subjects and Program

The results we report here represent multi-disciplinary studies with carefully selected adolescent WMS subjects. We chose to begin our studies with WMS subjects at a point at which many of the basic milestones of language and cognitive functioning had been attained, and thus these studies were conducted with subjects ten years of age and above. Subject selection criteria were both inclusive and exclusive and were strictly observed, requiring diagnosis by a medical geneticist with confirmation by dysmorphologist Dr. Kenneth Lyons Jones, a colleague at the University of California at San Diego, who has long been involved in important studies delineating the consistent features of WMS for purposes of diagnosis (Jones & Smith, 1975). Moreover, the clinical diagnosis was confirmed where possible with the use of a neuroendocrine marker developed by Dr. Floyd Culler (Culler, et al., 1985; Bellugi & Culler, 1987).

Over 50 WMS subjects have been tested by the LCN, to date. The results presented here focus primarily on a core group of ten adolescents, ranging in age from 10 to 20 years (Bellugi, Bihrle, Neville, Jernigan, & Doherty, 1992; Bellugi, Bihrle, Jernigan, Trauner, & Doherty, 1990). They are contrasted with Down syndrome (DNS) subjects, matched for age, sex, and mental function on IQ measures. (Mean full scale IQs were 50.8 for the WMS group, and 48.8 for the DNS group. Mean ages were 14.4 and 15.4, respectively.) In addition, subjects from each group were generally in similar classrooms for educable mentally-retarded students. The DNS adolescents thus provide a relatively homogeneous control group of mentally retarded subjects.

In order to evaluate components of language and cognition in WMS, we are engaged in a program of systematic studies of the neurobehavioral profile of adolescents and adults. A number of these studies are undertaken in the context of a multi-institutional, multi-disciplinary NIH-sponsored Center for the Study of the Neurological Bases of Language and Communication Disorders. The WMS and DNS subjects undergo neurological examination (Trauner, Bellugi, & Chase, 1989), metabolic screening and diagnostic behavioral screening. These same subjects have had Magnetic Resonance Imaging (Jernigan & Bellugi, 1990 and this volume), and take part in neurophysiological studies (Bellugi, et al., 1992, and this volume), as well as our battery of neurobehavioral studies. Moreover, the WMS subjects are involved in our studies of the neurobiological basis of the disorder (Bellugi, 1991; Bellugi, Bihrle, Jernigan, Swanson, & Culler, 1987). These investigations apply experimental probes to test the specific abilities of not only WMS subjects, but also subjects with specific language impairment, certain metabolic disorders, and children with focal lesions to the right or left hemisphere.

Equivalent Cognitive Impairment in WMS and DNS

Studies from the LCN show not only that WMS and DNS subjects are equivalently low on IQ tests, but also that they characteristically fail on other cognitive probes, including Piagetian tests of conservation skills (for number, weight, and substance), and Piagetian tests of seriation skills (Bellugi, Marks, Bihrle, & Sabo, 1988; Bellugi, Sabo, & Vaid, 1988). These tasks tap general cognitive ability and normally are mastered early in the course of cognitive development. Figure 1a illustrates an example of conservation of volume: a quantity of water transferred from one container to another retains the same volume regardless of the shape of the container. Figure 1b shows the uniformly poor performance of WMS adolescents: whereas mental age-matched controls have full command of the concept of conservation, WMS subjects exhibit no evidence of such mastery. We note that their matched DNS counterparts fail similarly on the same tasks. **Figure 1: Conservation.**

Equivalent deficits in WMS and DNS in the general cognitive skills needed for concept formation are exhibited on the Reitan-Indiana version of the Category Test (Bellugi, et al., 1992). This test requires subjects to note similarities and differences in stimuli and to formulate hypotheses regarding the principles used to organize the stimuli. Although normal subjects readily discern these organizational principles, the matched WMS and DNS adolescents require markedly more training in the task, do not seem able to benefit from examiner feedback, and ultimately perform well below their chronological age, at the level of 7-year-olds. In summary, both WMS and DNS subjects in our sample are markedly impaired on a range of purely cognitive tasks such as conservation, concept formation, and problem solving, despite differences in performance on linguistic probes (see below).

Spared Language Abilities in WMS but not DNS

In the setting of this general cognitive impairment, the expressive language of WMS adolescent subjects is dramatically different from the language of matched DNS subjects. Consider, for example, the following excerpt from the spontaneous and fluent speech of an 18-year-old WMS subject whose IQ is 49.

> (Describing her aims in life.) You are looking at a professional bookwriter. My books will be filled with drama, action, and excitement. And everyone will want to read them. . . I am going to write books, page after page, stack after stack. I'm going to start on Monday.

This young WMS woman shows great facility with language, being able even to weave vivid stories of imaginary events and to compose lyrics to a love song. However, she fails all Piagetian seriation and conservation tasks, has academic skills comparable to those of a first-grader, and requires a babysitter for supervision. This unusual dissociation of language from other cognitive functions forms the basis for this series of studies. Here, we discuss tests of grammatical ability, semantic skills, and the interplay of linguistics with expression of affect.

Sparing of Syntax in WMS

Language is not a unitary phenomenon: rather it is composed of distinct components whose separate workings can be seen most clearly under unusual circumstances. WMS subjects provide a powerful vehicle for investigating the separability of linguistic and cognitive functioning, and even the components of language itself. Until now, there have been very few investigations of the linguistic capacities of WMS subjects. Results from our studies suggest that although our WMS and DNS subjects are comparably impaired cognitively, and in fact are selected on the basis of equivalent IQ scores, the differences between the two groups are highly marked in the linguistic domain, with WMS subjects showing an unusual profile of dissociations. Analyses of their language production indicates that lexical and grammatical abilities are remarkably spared in adolescent WMS subjects, given the extent of their cognitive deficits (Bellugi, et al., 1988a, b).

The grammatical facility of WMS subjects -- and their difference from IQ- and age-matched DNS subjects -- is apparent on formal tests of comprehension. The WMS adolescents perform much better than their DNS matches, and nearly at ceiling on tests of comprehension of passive sentences, negation, and conditionals (Figure 2a) (Bellugi, et al., 1990). For example, on a test of comprehension of passive sentences, the WMS subjects perform at a mean of above 90%, choosing correctly among the possible pictorial representations of the test sentences. The test sentences employed, semantically-reversible passives, such as ``the horse is chased by the man,'' cannot be solved solely from the knowledge of word meanings. They require an understanding of the underlying syntax of the sentence. While DNS subjects characteristically do poorly on such tests, WMS subjects give evidence of good syntactic comprehension and processing. **Figure 2. Sentence Processing Tasks.**

The ability to detect and correct anomalies in the syntax of a sentence depends on knowledge of syntactic constraints and the ability to reflect upon grammatical form. These are sophisticated metalinguistic abilities that may be mastered considerably after the acquisition of grammar and may never fully develop in certain at-risk populations. We are finding that the WMS subjects' remarkable linguistic abilities extend to tests of metalinguistic abilities in language as well (Bellugi, et al., 1992). Figure 2b shows results from tests of sentence completion, sentence correction, and the correct completion of syntactically complex tag questions. Such probes require the subjects to contemplate language as an object, by asking them to massage a stimulus sentence into new grammatical forms, or to correct ungrammatical sentences. The "tag question" task requires subjects to supply a specific syntactic form, which serves as a request for confirmation, as in ``John and Mary like apples, <u>don't</u> <u>they?</u>'' Provision of tag questions involves mastery of the rules of question formation, the auxiliary verb system, pronoun usage, and negation, all for a trifling semantic effect. WMS subjects show good performance on a probe for the linguistic ability to form tag questions, while DNS subjects are essentially unable to perform this linguistic task. On a metalinguistic task involving sentence correction, subjects are presented with sentences which may be ungrammatical, e.g., ``I hope you to eat all your supper.'' Subjects are asked to monitor and correct ungrammatical examples. While one WMS subject correctly responded ``I hope that you will eat all your supper,'' the DNS match was unable to provide a correct answer, and instead, responded ``Chicken.'' There were significant differences across the board between the two groups on these linguistic and metalinguistic probes, with WMS subjects performing well, and DNS subjects performing very poorly.

Analysis of the spontaneous expressive language of adolescent WMS subjects shows that they characteristically produce well-formed, grammatically-correct sentences. They characteristically employ a rich variety of grammatically complex forms, including passive sentences, conditional clauses, and embedded relative clauses, although there are occasional errors, and even some systematic ones (Rubba & Klima, 1991).

Importantly then, the WMS subjects are able to manipulate, process and comprehend complex grammatical structures, and they also are able to monitor and correct ungrammatical sentences. Despite the occasional errors, WMS subjects generally use morphological markers appropriately and correctly, including markers for tense, aspect, as well as auxiliaries and articles. By contrast, the language of the matched DNS subjects is simpler and less varied in construction, often with errors and omissions in both morphology and syntax. These differences in linguistic competence, on both production and comprehension tasks, evidence a remarkable preservation of linguistic knowledge in WMS, in the context of otherwise widespread general cognitive impairment.

