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10. LANGUAGE AND WILLIAMS SYNDROME

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Most aspects of human life—from gene expression, to brain structure/function, to underlying linguistic and cognitive processes, through to overt language production and comprehension behaviors—are the result of dynamic developmental processes, in which timing plays a crucial role. So, the study of language acquisition in developmental disorders such as Williams syndrome (WS) needs to change from the still widely held view that developmental disorders can be accounted for in terms of spared versus impaired modules to one that takes serious account of the fact that the infant cortex passes from an initial state of high regional interconnectivity to a subsequent state of progressively increasing specialization and localization of functional brain networks. With such early interconnectivity in mind, developmental neuroscientists must explore the possibility that a small perturbation in low-level processes in one part of the brain very early in development can result in serious deficits in higher-level processes in another part of the brain later in development. Therefore, in profiling developmental disorders of language such as in WS, it is vital to start in early infancy, from which to trace the full trajectory of the interactions of language and other cognitive processes across infancy, toddlerhood, and childhood, through to adolescence and adulthood.

> Overall, the *genetic double dissociation* is striking. . . . The genes of one group of children [Specific Language Impairment] impair their grammar while *sparing* their intelligence; the genes of another group of children [Williams syndrome] impair their intelligence while *sparing* their grammar.
>
> —Pinker (1999, p. 262, emphasis added)

Introduction

The view that there might be a gene or specific set of genes for grammar (Gopnik, 1990; Pinker, 1994, 1999; Wexler, 1996) stems from a focus on the *adult* brain and from dissociations found in agrammatic patients whose brains had completed their normal developmental specialization prior to their brain trauma

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(Karmiloff-Smith, 1998, 2006). The *developing* brain is very different. Cortical regions do not start out functioning independently. Rather, in the normal case, they are highly interconnected (Huttenlocher & Dabholkar, 1997; Huttenlocher & de Courten, 1987; Neville, 2006), with the neonate cortex neither localized nor specialized at birth (Goldman-Rakic, 1987; Johnson, 2001; Johnson, Karmiloff-Smith, Pennington, & Oliver, 2000). This allows interaction with the physical and social environments to play a crucial role in gene expression and in the ultimate linguistic phenotype (Elman et al, 1996; Karmiloff-Smith, 1997, 1998; Kuhl, 2004; Majdan & Schatz, 2006; Meaney & Szyf, 2005). Notions such as *spared* (or *intact* or *preserved*) are questionable when we consider how much the brain changes over developmental time and how a tiny deficit early on may have widespread effects on subsequent development. For example, early on, in response to linguistic input the typically developing brain displays widespread activity across multiple regions of cortex in both hemispheres (Casey, Giedd, & Thomas, 2000; Neville, 2006). This is followed by subsequent pruning, giving rise to *gradual* specialization and localization of function (Bourgeois & Rakic, 1993; Johnson, 2001). So, rather than thinking of the atypical brain as having spared versus impaired functions, it may be more fruitful to ask whether this gradual process of specialization and localization of function occurs in the atypically developing brain (Karmiloff-Smith, 1998, 2006, 2007). There are certainly indications that it does not. For example, older children, adolescents and adults with Williams syndrome (WS) tend to continue to display more bilateral brain activation than in the normal case (Mills et al., 2000; Neville, Mills, & Bellugi, 1994). Likewise, the brains of individuals with fragile X syndrome have been shown to have abnormally high synaptic densities, that is, they have undergone less pruning than in the normal case (Comery et al., 1997; Huttenlocher & Dabholkar, 1997; Huttenlocher & de Courten, 1987). In other words, synaptic pruning and gradual specialization of function constitute an essential part of normal development (Bourgeois & Rakic, 1993; Huttenlocher & Dabholkar, 1997; Huttenlocher & de Courten, 1987; Lund, Boothe, & Lund, 1977), and are an important consideration when endeavoring to understand the ways in which development goes awry in the atypical case, such as in WS.

