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Language and Visuospatial Abilities in Down Syndrome Phenotype: A Cognitive Neuroscience Perspective

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1. Introduction

Down syndrome (DS) is the most common genetic disorder with a prevalence that ranges from 1:700 to 1:100 live births and accounts for 25–30% of people with intellectual disability (Nadel, 1999; Rogers, Roizen, & Capone, 1996; Rondal, 1988, 1998; Rondal, Perera, & Nadel, 1999). Trisomy 21, one of the three forms of DS, is caused by the presence of a third chromosome at band 21q22 of the long arm. The other two forms, namely translocation 21 and mosaicism, account for only 6% of children with DS (Rogers et al., 1996). Recent medical advances suggest that over 300 genes are affected, making the genetic etiology of DS a complex mechanism that implicates gene interactions that are not clearly understood (Pennington, Moon, Edgin, Stedron, & Nadel, 2003; Antonarakis et al., 2004). The syndrome is characterized by specific phenotypic characteristics, health related problems, cognitive and language impairments, neuromotor dysfunction and early aging, often associated with increased prevalence of Alzheimer's disease.

Interest in the cognitive profile of DS has been robust during the past decades, with a large number of published studies discussing the atypical and unique profile of cognitive abilities in this population. Yet, there is no clear understanding of the cognitive profile of individuals with DS and how this differentiates from other forms of intellectual disability. The uniqueness of the cognitive make-up of individuals with DS will contribute to a better understanding of the specific strengths and impairments of this population, as well as to the development of more effective educational programs suitable for them. This chapter will focus on language and visuo-spatial abilities of individuals with DS from a cognitive neuroscience perspective. The chapter is organized in four parts. The first part discusses language abilities in individuals with DS, with particular emphasis on expressive and receptive vocabulary and grammar. In the second part, research in visuospatial abilities in individuals with DS is reviewed. The third part deals with the concept of atypical cerebral laterality (ACL) in DS individuals and, in particular, how ACL may affect their language and visuospatial abilities. Finally, the last part discusses the contribution of laterality research in understanding the unique pattern of cognitive abilities in DS.

2. Neurobiology of DS

At birth, the total brain volume of individuals with DS is close to normal, although microscopically some changes have been observed as early as 22 weeks of gestation that become more obvious by 6 months of age (Nadel, 2003). This condition has been linked to neural density reduction in the cerebral cortex (Florez, 1992). Indeed, the most affected area of the brain of individuals with DS is the cortex, both in neural density and in weaker neural synapses, caused by fewer dendritic spines. (Florez, 1992; also see Lubec & Engidawork, 2002 for a review). Although, the reduced brain volume cannot be directly associated with the observed intellectual disability of this group, it is suspected that these abnormalities in the neural density of the cortex may contribute to the weak cognitive deficits associated with the syndrome (e.g., memory and attention). Shapiro and colleagues (1992) reported abnormal neuronal interactions between the frontal and parietal lobes of individuals with DS, suggesting the involvement of Broca's area. More specific differences in the brain's neuroanatomy of individuals with DS include reduced growth of the frontal lobes (Kesslak et al. 1994), narrowing of the superior temporal gyrus, smaller brain stem and cerebellum (Cole et al., 1993).

Research using magnetic resonance imaging (MRI), comparing demented and non-demented individuals with DS, indicates the presence of reduced volume of left hippocampus and amygdala in the former group (Pearlson et al., 1998). In a different MRI study, measuring hippocampal and amygdala volumes, non-demented individuals with DS exhibited smaller hippocampal size compared to age-matched typically developing controls, but there were no differences in amygdala volumes between the two groups (Pinter, Brown, Eliez, Schmitt, Capone, & Reiss, 2001). In their study, Pinter and colleagues (2001) confirmed that individuals with DS have smaller brain volumes, both in gray and white matter, smaller cerebellar volumes, and relatively larger subcortical gray matter volumes, both in parietal and temporal structures. Finally, Teipel and colleagues (2003) found decreased size of the corpus callosum in a group of non-demented individuals with DS, even when total brain volume was controlled for (Teipel et al., 2003). Thus, although the neuropathology of individuals with DS is widespread, particularly in older adults, it is also selectively affecting mainly cortical areas that are involved in higher cognitive processes.