Unusual Semantic Organization

WMS adolescents clearly show that they have understanding of words and are able to provide appropriate contexts of use. Unlike DNS subjects, they often use unusual words in spontaneous conversation, exhibiting considerable knowledge about words, that belies their lack of cognitive understanding of the world. The WMS subjects' knowledge of the meanings of words is exhibited on standard tests of word knowledge, such as the Peabody Picture Vocabulary Test (Figure 3). The WMS subjects were often able to correctly match a word to one of four possible pictures, even with advanced items such as ``abrasive'' ``cooperation'' and ``solemn.'' As the figure shows, the WMS subjects characteristically score above their mental age, while the DNS counterparts typically score below their mental age, accentuating the differences between the two groups. **Figure 3. Vocabulary Abilities in WMS versus DNS.**

However, studies from LCN have found that WMS subjects show both a preservation of ability and a possible deviance in that ability (Bellugi, et al., 1992). For example, the spontaneous language of WMS adolescents often includes unusual word choices, such as ``The bees abort the beehive'' (meaning (``they leave the hive''), and ``I'll have to evacuate the glass'' (meaning ``empty the glass''). This unusual semantic organization also is seen on tests of word fluency (Bellugi, et al., 1990). When asked to name as many animals as they can in a minute, WMS subjects provide significantly more responses than DNS subjects do (Figure 4). Whereas DNS responses are typically fewer, and more often involve perseverations or category errors (e.g. ``horsie, dog, ice cream''), WMS responses are nearly all within category; moreover, they are peppered with unusual items such as ``weasel,'' ``newt,'' ``salamander,'' ``chihuahua'' ``ibex'' and ``yak.'' We have found that WMS adolescents give a larger number of uncommon responses than do control children who are matched on the number of common responses. [Here, commonality refers to the frequency with which a word appears in reading materials (Carroll, Davies, & Richman, 1971).] Only normals who give a greater number of common responses give as many uncommon items as WMS adolescents do. Thus, WMS subjects show a proclivity for unusual words that is not seen in either matched normal or DNS subjects. **Figure 4. Unusual Semantic Organization in WMS.**

Preservation of Narrative in WMS Subjects

Beyond the abilities needed for the production and comprehension of syntactically well-formed sentences lie narrative and discourse abilities. They include the ability to structure a story, and the skills necessary for fluent and cohesive conversation. Moreover, the components of good storytelling include both paralinguistic devices (e.g. affective prosody) and lexically-encoded devices (references to affective states, other frames of mind, causal connectors, and the like) that allow the narrator to highlight particularly significant developments in the stories and are relevant to the capacity to engage an audience's interest and maintain it. The abilities of WMS and DNS subjects in these areas were assessed on a story-telling task (Reilly, Klima & Bellugi, 1991). A wordless picture book Frog, Where Are You? (Mayer, 1969) illustrates in pictures the adventures of a boy and a dog during their search for a lost frog. (A sample illustration appears in Figure 5a) Subjects are asked to tell a story from the pictures as they progress page by page through the book. No framework is provided to the subjects beyond the pictures themselves. **Figure 5. Affective Enhancers in WMS.**

On analysis of their responses to this task, marked differences were found between the matched WMS and DNS subjects. The number of WMS utterances was on average three times that obtained from the DNS subjects, and the mean length of utterance by WMS subjects averaged 3-4 times longer than for the DNS subjects. The spontaneous language displayed by WMS subjects was phonologically and syntactically sophisticated, and also effective in using subordinate clauses to foreground and background information. This is in stark contrast to language samples from the matched DNS counterparts. Characteristically, DNS subjects provided minimal descriptions of the individual pictures, often in simple fragments that were not well-formed sentences. Moreover, the DNS subjects frequently failed to establish an orientation for the story, and provided no cohesion from one picture to the next. Many of these subjects failed to explain that the boy and the dog were searching for the frog. In short, they often seemed to miss the point of the story. By way of contrast, WMS subjects characteristically provide well- structured narrations, establishing a clear orientation, introducing time, characters and their states and behaviors (``Once upon a time, when it was dark at night''), stating the problem (``Next morning. . .there was no frog to be found''), and including a resolution (``Lo and behold, they find him''). In short, the WMS subjects' narratives, in contrast to those of the DNS, tended to be well-formed stories, with well-formed story grammar and a variety of narrative enrichment devices, as we explain below.

Narratives as a Context for Affective Expression in WMS

The modulation of voice tone and stress, evident in linguistic expressions such as ``OH, my POOOOOOR little wabbit,'' is a paralinguistic affective device. Language may be emotionally enriched through the use of such devices, as well as through the use of lexically-encoded devices (i.e. the use of words that refer to emotion and affect). We examined the ability of WMS and DNS subjects to use such devices to express affect and to engage the audience on the same Frog story narration task (Reilly, et al., 1991).

In their Frog story narrations, WMS subjects were found to use affective prosody far more frequently than either DNS matches, or normal children with a higher mental age. In fact, WMS subjects continued to use high levels of affective prosody even on second and third re-tellings of the story. (In this respect, their expressivity contrasts markedly with both normal child behavior and that of disordered populations such as autistic subjects). This extensive use of prosody by WMS subjects confirms observations of affective expressivity in their casual conversations as well as in their storytelling.

The affective richness of the WMS narratives was reflected also in their lexical choices. Their narratives included frequent comments on the affective state of the characters in the stories (e.g. ``And ah! he was amazed'' or ``The dog gets worried and the boy gets mad''), as well as the use of dramatic devices such as sound effects and character speech (``And BOOM, millions of bees came out and tried to sting him.'' or ``He goes, `Ouch! oh uh get outta here bumblebees!' ''). These devices were notably absent in the DNS subjects' tellings. The attention of WMS narrators to the state of their story-telling audience was evident through their use of exclamatory phrases and other audience engagement devices that convey surprise to the listener, such as ``Suddenly splash! The water came up'' or ``Lo and behold'' and ``Gadzooks! The boy and the dog start flipping over.'' The unique proclivity for WMS narrators to employ a wide variety of affective enhancers is shown in Figure 5b, compared to DNS subjects and controls.

In sum, the WMS stories are replete with narrative enhancement devices, which contributed immensely to the drama and immediacy of the story, and contribute to the impression that adolescents with WMS are extremely expressive. It is clear that despite their mental retardation and severe cognitive deficits, WMS subjects are able to employ paralinguistic and linguistic devices for expressive purposes and to maintain audience interest. The contrast between children with WMS, children with DNS, and autistic children is marked and illuminating. The fact that the WMS subjects continue to use the same level of expressivity regardless of how many times they have told the story, and irrespective of their audience, suggests that their extreme expressivity may turn out to be aberrant. In general, these findings corroborate the anecdotal experience of parents and professional caretakers of WMS subjects. WMS adolescents appear acutely attentive to the emotional state of others, and often express exquisite emotions themselves. In contrast to the flatter affectual appearance of DNS subjects, WMS subjects are animated and vivid in their everyday deportment.

Peaks and Valleys of Ability in Spatial Cognition in WMS

Unlike language, which includes the well-defined components of phonology, morphology, syntax, semantics and prosody, spatial cognition has resisted fractionation into components (Stiles-Davis, Kritchevsky, & Bellugi, 1988). Studies from the LCN are showing, however, that WMS subjects display a markedly non-uniform pattern even within the domain of spatial cognition. The WMS subjects' pattern of peaks and valleys of spatial performance may provide insight into the structural components of spatial cognition. Here we review the remarkable profile of preservation and impairment in spatial cognition in WMS, in contrast with matched DNS counterparts.

Marked Dissociation between Linguistic and Spatial Cognition in WMS

On many visuo-spatial tasks, we have found that WMS subjects perform poorly (Bellugi, et al., 1988; 1990). For example, WMS subjects show tremendous difficulty on a simple test of spatial perception, the Benton Line Orientation Test. This test requires subjects to designate which of several slanted lines matches the orientation of model lines. Both WMS and DNS subjects fail on this task, characteristically unable to complete even the practice items correctly.   On a standardized visuoconstructive measure, the Developmental Test of Visuo-Motor Integration, subjects are required to copy a series of figures (lines, triangles, and combinations of forms). On this task, both WMS and DNS subjects are markedly impaired, with WMS subjects at a mean age equivalent of 4;8 years and DNS at 5;6 years. We note that WMS subjects appeared to show a selective disability on items that required integration of component parts (a triangle made out of circles).

The dramatic dissociation between WMS visuospatial skills and their linguistic abilities is clearly illustrated in Figure 6, which compares the drawing of an elephant with the verbal description of one by a WMS subject, age 18 with an IQ of 49. The drawing shown is typical of the impoverished and disorganized drawings produced by the WMS adolescents in our studies. Without the subject's verbal labels, the drawing would be unrecognizable. By contrast, the linguistic description is fluent and rich (what an elephant is, what an elephant does, and what an elephant has ... ``It has long grey ears, fan ears, ears that can blow in the wind. It has a long trunk that can pick up grass or pick up hay"). Indeed, WMS subjects often seem to talk their way through drawings, as if using their verbal skills to mediate the severely impaired act of drawing, although the results often belie this effort (Figure 6). In general, WMS subjects, like right-hemisphere damaged patients with lesions in the parietal lobe, often depict the parts of an object scattered on the page with no attempt at integration into functional objects, and fail to represent spatial orientation, perspective, or depth (Bellugi, Poizner, & Klima 1989; Bihrle, et al., 1989; Bihrle, 1990). **Figure 6. Contrast between Visuospatial and Language Abilities.**

Local and Global Modes of Processing

In the context of their low-scoring results on some visuospatial tasks, an analysis of the characteristics of WMS versus DNS responses is highly revealing. Consider the Block Design subtest of the WISC-R, where both WMS and DNS subjects score extremely poorly. When we examine the final performance on the designs, we find that the processes by which they arrive at their poor scores demonstrate remarkably different approaches (Bihrle, 1990; Bihrle, et al., 1989). Although they fail to provide correct designs, DNS subjects generally adhere to the overall configuration of the block arrangements, with internal configurations of the designs incorrect. WMS subjects, by contrast, fail to adhere to the global conformation of the designs, appearing biased to the details of the designs, as shown in Figure 7. We note that the DNS responses, with errors of internal detail, resemble the performance of left-hemisphere damaged patients, while the WMS responses exhibit a fragmented approach as is typical of right-hemisphere damaged patients on this task. Thus the two groups show marked processing differences between them with respect to parts and wholes of objects. **Figure 7. Block Design.**