Williams Syndrome: A Brief Description of the Genotype and Phenotype

Williams syndrome is a neurodevelopmental genetic disorder with a specific physical, behavioral, and cognitive profile. It is caused by a microdeletion on the long arm of chromosome 7, affecting some 28 genes (Donnai & Karmiloff-Smith, 2000; Semel & Rosner, 2005; Tassabehji, 2003). In most cases, the deletion is sporadic, although a few cases of parent-to-child transmission and concordant monozygotic twins have been reported (Morris, Thomas, & Greenberg, 1993; Pankau, Gosch, Simeoni, & Wessel, 1993). For a long time, the prevalence of WS was estimated to be between 1 in 20,000 and 1 in 50,000 (Morris, Demsey, Leonard, Dilts, & Blackburn, 1988), but more recently a Norwegian study has situated the prevalence much higher, at closer to 1 in 7,500 (Strømme, Bjørnstad, & Ramstad, 2002). WS was first described by two cardiology groups (Beuren, Apitz, & Harmjanz, 1962; Williams, Barratt-Boyes, & Lowe, 1961), both identifying the association of several clinical features in affected individuals: narrowing of the aorta (supravalvular aortic stenosis

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[SVAS]), distinctive facial dysmorphology, slow physical growth, and learning difficulties. It took another couple of decades before the syndrome started to be extensively investigated by cognitive psychologists and neuroscientists, hoping thereby to gather data that might contribute directly to the question of whether or not the human mind/brain starts out with innately specified, cognitive-level modules (like grammar, face processing, spatial cognition, number, etc.) that operate independently of one another and of general intelligence. The widely held view was, and still is to some extent, that WS involves a juxtaposition of intact and impaired modules, including intact grammar, as the quotation from Pinker at the beginning of this article suggests. But, as we shall see, the real picture of the WS phenotype is far more complex.

At the level of the brain, WS is characterized by structural abnormalities, with total brain volume being about 80% of normal brains (Neville et al., 1994). Once overall brain volume is controlled for, structural imaging studies point to specific reductions in parietal cortex (Eckert et al., 2005) as well as in the brainstem (Reiss et al., 2000). The corpus callosum is particularly small (Schmitt, Eliez, Warsofsky, Bellugi, & Reiss, 2001) but primary auditory cortex is proportionally large, with atypical cytoarchitecture (Holinger et al., 2005). Although the cerebellum is also large in WS brains (Jones et al., 2002), this is an area in which we identified abnormal brain biochemistry (Rae et al., 1998). Atypical neuronal size, orientation, and density have also been identified (Galaburda, Holinger, Bellugi, & Sherman, 2002), as has increased cortical gyrification in the right parietal and occipital regions and the left frontal areas (Schmitt et al., 2002). Gray-matter volume is close to that found in normal controls, but white-matter volume is reduced (Reiss et al., 2000). Finally, the hippocampus in WS brains appears to have an atypical shape (Meyer-Lindenberg, Mervis, et al., 2005). Apart from these structural abnormalities, other studies using functional magnetic resonance imaging (fMRI; Meyer-Lindenberg, Hariri, et al., 2005) and high-density event-related potentials (ERPs; Grice et al., 2001, 2003; Mills et al., 2000) point to atypical functioning in the WS brain. It is worth noting, however, that most of the studies of the WS brain structure and function have been based on adult brains. We have as yet little understanding of the developmental mechanisms that yield these brain abnormalities. This is obviously vital when attempting to account for language acquisition in a developmental disorder like WS.

The Importance of Tracing Full Developmental Trajectories

Although research into normal language acquisition has focused on infant precursors, it is still relatively rare to find such a focus in work on developmental disorders. Yet, in previous research we have shown that the profile of proficiencies and deficits in infancy can be very different from the subsequent profiles in adolescence and adulthood (Karmiloff-Smith, 1998; Paterson, Brown, Gsödl, Johnson, & Karmiloff-Smith, 1999). Pinker's (1999) aforementioned claim of "spared" language in WS is based on adult data where some individuals with WS do display surprisingly proficient (albeit not intact) language abilities by adolescence or adulthood. But if language were spared in this clinical group, as Pinker and others

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claim, why is its onset so frequently delayed? Is it just a case of the delayed maturation of a "language module," or is there a *developmental* explanation?