3. Cognitive profile of individuals with DS

Individuals with DS demonstrate a unique cognitive profile of strengths and weaknesses that is characteristic to the syndrome. The general intellectual ability of individuals with DS ranges from mild to severe mental retardation, with a decline as they grow older (e.g., Hoddap & Zigler, 1990; Pennington, Moon, Edgin, Stedron, & Nadel, 2003). This decline, which begins early in adulthood, has been related to the gradual deterioration of several brain areas, such as the hippocampus and the cerebellum (Pennington et al., 2003). Alternatively, this decline has been linked to the increased prevalence of dementia in adults with DS (Takashima, Ieshima, Nakamura, & Becker, 1989).

Hippocampal function that supports tasks that tap short-term and long-term memory are severely affected in individuals with DS, as opposed to those supported by prefrontal areas (e.g., executive functions) (Pennington et al., 2003). Explicit memory (verbal and non-verbal) is particularly weak when compared both to typically developing (TD) individuals matched for mental age, and non-Down syndrome individuals with intellectual disability (ID)

(Carlesimo, Marlotto, & Vicari, 1997). These findings suggest that memory is disproportionately affected in DS due to the specific neurological abnormalities mentioned earlier (i.e., hippocampal dysfunction, reduced brain volume) (Lubec & Engidawork, 2002). Sustained attention has been also examined in infants with DS (Brown, Johnson, Paterson, Gilmore, Longhi, & Karmiloff-Smith, 2003). Results showed that infants with DS exhibit poor engagement and less duration in sustained attention than TD mental-age controls (Brown et al. 2003). These results are unlikely to reflect lack of motivation or task difficulty. In older individuals with DS, this condition has been associated with other dementia symptoms, such as lack of orientation (e.g., Granholm, Sanders, & Crnic, 2000).

Language is the most extensively studied domain within the cognitive system in individuals with DS. Most authors agree that language is severely affected in these individuals, with expressive vocabulary, grammar and syntax being the weakest areas of function. Indeed, individuals with DS document an unusual disparity in performance in expressive and receptive vocabulary tasks, with the latter being more affected than the former. Particular emphasis has been placed in identifying the specific nature of the expressive language difficulties, their neural substrates, as well as the developmental changes throughout the life span.

Grammar and syntax are disproportionately affected in individuals with DS as well. Spoken language is characterized by a systematic omission of tense-related grammatical morphemes that persists throughout development. Surprisingly, in most studies examining English-speaking children with DS, regular past tense formation is more affected than irregular past tense formation, suggesting a difficulty with understanding and applying grammatical and syntactic rules, as opposed vocabulary entry and retrieval.

Visuo-spatial abilities have been less extensively investigated in DS. Some authors propose that visuo-spatial working memory is relatively preserved compared to verbal working memory in DS individuals (e.g., Lanfranchi, Carretti, Spanò & Cornoldi, 2009). In fact, they have often been characterized with relative strengths in visuo-spatial processing and poor verbal processing skills (Jarrold, Baddeley & Hewes, 1999; Klein & Mervis, 1999; Wang & Bellugi, 1994). The relative strength of visuo-spatial skills is supported by strong fine motor skills documented through the use of gestures in early development (Bilovsky & Share, 1965). More specifically, it has been reported that children with DS are better at the construction subtests of the Stanford-Binet (e.g., block building, drawing line, copying, folding), compared to mental age controls, due to their strong visuo-motor abilities (Silverstein, Legutski, Friedman, and Takayama, 1982). Pueschel and colleagues (1987) documented that young children with DS were better at figure closure and hand movement tasks, compared to verbal tasks (using the Kaufman Assessment Battery for Children), while TD children exhibited the reverse pattern of performance and children with IDs without DS exhibited equally weak performance in both tasks.