An experimental task which distinguishes local and global features more rigorously was employed to investigate and characterize these visuoconstructive impairments. In the Delis Hierarchical Processing Test (Figure 8a) each stimulus item is composed of local components that together take a recognizable global form (i.e., a big D made up of little Y's). When asked to copy these items, WMS subjects reliably draw only the local features and do not configure them in the correct global arrangement. DNS subjects on the other hand draw the global figure correctly, but omit all of the local detail (Bihrle, et al., 1989; Bihrle, 1990). These results suggest an unusual processing pattern in WMS, a specific pattern identifiable within the context of poor overall performance. **Figure 8. Hierarchical Processing.**

<u>Facial Recognition: An Island of Sparing in WMS</u>

Despite their spatial cognitive dysfunctions, there exist realms within spatial cognition where WMS subjects display selective preservation of abilities. The WMS subjects (but not the DNS subjects) demonstrate a dramatic ability to discriminate unfamiliar faces (Bellugi, et al., 1992). The Benton Test of Facial Recognition asks subjects to match either one or three of six pictures of faces with an original target photograph. The six stimulus pictures show faces at different angles and in different lighting conditions. (Figure 9a). On this test, WMS subjects perform significantly better than their DNS matches, and were not significantly different from the adult control group (Figure 9b). The difference between WMS and DNS is also found on an inverted version of the Benton Faces task, where the six match pictures are presented upside down. The DNS subjects did not vary on the upright and inverted task, scoring equally poorly on both. While the WMS subjects do show a decrement on the inverted task, as do normals, they still show unusual preservation of performance. **Figure 9. Recognition of Unfamiliar Faces.**

On the Mooney Closure Faces Test (Mooney, 1957), subjects are required to identify whether pictures like that in Figure 10a depict a male or female person, and whether that person is young, middle-aged, or old. Performance on this test has been shown to factor with closure ability rather than face recognition ability in studies of adult stroke populations (Wasserstein et al., 1987). Surprisingly however, WMS subjects perform very well on the this task (Figure 10b), even though they do poorly on other visual closure tests using non-face stimuli (Bellugi, et al., 1988). The biological organization of spatial cognition therefore appears to be different in WMS than in the adult populations previously studied. The neurobiological discovery that certain cells in the superior temporal sulcus respond selectively to visually-presented faces (Perrett, Rolls, & Caan, 1982) gives biological plausibility to the pattern of abilities found in WMS. **Figure 10. Mooney Faces.**

WMS subjects also do well in the identification of objects that are shown from unusual perspectives (Bellugi & Doherty, 1992). The Canonical / Non- canonical Views Test (Diamond & Carey, 1991) draws on this ability, by presenting objects either in a canonical orientation (e.g. a watering can from the side) or a non-canonical orientation (e.g. a teapot from above). On canonical orientations, WMS and DNS groups perform equally well, proving that they know the objects pictured. However, WMS subjects perform significantly better than DNS matches on non-canonical views. Results from these tests taken together suggest that WMS adolescents exhibit an unusual pattern of peaks as well as valleys of abilities within spatial cognition. We discuss later the possibility that these peaks are not randomly occurring, but that they reflect the preservation of (or over-reliance on) one particular cognitive processing mode.

Dissociations in Memory Function in WMS

The memory abilities of WMS and DNS subjects are also coming under scrutiny in the LCN, in studies of both short- and long-term memory. The digit span subtest of the WISC-R served as a starting point for these studies. It taps phonological short-term memory. Results from the same WMS and DNS subjects described above show a significant difference between the two groups on digit span (Wang & Bellugi, 1991), as shown in Figure 11. On forward repetition of the digits, every WMS subject was able to correctly repeat a sequence of at least four digits. Most DNS subjects had a span of 1-3 digits, with only two subjects able to repeat a sequence of four. On backwards repetition, WMS subjects averaged 2.5 digits, but DNS subjects averaged only 1.6. These group differences were observed even when subjects were not required to repeat the digits in the exact order of presentation, suggesting that the results are not accounted for by sequential ordering abilities. **Figure 11. Digit Span.**

Explicit vs. Implicit Memory

Long-term memory is thought to be divisible into at least two independent components. These are explicit and implicit memory. Explicit memory, also referred to as declarative memory, refers to the ability to store and retrieve information in a form that can be consciously reflected upon and expressed verbally (e.g. remembering a phone number). Implicit or non-declarative memory refers to a heterogeneous collection of abilities, including motor skills (riding a bike), perceptual skills (reading something in a mirror), and some cognitive skills (solving certain types of puzzle-problems). These different types of memory have been shown to be dissociated in particular disorders. For example, adults with Huntington's disease show preservation of explicit memory, but degradation of implicit motor skills, while Alzheimer subjects may show the opposite pattern (Heindel, Salmon, Shults, Walicke, & Butters, 1989).

Studies at the LCN are examining both explicit and implicit components of long-term memory.

Explicit skills in WMS and DNS were assessed with the California Verbal Learning Test - Children's Version (CVLT-C). Here, WMS subjects demonstrated better-preserved memory abilities than did DNS subjects. In a finding related to linguistic skills, WMS subjects used semantic clustering strategies in memory more often than DNS subjects did. That is, presented with a list of items from three categories (e.g. toys, clothes, fruit), WMS subjects are more likely to group items from the same category together when asked to recall all the items. More extensive tests of long-term explicit memory are in progress.

We have begun studies on implicit memory using a rotor pursuit task. This test of implicit motor learning requires subjects to maintain contact between a hand-held stylus and a small metallic disk which revolves on a turntable. As a pure motor task, it does not admit verbally-mediated cognitive strategies. Pilot results from groups of 5 WMS and 5 DNS subjects suggest that WMS and DNS subjects have comparable initial levels of performance on this task. With practice, however, it appears that DNS subjects learn more quickly and reach a higher level of performance than do WMS subjects. These results suggest that at least one type of non-verbal memory and learning, as evidenced by performance benefit, is superior in DNS, showing an <u>opposite</u> pattern of abilities than on the tests of explicit memory described above. However, confirmation of these results, and the double dissociation of explicit and implicit mnestic abilities, will require further testing.

Contrasting Syndromic Profiles: Brain Implications

A general goal of our research is to relate cognitive functions to underlying neural substrates. In the case of WMS, our studies show marked and specific alterations in behavioral development, pointing to the dissociability of various linguistic and cognitive functions. The resulting neuropsychological profiles of adolescent WMS subjects clearly point to the possibility of abnormal development of neural systems, and the potential implications for understanding both brain function and brain structure. Such syndromic patterns of neurocognitive deficits may provide insight into the development of the neural systems underlying higher cognitive functions.

Contrast between Linguistic and Cognitive Functions in WMS

WMS and DNS present interesting contrasts in both language and in spatial cognition. First, the language profiles in these two syndromes suggest that certain linguistic skills may become functionally independent from general cognitive ability. As the data presented above suggest, WMS subjects are far superior to DNS subjects on both receptive and expressive grammatical abilities, despite similar levels of general cognitive impairment. This broad argument for the dissociation of cognitive and linguistic skills is iterated at a more specific level, in the relationship between particular cognitive and linguistic abilities. It has been argued that mastery of the Piagetian concept of conservation, which embodies ideas of reversibility and transitivity, is a prerequisite to the full understanding of passive sentences in language and co-occurs in development in the normal child (Beilin, 1975). However, despite their manifest inability to conserve, WMS subjects correctly produce and comprehend semantically-reversible passive sentences (such as ``The horse is chased by the man'') without difficulty.

Semantic knowledge, which allows us to attribute meaning to words and phrases, intuitively seems dependent on our understanding of the world, items in it, and relationships among those items. In WMS, we are finding evidence of semantic deviance as well as preservation, supporting the notion that semantic knowledge may depend on general cognition. So too, prosody and discourse rely on knowledge of cultural expectations, on affective astuteness, and on other aspects of cognition. WMS subjects' performance on the Frog stories tended to show deviantly persistent use of affective prosody. Grammar, by contrast, can more readily be construed as an independent, formal system. Thus, it would seem less likely for grammatical skill to depend on some non-linguistic ability. The selective, non-deviant preservation of grammar in WMS suggests that this may be the case.

WMS, DNS, and Lateralization of Brain Function

The pattern of linguistic preservation and marked spatial cognitive deficit found in WMS is suggestive of the effects of right-hemisphere damage on these domains. Focal lesions (e.g. strokes) to the right hemisphere frequently spare most core linguistic functions, while severely disrupting spatial skills (Bellugi, Poizner, & Klima, 1989). This spatial cognitive disruption may consist of preservation of some spatial skills, but loss of others, as in WMS. The contrast between WMS and DNS in their respective proclivities for local and global modes of spatial processing also is reminiscent of the effects of left- and right-hemisphere damage (Delis & Bihrle, 1989; Delis, Kiefner, & Fridlund, 1988; Lamb, Robertson, & Knight, 1989). Right-hemisphere damage tends to result in a bias toward local spatial processing, as in WMS. Left-hemisphere damage results in a bias toward global processing, as in DNS. However, the MR imaging studies of Jernigan and Bellugi show no pattern of focal cerebral lesions, right or left, in either WMS or DNS (see Chapter 4). These studies find that dissociations between language and spatial cognition, and differential modes of processing (parts versus wholes) can arise even in the absence of lateralized focal lesions.