In fact, many interacting delays and deviances are contributing factors. For example, infants with WS are extremely delayed in the onset of babbling (Masataka, 2001) and in the segmentation of the speech stream (Nazzi, Paterson, & Karmiloff-Smith, 2003). Curiously, unlike typically developing children, production precedes referential pointing in WS (Mervis & Bertrand, 1997), suggesting that early productive language may not be referential in nature. Comprehension does not show the usual advantage over production in this clinical group (Paterson et al., 1999). Moreover, despite their fascination with faces, toddlers with WS do not follow the eye gaze of their interlocutors, nor do they pay attention to the referential targets of pointing (Laing, Hulme, Grant, & Karmiloff-Smith, 2002). And, even when they have greater vocabularies than their healthy controls, they show the opposite pattern from the controls and rely more on perceptual cues than on linguistic labels (Nazzi, Gopnik, & Karmiloff-Smith, 2005), pointing to an synchrony in the cognitive and lexical development of young children with WS (see also Nazzi & Karmiloff-Smith, 2002). In other words, the early stages of language acquisition in WS are not spared; multiple causes contribute to its late onset and atypical trajectory. This highlights how important it is to trace developmental trajectories across time, ideally longitudinally (Annaz, 2006; Annaz, Karmiloff-Smith, & Thomas, 2008; Ansari & Karmiloff-Smith, 2002; Karmiloff-Smith, 1992, 1998, 2007; Thomas et al., 2001, in press).

The Development of Language in Williams Syndrome

In spite of claims to the contrary (Bellugi, Wang, & Jernigan, 1994; Piatelli-Palmarini, 2001; Pinker, 1994; Rossen, Klima, Bellugi, Bihrle, & Jones, 1996; Smith & Tsimpli, 1995), it is questionable whether any domain of language, for example, syntax, semantics, phonology, or pragmatics, is intact in WS. Indeed, many empirical studies from different laboratories across the world have challenged intactness claims in respect of all aspects of WS language (e.g., the lexicon: Jarrold, Hartley, Phillips, & Baddeley, 2000; Stevens & Karmiloff-Smith, 1997; Temple, Almazan, & Sherwood, 2002; morphosyntax: Grant, Valian, & Karmiloff-Smith, 2002; Karmiloff-Smith et al., 1997; Stojanovik, Perkins, & Howard, 2004; Thomas et al., 2001; Volterra, Capirci, & Caselli, 2001; phonology: Grant et al., 1997; Laing et al., 2001; pragmatics: Laws & Bishop, 2004). Clahsen and Almazan (1998) tried to retain the innateness hypothesis, but for morphosyntax only instead of a whole language module. They argued for a dissociation in WS between impaired vocabulary but intact grammar. However, their claims are questionable because they were based on a very small sample of children with WS ($N = 2$ for $MA = 5$ years, and $N = 2$ for $MA = 7$ years, with considerable individual variation between the few participants). By contrast, Thomas et al. (2001) conducted a much broader and in-depth study using the same tasks and compared the performance of 21 individuals with WS with that of four groups of typically developing controls at ages 6, 8, 10 and adult. Thomas and colleagues argued that it is not sufficient to demonstrate that one aspect of language is relatively poorer than another, because this also obtains at younger stages in typical

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development. Rather, it is necessary to demonstrate that the level of a specific aspect of language is poorer that would be expected in WS, given their overall level of language development. The Thomas et al. study further reported that when verbal mental age was controlled for, the WS group was not only generally impaired, but displayed no selective deficit across vocabulary and morphosyntax. In a subsequent study of rapid naming in WS (Thomas et al., 2006), the results also pointed to atypicality in WS: slower and less accurate naming in the clinical group compared with both chronologically age matched and receptive vocabulary age-matched controls. In fact, Mervis and colleagues (e.g., Klein & Mervis, 1999) have concluded that the best way to characterize WS language is that it is delayed, reflecting patterns typical of considerably younger children. Indeed, a meta-analysis of a large number of language studies reveals that WS language is neither intact nor at the level expected for chronological age; rather, it is often no better than would be expected for nonverbal mental age (Brock, 2007).