Bellugi and colleagues (1994) proposed that individuals with DS are better at sustaining the global configuration of objects, as opposed to local forms, a pattern that is reversed in individuals with intellectual disability of different genetic origin. Similar findings have been reported in drawing, where individuals with DS tend to reproduce the global features of a stimulus and omit the local details of the object. This pattern of performance is often encountered in patients with left hemisphere damage, suggesting lateralized brain lesions in individuals with DS. However, MRI data do not exhibit asymmetrical damage in

individuals with DS. This evidence supports the existence of an atypical functional lateralization in this clinical group (Jernigan & Bellugi, 1990).

4. Language of individuals with DS

One of the earlier studies on language of individuals with DS explored speech reproduction and observed weak expressive skills in this population (Dodd, 1975). During the same decade Gibson (1978) discussed the language production of individuals with DS during the first two years of life. He suggested that some aspects of language, particularly expression, fall behind their chronological age. Almost a decade later, Cardoso-Martins and colleagues (1985) found weaknesses in speech production in individuals with DS. Since then, it has been repeatedly documented that children with DS exhibit an unusual disparity between expressive and receptive language, compared to what would be expected, based on their mental age, with the latter being less affected than the former (e.g., Jenkins, 1993; Chapman, 1997). This delay in expressive performance is evident from infancy, even prior to development of formal vocal speech.

Likewise, it has been found that infant gesture development in DS population is delayed, compared to TD infants (e.g., Miller, 1992). Longitudinal studies examining one-to-two word formations, found that individuals with DS exhibit a delay in speech production up to 18 months, with large individual variation that reached 19 months (e.g., Oliver and Buckley, 1994). The “vocabulary spurt”, typically observed in TD 24-month old infants, was commonly absent in individuals with DS. As the syntax becomes more complex and the vocabulary for speech production more demanding, the discrepancies between DS and TD individuals become more pronounced (Miller, 1992).

Receptive language and comprehension appear to be more advanced than expressive speech in DS adolescents (Chapman, Schwartz, & Kay-Raining Bird, 1991). However, some evidence suggests that comprehension declines with age in non-demented individuals with DS (Chapman, Hesketh, & Kistler, 2002). In our study, receptive and expressive vocabulary was investigated in DS and TD individuals matched for mental age (Ypsilanti, Grouios, Alevriadou & Tsapkini, 2005). Four subtests of the Test of Word Knowledge (TOWK) (Wiig & Secord, 1992) were used to assess naming pictures (expressive vocabulary), matching a spoken word to a picture among four semantically related detractors (receptive vocabulary), relational word knowledge and ability to provide definitions to orally presented words. We found no differences between the two groups in three of the four tasks of expressive and receptive vocabulary. The only reliable weakness of individuals with DS was evidenced in the word definitions subtest that demands complex syntactic constructions, requirement which is challenging for these individuals.

Surprisingly, narrative production, which is closely related to expressive language and syntax, seems to be less affected in individuals with DS. Chapman, and colleagues (1998) compared the performance of 33 individuals with DS with two TD control groups matched for syntactic comprehension and for mean length of utterance (MLU), respectively, and failed to find reliable differences in number of episodes (stories) described by the three groups. Individuals with DS documented syntactic errors that included verb omissions, suggesting that narrative production may be weak due to syntactic deficits and not vocabulary restrictions.

Grammatical word formation, particularly the omission of tense-related morphemes, is another area of difficulty for individuals with DS (e.g., Laws & Bishop, 2003). Regular past

tense formation is more affected than irregular in individuals with DS (Laws & Bishop; Eadie, Fey, Douglas, & Parsons, 2002). This peculiar finding suggests that irregular past tense formation resembles accessing vocabulary entries, which does not rely on understanding and applying grammatical rules (Pinter, 1991). This theorization has been subsequently supported by evidence indicating significant correlation between irregular past formation and vocabulary level in individuals with DS (Laws and Bishop, 2003).