In WMS and DNS, these processing preferences presumably result from aberrant neural organization. It would be unlikely for this aberrant organization to mimic perfectly the left- and right-hemisphere differences seen in adults with focal lesions. In fact, WMS teaches us something new about the behavioral patterns that may arise in a neurodevelopmental disorder. For example, in WMS there is preservation of facial discrimination ability despite their other deficits and biases in spatial processing, and despite the usual pattern of right-hemisphere specialization for these tasks. In the case of the Mooney Closure Faces Task, where we have seen that subjects with WMS perform surprisingly well, it has been shown that neurological patients do worse after the removal of right temporal lobe than left (Lansdell, 1968 and 1970). Thus, the genetic paradigm that is WMS results in aberrant neurodevelopment and a behavioral pattern that is distinct from the pattern revealed by split-brain and focal lesion paradigms.

We note that there are also aspects of WMS language that demonstrate preservation where right-hemisphere damaged subjects fail. The first of these is in semantic processing. As discussed previously, WMS subjects make frequent use of semantic clustering strategies in verbal memory tasks. Right-hemisphere damaged subjects, on the other hand, are impaired in their ability to use semantic clustering strategies (Villardita, 1987). This distinction also is evident on semantic fluency tasks, where subjects are asked to name as many members of a category as they can (e.g. all the animals they can think of). As discussed, WMS subjects provide far more responses than DNS subjects matched for IQ. Right-hemisphere damaged subjects, however, perform worse than matched controls on semantic fluency, despite normal performance on other fluency tasks (e.g. name all the words staring with an "s" sound) (Laine & Niemi, 1988).

A second distinction between WMS and right-hemisphere dysfunction is in affective prosody. Several studies of adults with focal cerebral lesions have shown that the right hemisphere is specialized for affective prosody. Subjects with right-hemisphere damage have difficulty expressing and comprehending different emotional tones of voice (Heilman, Bowers, Speedie, & Coslett, 1984; Tucker, Watson, & Heilman, 1977). However, the speech of WMS subjects evidences good command and frequent utilization of affective prosodic devices, as discussed before. Thirdly, right-hemisphere damaged subjects are poor at organizing narrative into a coherent whole, and they often show a tendency to miss the gist or moral of a story (Wapner, Hamby, & Gardner, 1981). The Frog Story data on WMS subjects, by contrast, shows particular preservation of this ability, and its absence in the comparison DNS group. Three domains of WMS language thus display preservation despite their usual right hemispheric dependence. Rather than mimicking right hemisphere, WMS presents a consistent but new and different biologically-determined neurobehavioral pattern.

WMS and Autism: Syndromic Contrasts

To date, a distillation of the neurobehavioral profile of WMS yields what appear to be three notable features. We suggest that on all three of these axes, an intriguing syndromic contrast to WMS might be found in autism, although the same studies have not been done across both groups. The first of these contrasts is in the area of language. While WMS language is spontaneously fluent and engaging, the DSM-III-R definition of autism cites impairments in verbal and non-verbal communication (APA, 1987). As Rapin reviews (Rapin, 1991), children with autism show a wide range of competence on tests of specific linguistic skills, and a wide range of deficits as well. These deficits can include comprehension deficiencies, semantic irregularities, and prosodic peculiarities. It seems then that at least a large fraction of subjects with autism fail to employ language in the effective, communicative manner that WMS adolescents in our studies do (Reilly et al., 1991).

Sigman and her colleagues emphasize the role that social interaction (and its perturbation) has in the aberrant language development of children with autism (Sigman, this volume). In this realm of social interaction and emotional affect, we suggest that WMS and autism may pose an even more dramatic contrast. Evidence from their Frog Story narrations suggests that WMS subjects are acutely attentive to the affect of others and reflect this affectual concern in their language. During social interactions, WMS adolescents can be lively and engaging. Sigman et al. (Mundy & Sigman, 1989; Mundy, Sigman, & Kasari, 1990) have demonstrated that children with autism characteristically show deficits in joint social attention and affective sharing. The DSM-III-R definition of autism summarized these features as a marked lack of awareness of the existence and feelings of others, and a unique ``aloneness'' (APA, 1987). Courchesne (Akshoomoff, Courchesne, & Press, 1990; and this volume) suggests that the basis for these behavioral distinctions may lie in neocerebellar structures, on which WMS and autistic subjects show divergent morphology (Jernigan & Bellugi, 1990). He argues that these structures are integral to the mechanisms necessary for attentional shifting. The third distinctive finding in WMS, the excellent facial recognition ability, would seem to bear on these issues of sociability. In informal situations, we have noted that WMS subjects attend intensely to their social partners' faces, seeming receptive and responsive to any and all facial cues. Children with autism are thought to be unresponsive to such cues, failing to notice another person's distress, for example (APA, 1987). Additionally, it has been found that Fragile X subjects characteristically avoid eye contact during social greetings (Wolff, Gardner, Pacia, & Lappen, 1989).

A strong distinction between WMS and autism also is found on a formal test of spatial cognitive skill - the Block Design subtest of the WISC-R. The poor and fractionated performance of WMS subjects on this measure has been reviewed. Conversely, it has been reported that autistic subjects display a performance peak on Block Design, actually solving the designs faster than normal subjects of the same age (Shah & Frith, 1983). In a recent study, we contrast matched WMS, DNS, and autistic subjects on a block design task (Chen, 1992), Figure 12. We found striking differences between the subjects, with the WMS subject using a fragmented piecemeal approach, never gaining the correct overall configuration, requiring multiple trials even on simple designs, including many counterproductive isolating movements (in which one block is isolated from the others, rather than brought together with the other blocks), and trying to talk their way through the task. By contrast, the matched autistic subject solves the puzzles rapidly and with great economy of effort, making very few unnecessary or non-productive manipulations, never making isolating moves, and working with almost mechanical precision and accuracy (Chen, 1992). **Figure 12. Contrast between WMS and Autistic Subjects on Block Design.**

Neurophysiological Studies of Brain Function in WMS

We report on a series of studies with Neville and colleagues (Neville, Holcomb, & Mills, 1989, and this volume) to assess the timing and organization of neural systems active during sensory, cognitive and language processing in Williams syndrome subjects. These studies employ the event-related potential (ERP) technique, one of few non-invasive techniques that permits a millisecond by millisecond monitoring of brain activity that precedes, accompanies, and/or follows particular types of cognitive processing. In this chapter, we mention studies of two characteristics of the WMS behavioral profile. First, we examine their auditory recovery cycle for indices that might provide clues to the basis of their apparent hyperacusis (i.e., increased sensitivity to sounds). Is there evidence for hyper-excitability at any stage along the auditory pathway? Second, we examine auditory sentence processing. Are the relatively preserved language capabilities of these otherwise mentally retarded adolescent WMS subjects mediated by brain systems that resemble or differ in some principled manner from those that are active in normal age- matched control subjects?

Auditory and Visual Recovery Paradigm. As mentioned above, a psychophysical feature of WMS is an unusual sensitivity to specific classes of environmental sounds, manifested in specific ways. In subjects tested to date, auditory brainstem evoked responses are normal in WMS subjects, suggesting that hyperexcitability does not occur at the brainstem level. However, the auditory recovery data suggest a possible cortical mechanism subserving the apparent sensitivity to sounds. As Neville et al. report, WMS and normal subjects listened to tones presented at different repetition rates (monitoring for frequency shifts) in order to index the rate of recovery or refractory period of the auditory sensory evoked response. The overall morphology of the ERP to tone stimuli (i.e. the N100-P200 response) was very similar in WMS and control subjects over both hemispheres. However, WMS subjects displayed larger responses at high repetition rates than did controls, suggesting that their responses were less refractory (i.e. more excitable) than in normals. This effect is only evident over temporal cortex and only occurs to auditory stimuli. These data suggest that although similar brain systems are activated by tones in WMS and normal subjects, WMS subjects display hyperexcitability compared with normal controls. Importantly, on a visual recovery cycle paradigm, the same WMS subjects showed results that were indistinguishable from those of normal controls, suggesting that the hyperexcitability effect is specific to auditory information. Taken together, these studies suggest that the hyperacusis observed in WMS subjects may reflect specific mechanisms in the cortical areas that are utilized in processing acoustic information.

Abnormal Brain Function During Language Processing. In studies with WMS subjects, ERPs were recorded to auditorily presented words that formed sentences. Responses to open and closed class words in sentence medial position were compared. In addition, one-half of the sentences were highly contextually constrained, ending with an expected word (semantically appropriate), and the other half ending with an anomalous unexpected word (semantically inappropriate), as in ``I take my coffee with cream and paper.'' Normal subjects show a large negative response at 400 msec (N400) to semantically unprimed words, which is thought to be an index of how the mental lexicon is organized. Results from this study are highly revealing. Analysis of the responses to sentence-middle words (i.e. not the semantically-primed words) revealed that WMS subjects displayed responses that were highly abnormal within the first 200-

300 msec following word onset. The abnormality consisted of a large positivity not apparent in control subjects at any age. This effect, only apparent over temporal brain regions, may relate to the hyperacusis these subjects display. Furthermore, the WMS responses do not display the asymmetry (left temporal regions more negative than right) that is normally apparent by about 7 years of age, suggesting that there may be an unusual pattern of brain organization underlying language.