A number of other empirical findings suggest that the WS language system is not only delayed but actually develops along a different trajectory compared to typical controls (Karmiloff-Smith et al., 1997; Klein & Mervis, 1999; Mervis, Morris, Bertrand, & Robinson, 1999; Thomas & Karmiloff-Smith, 2003; Thomas et al., 2001, 2006). For instance, unlike healthy controls, young children with WS use pointing *after* the appearance of naming. Exhaustive sorting follows the vocabulary spurt in WS, rather than preceding it as in typical development (Mervis et al., 1999). Furthermore, increased iconic gestures accompanied WS children's performance on a picture-naming task compared to the control group of children (Bello, Capirci, & Volterra, 2004). It has been suggested that sensitivity to the sound patterns of the language may act as a greater constraint on WS language than sensitivity to meaning (Grant et al., 1997; Klein & Mervis, 1999; Laing et al., 2001). Overgeneralization of regular plural *-s* to irregular plurals was reported to be more prevalent in WS compared with typically developing children (Clahsen & Almazan, 2001). Finally, supporting evidence from several studies across different languages (e.g., Karmiloff-Smith et al., 1997, in French; Klein & Mervis, 1999, in English; Levy & Bechar, 2003, in Hebrew; Lukacs, Pleh, & Racsmany, 2004, in Hungarian; Vicari, Carlesimo, Brizzolara, & Pezzini, 1996; Volterra, Capirci, Pezzini, Sabbadini, & Vicari, 1996; and Volterra, Caselli, Capirci, Tonucci, & Vicari, 2003, in Italian) suggest that the problems that individuals with WS have with semantics, morphosyntax, and pragmatics are often camouflaged by their good verbal memory, challenging the popular belief that their language is intact.

Taken together, these and many other studies point to the fact that individuals with WS follow a deviant developmental trajectory while acquiring language as children as well as when processing language as adults. Behaviorally WS language may appear to be proficient, but cognitively it seems increasingly likely that it involves different cognitive processes from the language of typically developing individuals. This is also true of the brain. A recent study (Hsu, Karmiloff-Smith, Tzeng, Chin, & Wang, 2007) of semantics in WS memory reported that while the brains of normal adults differentiated between semantically related words and semantically unrelated words, the brains of individuals with WS did not. Moreover,

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unlike normal adults, the brains of individuals with WS showed a difference between previously presented words and semantically related words. These findings suggest that the WS proficient performance at the behavioral level is underpinned by a deviant neural pathway, which highlights the need to go beyond behavioral measures and to examine brain processes to understand language in this and other clinical groups.

The Importance of Cross-Domain Studies

Multiple contributing factors to the delay in the onset of language in WS have been listed here in the previous section, on the development of language in WS. But they were all within the general domain of communication. Should scientists merely probe closely related domains when endeavoring to understand atypical development? Again, recalling the early interconnectivity of cortical regions, it is wise not to limit research to the specific areas of language and communication when trying to seek the causes of atypically developing language. It is vital for understanding higher-level linguistic phenotypes to explore how they originated in low-level processing mechanisms early on in development. For example, we have demonstrated a serious deficit in visual saccadic planning in WS (Brown et al., 2003), which leads to atypical triadic interaction (Laing et al., 2002), thereby altering the way in which toddlers with WS learn vocabulary. So, not only should we explore the communication-relevant contributions to a delay in language, but we should also examine other domains like vision, memory, and attention. Timing plays a critical role in development, particularly if one considers how different domains may interact at different moments across the developmental trajectory. So, something that might at first blush seem irrelevant to the acquisition of grammar, that is, saccadic eye movement planning, may have been critical at the earlier stage of development for subsequent language acquisition.

The myth of intact language in WS is also due to a frequent slippage in which *relative* differences in abilities are often reported as *absolute* claims. The fact that a clinical group does *better* at, say, vocabulary tasks than at spatial tasks, does not confirm the claim that vocabulary is intact, spared, or preserved, and spatial cognition impaired. In many instances, both verbal and nonverbal abilities are below chronological age; it is simply that one is less impaired than the other. And, even when scores fall in the so-called normal range, it is crucial to ascertain whether the behavior may be underpinned by atypical cognitive and brain processes (Karmiloff-Smith, 1998; Karmiloff-Smith et al., 2004).