In summary, most published studies agree that expression is more affected than reception in individuals with DS (for a review see Ypsilanti & Grouios, 2008) and that phonological short-term memory may be mediating the performance on such tasks. This hypothesis is supported by research findings indicating that auditory short-term memory predicts early vocabulary entry in individuals with DS (Chapman & Hesketh, 2001). Several investigators have proposed that children with DS may exhibit difficulties in naming and sentence repetition tasks due to strong anatomical and functional deficiencies in the corpus callosum (e.g., Wang, Hesselink, Jernigan, Doherty, & Bellugi, 1992). Bunn et al. (2002) argued that if interhemispheric communication is necessary for picture naming before speech production, then deficiencies in the corpus callosum, such as those observed in individuals with DS, would influence performance on naming, but not on reading tasks.

5. Visuospatial abilities in DS

Studies on visuospatial abilities of individuals with DS reveal the existence of strengths and weaknesses within this domain. In particular, individuals with DS are stronger in visuomotor integration and visual memory, compared to spatial memory and spatial construction (Fidler, 2005). Visuospatial short-term memory was found to be relatively unaffected in individuals with DS (e.g., Jarrold & Baddeley, 1997). Bellugi and colleagues (1999) found a unique dissociation in the visuospatial abilities of individuals with DS and Williams Syndrome (WS) (a genetically linked disorder associated with intellectual disability). Individuals with DS tended to maintain a holistic strategy in drawing tasks, while those with WS matched for mental age, reproduced local features of the drawing objects (Bellugi, Lichtenberger, Mills, Galaburda, & Korenberg, 1999). Moreover, individuals with DS exhibited increased difficulty in depicting internal details of objects in block construction and integrating simple shapes. In the same study, a clear dissociation in global/local features of individuals with DS was illustrated using the Navon task, in which participants were asked to maintain the global or local form of letter stimuli. Individuals with DS were unable to reproduce the local details of the stimuli, maintaining only the global aspect of the presented letter.

In another study, Bellugi and colleagues (2000) presented comparative data from drawings of individuals with DS and WS demonstrating that individuals with DS produce drawings conforming with gestalt rules (such as, closure and continuation) that lack detail, but are easily recognizable (Bellugi, Lichtenberger, Jones, Lai, & St. George 2000). Interestingly, the two groups were equally weak in the block design subtest of the WISC-R (Wechsler, 1974). However, further analysis of the process of block design indicated that although erroneously, individuals with DS maintained the global configuration of the block arrangements, while individuals with WS exhibited a more local perspective in their arrangements (Bellugi et al., 1999). The characteristic profile of the visuospatial abilities of individuals with DS implicates the neural substrates supporting these processes that are ultimately linked to the chromosomal abnormality of the disorder and its unique

phenotype. This profile may also indicate variations in neuronal plasticity in different disorders with intellectual disability (Bellugi et al., 2000).

6. Atypical cerebral laterality in individuals with DS

Atypical cerebral laterality (ACL) has been associated with the cognitive deficits of individuals with intellectual disability since the early 1920s (Gordon, 1921). ACL refers to the reverse or weak or bilateral representation of language in the two cerebral hemispheres (Geschwind & Galaburda, 1985). The majority of right-handed individuals (97%) exhibit left-hemisphere lateralization for language. Only about 60% of left-handed individuals exhibit left-hemisphere lateralization for language, 30% bilateral lateralization and 10% right-hemisphere lateralization for language (Bishop, 1990). Geschwind & Behan (1982) termed atypical laterality any laterality pattern that differed from the “standard dominance pattern” (pp. 70). According to Geschwind & Galaburda (1985a; 1985b), atypical dominance may involve the inverse or weak dominance of three features; hand dominance, language dominance and visuospatial dominance.