Hypersemanticity. In the same studies, the N400 response to the semantically anomalous sentence endings is similar in WMS and control subjects; there is a large negative peak around 400 msec just as in the normal subjects. However, the effect of the semantic priming appears to be larger in WMS than in controls. An abnormally large effect of semantic priming may be related to behavioral findings discussed above, in which these same WMS subjects tend to generate low frequency and non-prototypical lexical responses. The effect of greater priming may indicate an abnormally large degree of activation which extends to less frequent and non-prototypical items within the mental lexicon.

These neurophysiological studies raise the possibility that at least some of the brain systems that mediate the remarkably preserved language in the WMS population differ from those that mediate language in the normal population. Implications from these studies are discussed in Neville et al., this volume. Further studies of WMS will help to clarify the role of different factors in the development of functional differentiation in the brain.

Implications for Biological/Behavioral Correlation

These studies on neurophysiological function in WMS raise an important caveat for the study of biological/functional relationships in our populations, or in other disordered populations. They point out that the neural systems employed by WMS subjects for sensory, cognitive or language processing need not be identical to the systems employed by the normal population for the same tasks.

Semantic processing in WMS is a case in point. The coincidence of well-preserved word knowledge, good semantic fluency, and volume preservation of frontal brain regions (see below and Jernigan, this volume) might imply the existence of an intact and normal neurobiological substrate for semantic function in WMS. However, the unusual semantic organization evident in the fluency behavior of WMS subjects, and the deviant ERP patterns on semantic priming suggest that the underlying brain systems may be deviant as well. The aberrant ERP patterns seen for open and closed class words remind us that the brain systems mediating WMS behavior may be either an aberrantly-organized deviation from the normal, or a system that is mechanistically and anatomically distinct from the system usually responsible for a given task in the normal population.

The facial recognition abilities of WMS subjects and their proclivity for a local mode of processing provide a second illustration of this caveat. The local processing mode pervades the spatial constructions of WMS subjects, from tests specifically designed to elicit this trait, to free drawing. Verbal clues given by the WMS subjects during testing suggest that they may employ a related processing mode during the facial recognition task. That is, rather than forming and utilizing a gestalt impression of the faces, as normal subjects do, WMS subjects may rely exclusively on a feature-by-feature analysis, responding that two items match because they have the same nose or same eyebrows. The same strategy may effect good performance on the Canonical/Non-canonical object identification task as well. If this alternative strategy obtains, then the neurobiological system underlying WMS performance may once again be distinct from that operating in normals during these particular tasks. These distinctions should not, however, dissuade us from studying these cognitive processes in abnormal populations. They merely point out the necessity of careful dissection of the cognitive processes whose neural mechanisms are sought.

MRI Studies of Brain Structure in WMS and DNS

As described above, the neurobehavioral results from WMS disclose a unique profile of cognitive skill. Since a genetic etiology underlies this fascinating neurobehavioral and neurophysiologic profile, the opportunity exists to examine its neurobiological underpinnings on multiple levels, from the genetic to the neuroanatomic and the neurophysiologic. Despite the caveats that we identify in the section above, and that Neville and colleagues reiterate (this volume), we find the opportunity posed by WMS to be provocative.

Within cognitive neuroscience, it is the neuroanatomical correlations to neuropsychology that are best studied. On the basis of this body of knowledge, one might expect that both WMS and DNS subjects would exhibit microcephaly, as often is seen in mental retardation. As Jernigan details in Chapter 4 of this volume, this is indeed the case (Jernigan & Bellugi, 1990; Wang, Doherty, Hesselink, & Bellugi, in press; Wang, Hesselink, Jernigan, Doherty, & Bellugi, in press; Jernigan, Bellugi, Sowell, Doherty, & Hesselink, submitted). More interesting is the pattern of regional cortical anatomy that might be predicted from the neurobehavioral evidence. We suggest that regions within the temporal lobe could be expected to show relative structural integrity in WMS, on the basis of multiple behavioral evidence. First, the pattern of spared affective and emotional ability argues for relatively good function of the limbic system. Similarly, the relatively stronger explicit memory skill of WMS subjects (as compared to DNS subjects) also suggests that the hippocampus and related mesial temporal structures would be preserved.

A second neuroanatomic prediction may be found in the psychological dichotomy between explicit and implicit memory processes. It has been proposed that whereas explicit / declarative memory is mediated through the medial temporal lobe (Squire & Zola-Morgan, 1991), the motor learning subset of the implicit processes may be mediated by the basal ganglia (Heindel, et al., 1989). Therefore, considering the superior behavioral results on motor learning, it would be intriguing if DNS subjects show greater integrity of the subcortical nuclei than WMS subjects.

The role of frontal brain regions in language, and especially in lexical and semantic processing, is increasingly supported by a number of lines of evidence. The Broca's aphasia that results from damage to specific frontal regions is well known; evidence from well studied subjects with frontal brain lesions is also telling (Damasio, 1990). Electrophysiologic and positron emission tomographic studies also suggest that frontal brain regions play a critical role in semantic processing (Peterson, Fox, Posner, Mintun, & Raichle, 1989). The relatively strong performance of WMS subjects on semantic and fluency tasks is compatible with the suggestion that their frontal areas may be better preserved than in DNS.

As Jernigan reviews in this volume, magnetic resonance imaging studies of the brain in WMS, DNS, and control subjects are consonant with some of the correlations postulated here. For example, the superior performance of WMS subjects on semantic fluency may be associated with proportional preservation of frontal volume, despite a decrease in overall cerebral volume relative to controls. Also, Wang et al. have shown that the most rostral fifth of the corpus callosum is better preserved in WMS than in DNS (Wang et al., in press). Studies of partial commisurotomy patients suggest that this region of the callosum is important for the interhemispheric transfer of semantic information (Gazzaniga, Kutas, VanPetten, & Fendrich, 1989; Sidtis, Volpe, Holtzman, Wilson, & Gazzaniga, 1981).

A major neuroanatomical contrast between WMS and autism is found in the cerebellum - a part of the brain that, until recently, was thought to contribute significantly only to motor function. In WMS, a particular portion of the midline cerebellar vermis is significantly larger in cross-section than in either DNS or normal controls (Jernigan & Bellugi, 1990). That portion, lobules VI and VII, comprises the neo-cerebellar part of the vermis. In proportion to a phylogenetically more ancient part of the vermis (lobules I - V), the neo-cerebellar vermis is again significantly larger in WMS than in either of the other groups. Although its role is not yet conclusively established, a growing body of evidence suggests that the neo-cerebellum participates in higher cognitive function, including possibly the coordination of the many cognitive resources necessary for fluent speech (Leiner, Leiner, & Dow, 1989). For example, animal studies have shown that lesions to the vermis may result in abnormalities in certain types of learning and in social interaction and approach behavior (Bernston & Schumacher, 1980). Courchesne et al.'s earlier demonstration of neocerebellar vermal hypoplasia in autism (Courchesne, Yeung-Courchesne, Press, Hesselink, & Jernigan, 1988) is interesting along these latter lines. The contrast between autism and WMS in communicative and affective behavior mirrors their differences in neocerebellar morphology. We thus find the neocerebellar findings in WMS particularly stimulating

(Wang, Hesselink, Jernigan, Doherty, & Bellugi, 1992). They represent the dynamic potential of the cross-level neuroscientific investigations in which we are engaged.

Current and Future Directions

Research in our laboratory is continuing along a number of promising lines. Critical among these is the exploration of the developmental trajectory of language and cognitive abilities in our special populations. Preliminary results from a survey of development in WMS suggests that their language and the language of DNS children are equivalently delayed at a young age. Continued longitudinal follow-up of these subjects will be needed to define when and in what manner the linguistic abilities of these subjects diverge from purported cognitive underpinnings. Investigations of non-linguistic cognitive development in the same children will allow us to address hypotheses on the cognitive correlates or prerequisites for language.

We also continue to explore the spatial cognitive abilities of WMS subjects. Their pattern of strengths and weaknesses provides a new hint about the nature of spatial cognition. Despite the efforts of many investigators, a broadly-applicable nosology of visual-spatial cognition has been difficult to construct. We believe that the unique profile of visual-spatial abilities in WMS is founded biologically and therefore may have broad implications. Our primary caveat, that some performance peaks may derive from non-standard performance strategies, will actually help guide our explorations, as long as it is kept in theoretical mind.

The biological foundation of WMS will permit invaluable study of the brain bases of behavior. The work reported by Jernigan and Neville marks the first major effort to illuminate the neural systems underlying the unique neurobehavioral profile of WMS as contrasted with other populations. With the advancing capabilities of non-invasive neuroimaging and neurophysiological probes, we will garner a more and more detailed account of the structures and mechanisms of the WMS brain (Damasio & Frank, in press). Also, we have recently obtained an autopsy brain specimen from a WMS subject. This will allow us to extend our biological explorations to the microscopic level of cortical organization and neuronal morphology. Lastly, investigations on the genetic basis of WMS are gathering speed, with the identification of the first certified family pedigree of WMS cases. We hope and expect eventually to give a full account of cognition in WMS, from the molecular biological level to the behavioral level.

Acknowledgements

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Figures

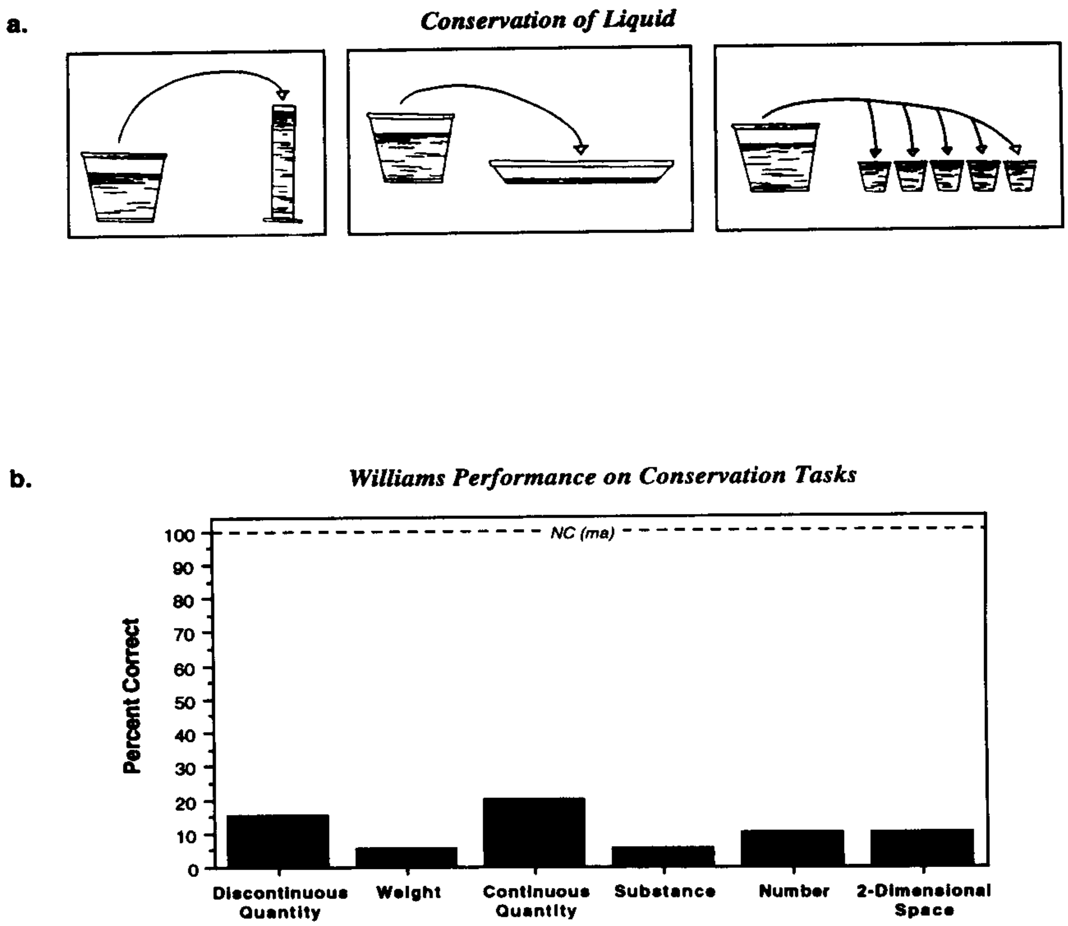


FIG. 2.1. Understanding of the Piagetian concept of conservation in WMS. (a) Illustration of the Piagetian concept of conservation. The total quantity of water remains the same regardless of the shape of the container. (b) Williams syndrome subjects perform at very low levels on tasks of conservation, equivalent to the level of 4- or 5-year-olds. Normal children show near perfect performance by 8 years of age.

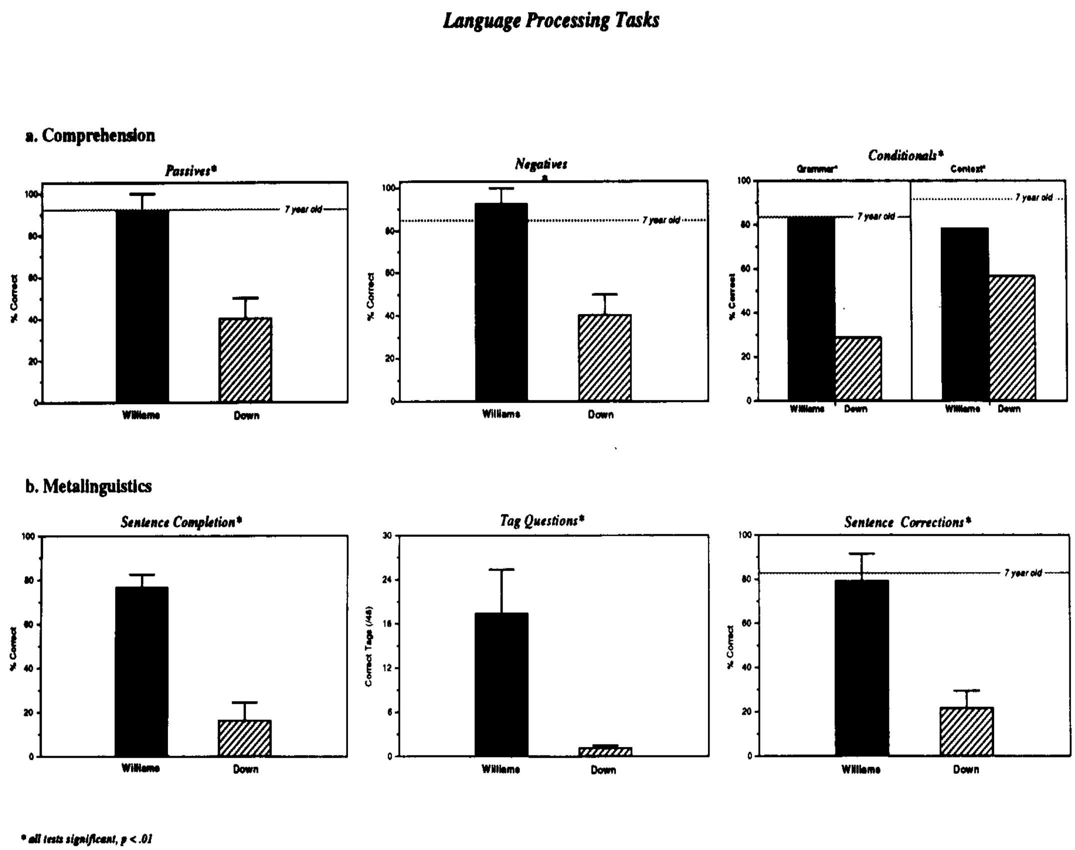


FIG. 2.2. Performance on sentence-processing tasks in WS and DS. Williams syndrome subjects show significantly better performance than Down syndrome subjects on (a) tests of sentence comprehension, and (b) metalinguistic tasks requiring the subject to correct ungrammatical sentences or to otherwise manipulate sentences.

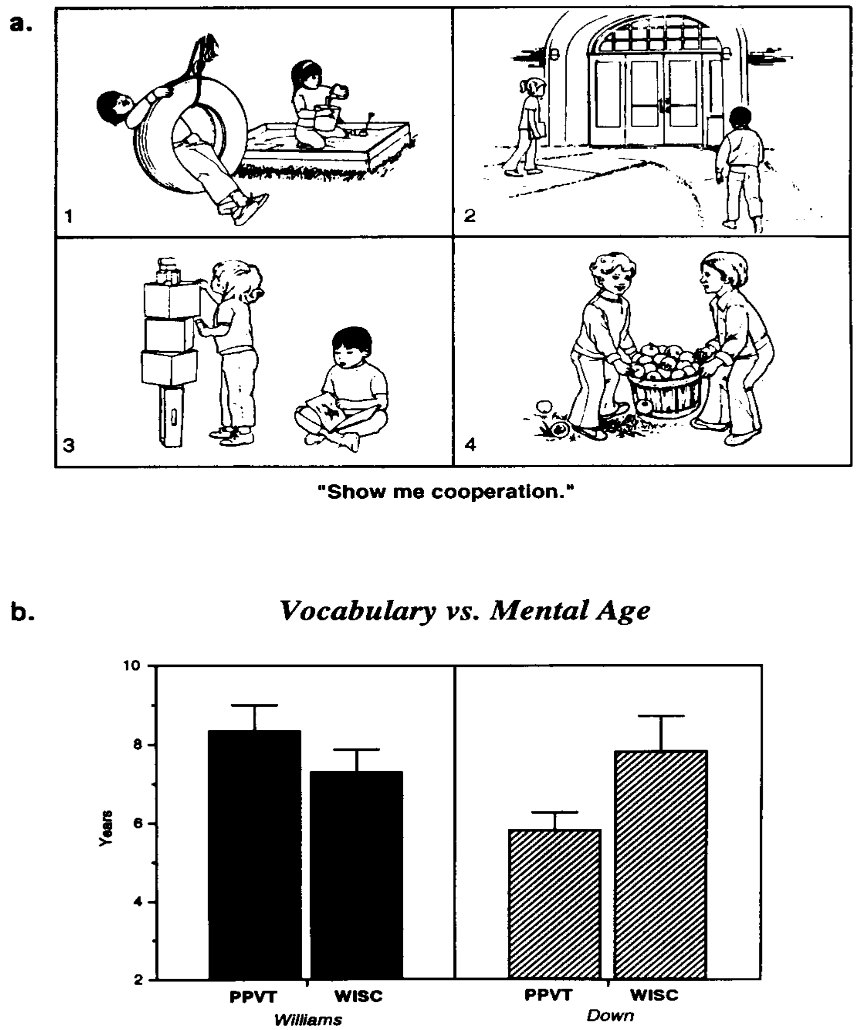
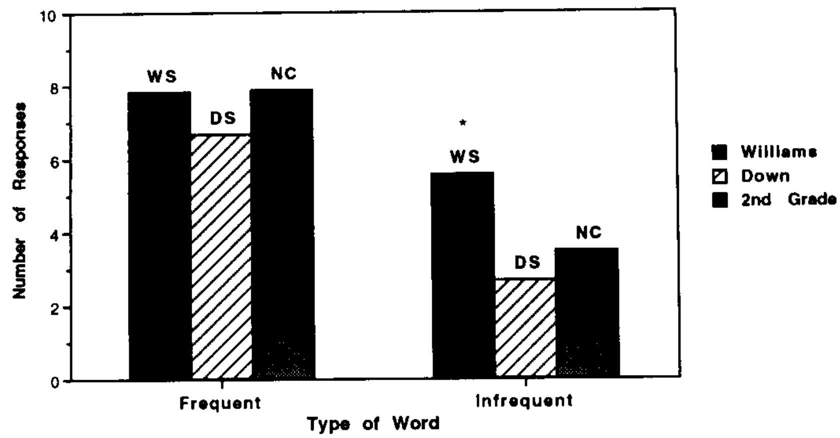


FIG. 2.3. Comparison of semantic knowledge and IQ in WS and DS. (a) Example of an item from the Peabody Picture Vocabulary Tests, testing knowledge of the word *cooperation*. (b) In Williams syndrome, semantic knowledge (given as age-equivalent score) often surpasses IQ-age, whereas semantic knowledge is significantly lower than IQ-age in matched Down syndrome subjects.