Several accounts have been put forward to explain the increased incidence of atypical laterality in individuals with neurodevelopmental disorders, which fall into four main categories: hormonal, genetic, pathological, and developmental. According to hormonal theories a number of exogenous and endogenous factors increase the secretion of prenatal testosterone in the fetus (Geschwind & Galaburda, 1987). This increment enhances the growth of the right cerebral hemisphere and inhibits that of the left cerebral hemisphere. In particular, their posterior regions, cortical areas tightly linked to intellectual disability and poor language development (Geschwind & Galaburda, 1985a, 1985b, 1985c). This speculation has been repeatedly challenged during the past decades for its complexity (e.g., McManus & Bryden, 1991; McManus, Bryden & Bulman-Fleming, 1994; Annett, 1994; Previc, 1994), although the implication of testosterone levels in the establishment of cerebral lateralization remains well supported (e.g. Witelson, 1985). For example, Witelson (1985, 1989) suggested that larger callosal isthmus is related to increased left-handedness in TD individuals, resulting from less axonal loss in the corpus callosum during foetal development, which is influenced by prenatal testosterone levels. Specifically, decreased levels of prenatal testosterone may cause decreased axonal loss in the corpus callosum, causing increased bilateral representation of cognitive functions and enhanced prevalence of non-right-handedness (Witelson, 1989, 1991).

Genetic theories argue that ACL results from genetic variation determined by a single gene (Annett, 1985; McManus & Bryden, 1982). Individuals who are not carriers of this gene will exhibit random hand preference (right or left). Any pathology during development may inhibit the expression of the right-hand gene causing ACL (Annett & Alexander, 1996). Alternatively, Satz (1973) proposed that ACL may be the result of early brain damage in the left hemisphere, causing a mild dysfunction of the contralateral hand for motor activities, which in turn, forces a genetically right handed person to switch to non-right handedness. According to this account, individuals with ACL are “pathological” left handers, genetically programmed to become right handers, but brain pathology altered this biological expression. From a developmental perspective, ACL may be caused by an atypical maturational process in motor development that initiates from the trunk, followed by the shoulders and then the hands. If this maturational process is arrested, or lagged, it could cause increased randomness which would be documented by lack of hand preference (i.e.,

ambiguous handedness) (Palmer, 1964). Bishop (1983; 1990) speculated that non right handedness is an indicator of an immature development of the motor system, caused by diffuse brain abnormalities in individuals with intellectual disability.

The characteristic dissociation of language being disproportionately affected to visuospatial abilities in individuals with DS that cannot be accounted by the hearing impairments (Laws, 2004) provides suspicion for the link between ACL and language problems in DS population. Indeed, an extensive review of the literature indicates that individuals with DS document an ACL pattern in speech perception and oral motor movements (e.g., Elliott & Weeks, 1993; Elliott, Weeks, & Chua, 1994; Heath & Elliott, 1999).

In a typical dichotic listening paradigm, two different auditory verbal stimuli are simultaneously presented in each ear using headphones. The participant is asked to repeat the stimulus that was best heard. TD right-handed individuals document a right-ear advantage (REA) for speech stimuli, which is indicative of left hemisphere lateralization for speech perception. According to the original account, auditory information incoming from the right ear is predominately represented in the opposite hemisphere (i.e., the left hemisphere) due to anatomical contralateral auditory pathways and, thus, closer to the language centers of the same hemisphere (Kimura, 1961). In order for verbal stimuli incoming from the left ear to reach the left-hemisphere's language centers, information crosses from the right to the left cerebral hemisphere via the corpus callosum, causing significant delays. In individuals with DS, a left-ear/right-cerebral hemisphere preference for speech sounds (Hartley, 1981; Pipe, 1988), or no ear advantage (Sommer and Starkey, 1977; Tannock et al., 1984) has been observed, instead of the typical right-ear/left-cerebral hemisphere preference found in TD controls. Using dichotic listening tasks, Welsh, Elliot, and Simon (2003) verified this hypothesis with right-handed individuals with DS exhibiting a left-ear/right-cerebral hemisphere advantage for speech perception, unlike the right-ear/left-cerebral hemisphere laterality for speech perception typically observed in TD adults. Similar results were obtained in a Japanese study with individuals with DS (Shoji, Koizumi & Ozaki, 2008).