Semantic Organization



* p < .02 Williams vs. Down
p < .05 Williams vs. 2nd Grade

FIG. 2.4. Unusual semantic organization in WS. WS, DS, and second-grade control children give similar numbers of frequent items, but WS children give significantly more infrequent items.

a.

b.

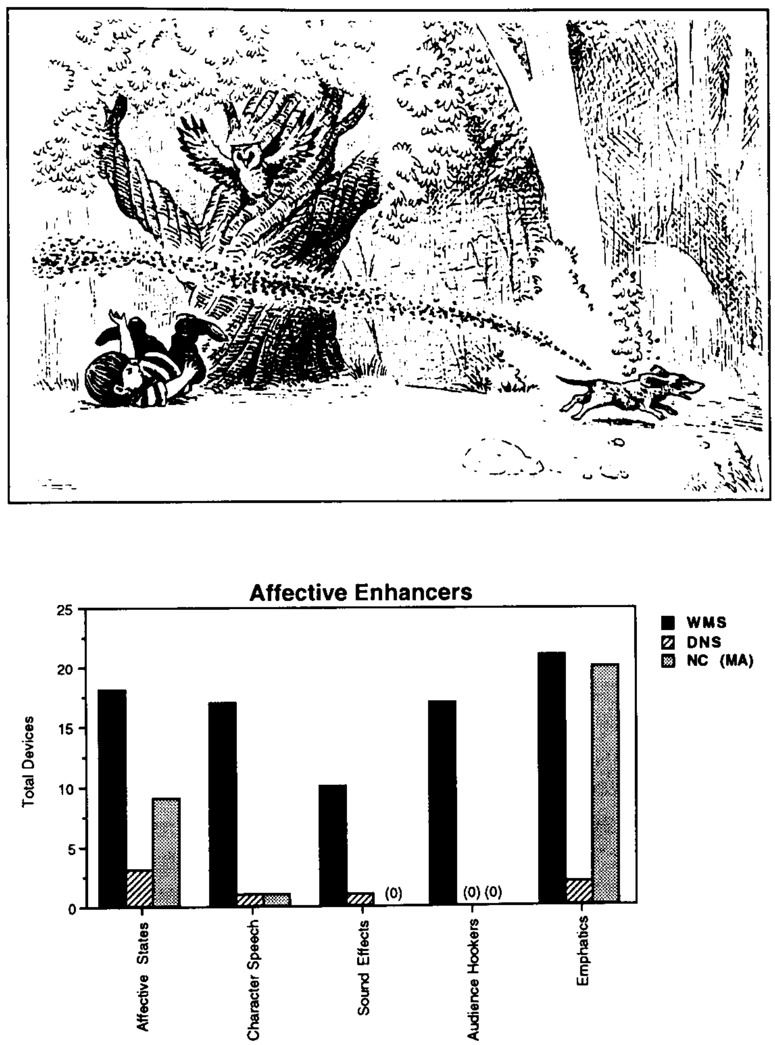
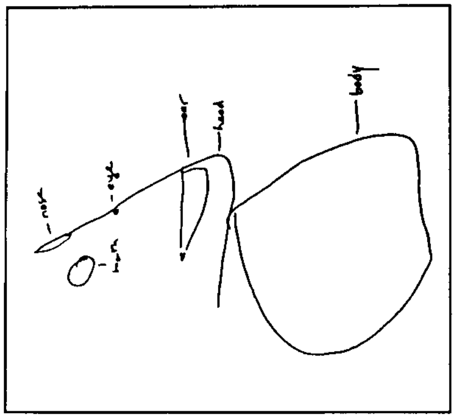


FIG. 2.5. Use of affective enhancers in narration. (a) Schematic of a page from the picture book narration task, reported in Reilly, Klima and Bellugi, 1991. (b) WS subjects use a greater number of various linguistic devices to affectively enrich their narrations than do DS or control children. From Reilly et al. (1991). Adapted by permission.

Contrast Between Visuo-Spatial and Language Abilities in Williams Syndrome

a.



b.

And what an elephant is, it is one of the animals. And what the elephant does, it lives in the jungle. It can also live in the zoo. And what it has, it has long gray ears, fan ears, ears that can blow in the wind. It has a long trunk that can pick up grass, or pick up hay....If they're in a bad mood it can be terrible...If the elephant gets mad it could stomp; It could charge, like a bull can charge. They have long big tusks. They can damage a car...It could be dangerous. When they're in a pinch, when they're in a bad mood it can be terrible. You don't want an elephant as a pet. You want a cat or a dog or a bird...

FIG. 2.6. Contrast between visuospatial and language abilities in WS. (a) Drawing of an elephant by an 18-year-old WS woman, whose IQ is 49. (b) Her verbal description of an elephant.

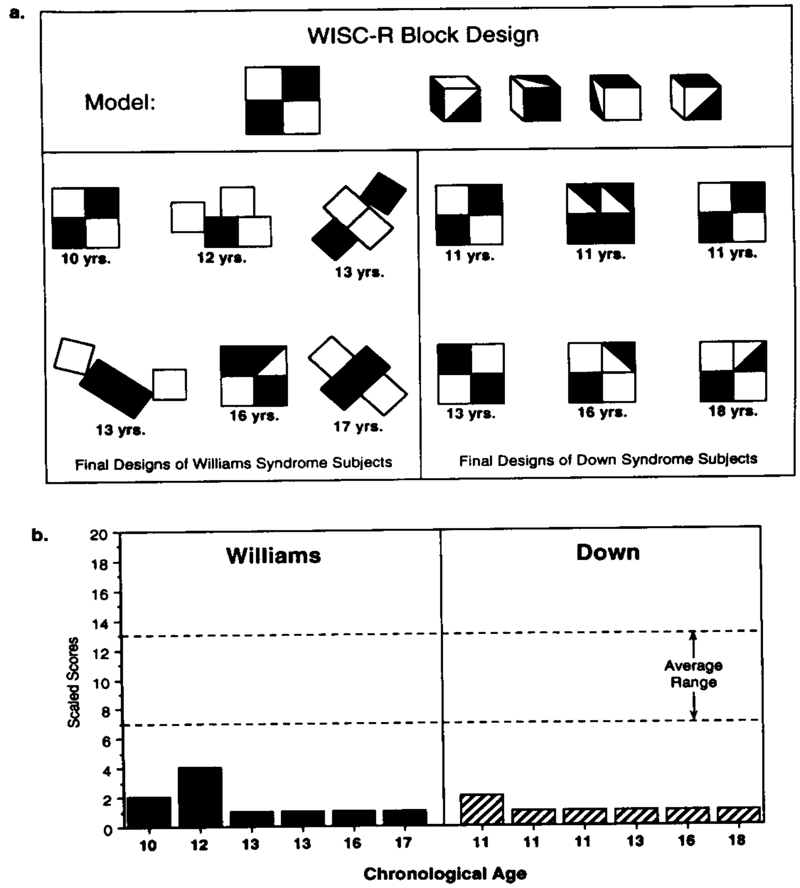


FIG. 2.7. Contrasting block design performance in WS and DS. (a) On the Block Design subtest of the WISC–R, both WS and DS designs reveal striking differences in their errors. WS subjects uniquely fail to reproduce the correct global configuration of blocks. (b) However, these differences are not reflected in quantitative scores, which are comparably low. From Bihrle, Bellugi, Delis, and Marks (1989). Adapted by permission. Also from Bihrle (1990). Adapted by permission.