Recently, Groen, Alku and Bishop (2008) used T-complex auditory event-related potentials to investigate whether individuals with DS show ACL, as reflected by atypical patterns of brain activity elicited by verbal and tone sounds presented in each ear. The relationship between atypical lateralization, language deficits and handedness was further explored. The laterality patterns of individuals with DS were significantly different, compared to TD individuals, confirming the existence of ACL for auditory processing in this population. However, this atypicality was not specific to verbal stimuli, but also to non-verbal stimuli, suggesting a more "generalized abnormality in auditory processing in individuals with DS" (Groen et al., 2008, p. 155).

Overall, in line with behavioral studies of language lateralization in individual with DS, there is reasonable evidence for the existence of ACL in this group.

Laterality studies indicate that individuals with DS exhibit increased non-right handedness, and inconsistent hand preference compared to healthy adults (Groen, Yasin, Laws, Barry & Bishop, 2008). This finding is in accordance with laterality studies examining handedness in other populations with intellectual disability of different etiology (e.g., Grouios, Sakadami, Poderi & Alevriadou, 1999).

7. Discussion

An overview of studies examining language and visuospatial abilities in individuals with DS suggests that there is a unique profile of cognitive abilities characteristic to the syndrome

that cannot be explained by intellectual disability. Individuals with DS exhibit diverse levels of strengths and weaknesses in both cognitive domains. Namely, the deficits in language abilities usually exceed impairments in visuospatial abilities. Recent studies demonstrate a more complex neuropsychological profile in this population, suggesting that the dissociation between language and visuospatial abilities is too simplistic. Indeed, we presented research that indicates that there are strengths and weaknesses in the visuospatial domain and the level of performance rarely exceed that of TD individuals matched for mental age. Moreover, the strength in visuospatial ability may be an artifact of comparisons with another genetic syndrome with intellectual disability, namely WS. The brain abnormalities of individuals with DS result in a complex pattern of a behavioral phenotype that involves a number of interacting cognitive systems. It also implicates atypical lateralization of function reflected in the abnormal auditory perception for speech stimuli and increased incidence of non-right handedness. According to the neuronal network hypothesis, the cognitive deficits of individuals with intellectual disability are the result of weak connectivity of different areas of the cerebral cortex (Ramakers, 2002). If this holds true, then processing difficulties are not limited to cognitive systems, but also perceptual systems such as auditory pathways. Indeed, difficulties in perceptual organization have been correlated with severity of intellectual disability, which is consistent with the hypothesis of a more general deficit in information processing (Ramakers, 2002). Future research should investigate the development of language and visuospatial abilities longitudinally to provide information on when the divergence of these cognitive domains becomes apparent.

8. References

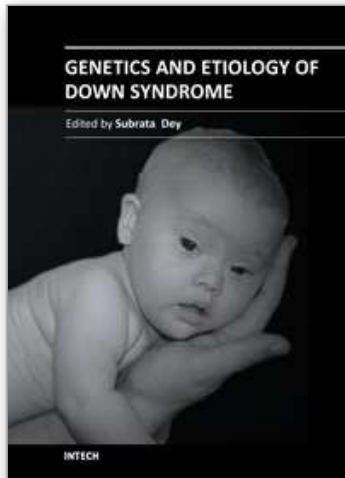
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This book provides a concise yet comprehensive source of current information on Down syndrome. Research workers, scientists, medical graduates and paediatricians will find it an excellent source for reference and review. This book has been divided into four sections, beginning with the Genetics and Etiology and ending with Prenatal Diagnosis and Screening. Inside, you will find state-of-the-art information on: 1. Genetics and Etiology 2. Down syndrome Model 3. Neurologic, Urologic, Dental & Allergic disorders 4. Prenatal Diagnosis and Screening Whilst aimed primarily at research workers on Down syndrome, we hope that the appeal of this book will extend beyond the narrow confines of academic interest and be of interest to a wider audience, especially parents and relatives of Down syndrome patients.

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