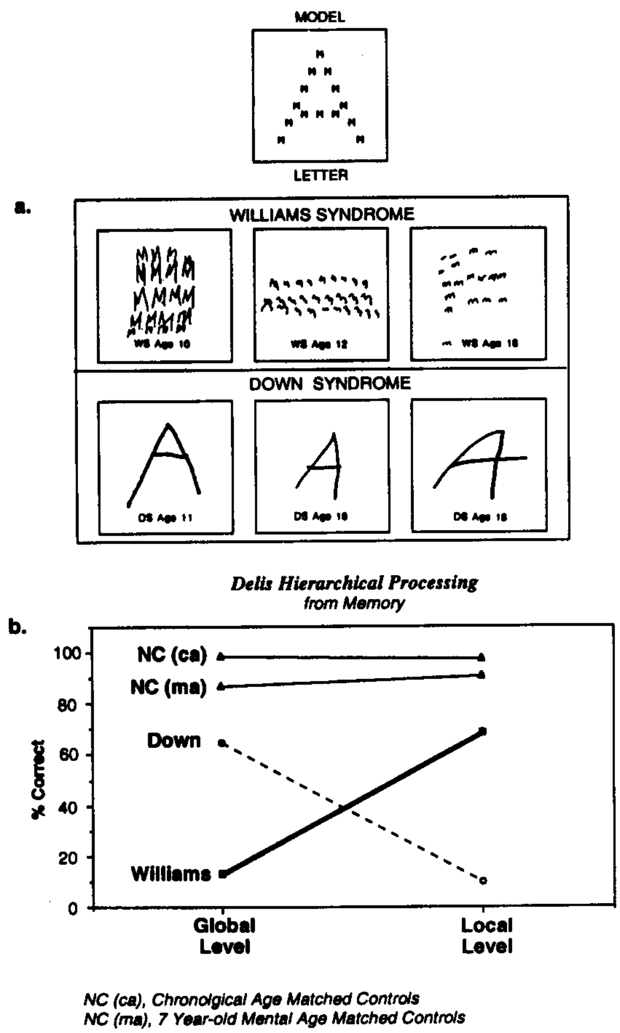


FIG. 2.8. Different error patterns in WS and DS on the Delis Hierarchical Processing Task. (a) In their reproduction of the model figure, WS subjects produce the correct local detail but omit the global configuration. DS subjects perform oppositely. (b) Quantitative assessment of these errors patterns reveals significant differences between WS and DS. From Bihrle, Bellugi, Delis, and Marks (1989). Reprinted by permission. Also from Bihrle (1990). Reprinted by permission.

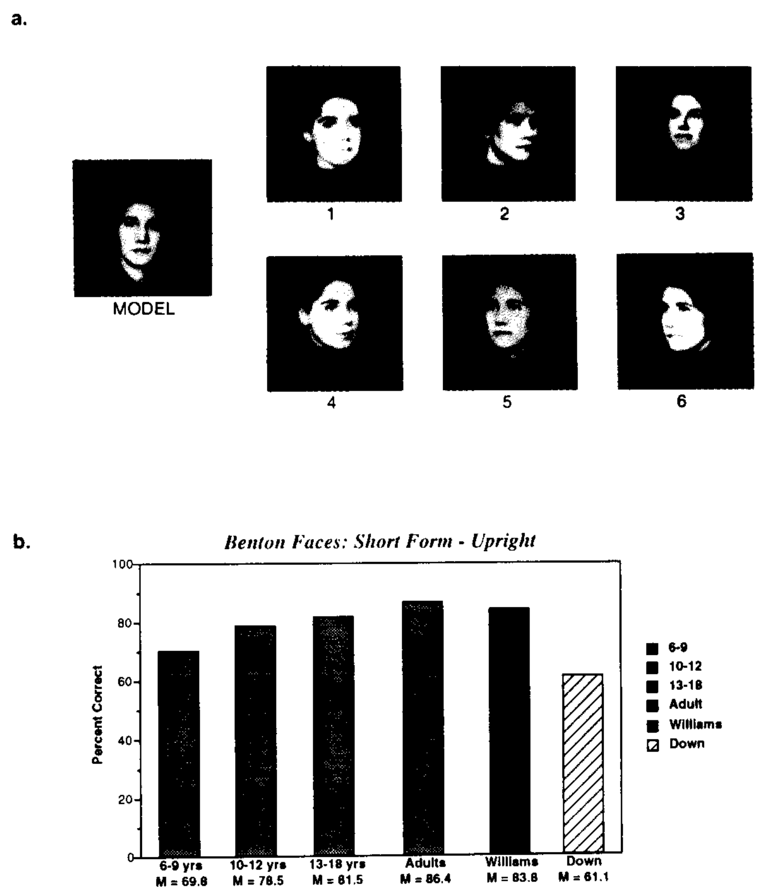


FIG. 2.9. Spared discrimination of unfamiliar faces in WS. (a) Sample items from the Benton Test of Facial Recognition. Subjects must match the picture at the left to one of the other six. (b) WS subjects perform significantly better than DS subjects on this task, and just as well as adult normal controls.

a.

b.

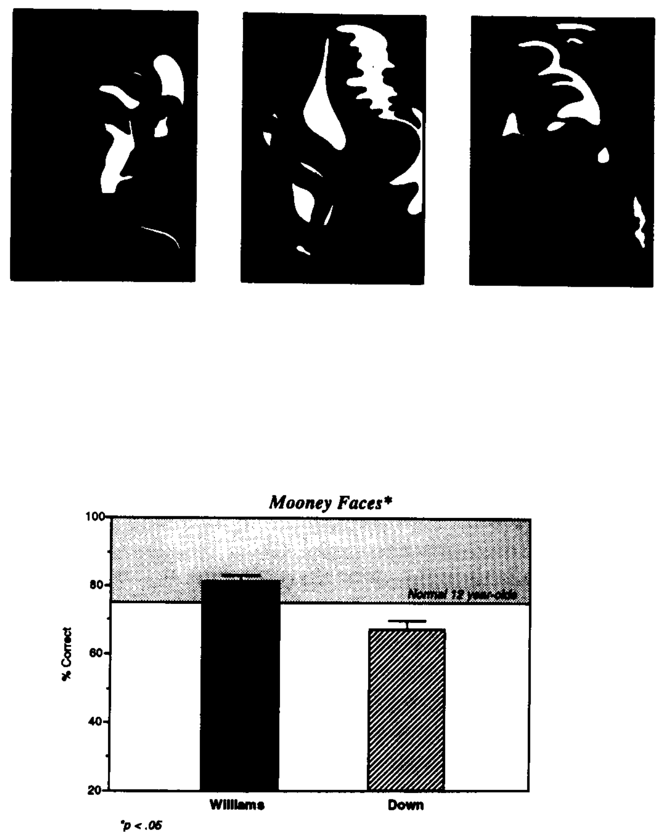


FIG. 2.10. Mooney Closure Test. Subjects must decide whether each face is of a young, middle-age, or old man or woman. (b) WS subjects perform significantly better than DS subjects on this task, and just as well as adult normal controls.

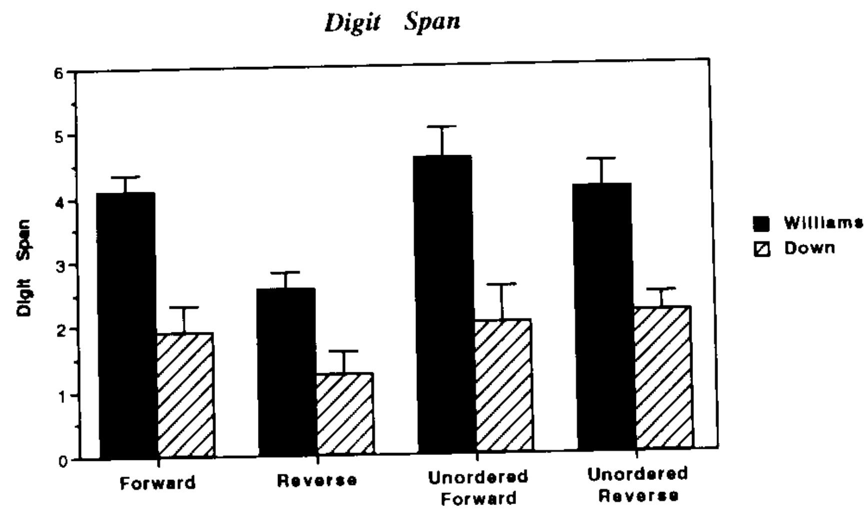


FIG. 2.11. Digit span subtest of the WISC-R. WS subjects score significantly higher than DS subjects on both forward and reverse digit span, regardless of serial ordering considerations.

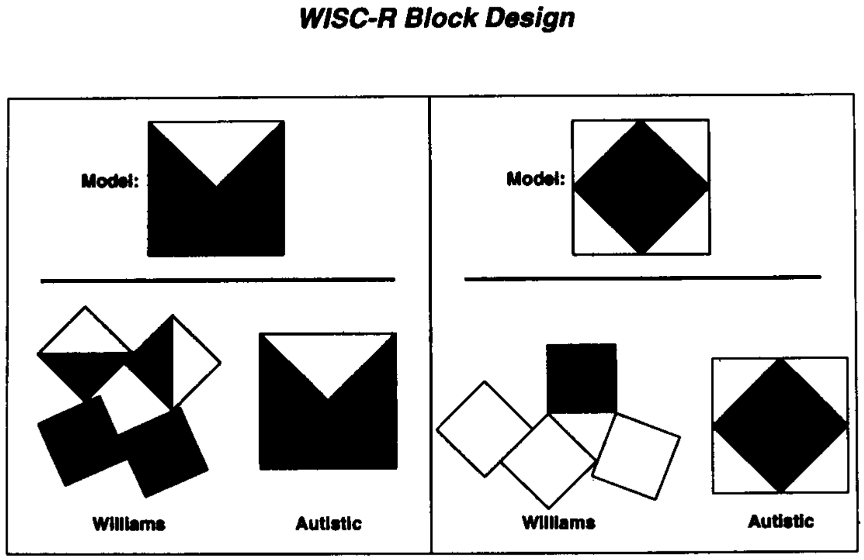


FIG. 2.12. Comparison between autistic and WS subjects on WISC–R Block Design. Comparison of performance between an autistic subject (perfect performance, very rapidly executed) and a matched WS subject (poor performance, fragmented, and slow). From Chen (1992). Reprinted by permission.

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