The Importance of Cross-Syndrome Comparisons

Interestingly, unlike infants and toddlers with WS, those with Down's syndrome (DS) are not impaired in their planning of saccadic eye movements (Brown et al., 2003), yet they are just as delayed in their vocabulary development as are infants and toddlers with WS (Paterson et al., 1999). Thus, the reasons for the similar delay and similar overall IQ in these two syndromes must be different, pointing to the

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importance of tracing full cross-syndrome developmental trajectories. And, in exploring cross-syndrome similarities and differences, it is important to analyze not simply success and failure, but also potential and informative differences in error patterns (Scerif, Cornish, Wilding, Driver, & Karmiloff-Smith, 2004).

Conclusion

In profiling atypical language development in disorders such as WS, neuroscientists need to keep in mind that the brains of atypically developing infants should not be viewed as normal brains with parts intact and parts impaired, but as brains that are likely to have *developed* differently throughout embryogenesis and postnatal development. If one views the healthy child brain as composed of prespecified independently functioning modules, and the atypical brain as a neat juxtaposition of intact and impaired modules, then the mind/brain can be theoretically represented by a number of segregated boxes, one or more of which will have a line crossed through if impaired. This kind of model implies that any damaged module has no effect on any of the other, purported independently functioning, so-called intact modules. Such a research strategy therefore frequently leads to a merely cursory check of the purportedly intact parts of the brain, to confirm that individuals' scores fall in the normal range, placing thereafter a major emphasis on the impaired part(s). By contrast, once one considers development as the dynamic result of many interrelated cortical regions in interaction with a constantly changing environment, then notions such as double dissociations (implying pure deficits) are theoretically dubious (Karmiloff-Smith, Ansari, Campbell, Scerif, & Thomas, 2006; Karmiloff-Smith, Scerif, & Ansari, 2003). Rather, the research focus must, in our view, shift to the delineation of longitudinal, cross-domain developmental trajectories of brain and behavior from infancy, toddlerhood, childhood, and finally to adulthood, and, where possible, even back to the final trimester of fetal life when auditory processing is very active (Hepper, 1991; Karmiloff-Smith, 1995). A lack of changes at the behavioral level does not preclude important changes at the brain level, and vice versa; and behavioral scores in the so-called normal range do not preclude atypical brain and cognitive processes.

Future research on language in WS must involve resource-intensive multidisciplinary studies, which should ultimately yield a rich body of knowledge about human language, allowing researchers to target intervention in low-level processes at the very earliest moments of development rather than waiting for more obvious higher-level deficits to emerge in later development. Let us always recall that development, whether typical or atypical, is not a *state*, but a *dynamic process of change over time*.

ANNOTATED REFERENCES

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This article is aimed at investigating whether there are selective impairments on regular and irregular inflections in language across developmental disorders. From the distinct pattern observed in people with WS and specific language impairment (SLI), the authors argued that they have demonstrated empirically the theoretical distinction between a computational system and an associative memory system for language.

Karmiloff-Smith, A. (1998). Development itself is the key to understanding developmental disorders. *Trends in Cognitive Sciences, 2*(10), 389–398.

The strict nativist approach to abnormal phenotypes, inspired by adult neuropsychology and evolutionary psychology, seeks to identify impairments to domain-specific cognitive modules and studies the purported juxtaposition of impaired and intact abilities. The neuroconstructivist approach differs in several respects: (1) it seeks more indirect, lower-level causes of abnormality than impaired cognitive modules; (2) modules are thought to emerge from a developmental process of modularization; (3) unlike empiricism, neuroconstructivism accepts some form of innately specified starting points, but unlike nativism, these are considered to be initially *domain-relevant*, only becoming domain-specific with the process of development and specific environmental interactions; and (4) different cognitive disorders are considered to lie on a continuum rather than to be truly specific. It is argued that development itself plays a crucial role in phenotypic outcomes.

Karmiloff-Smith, A., Thomas, M., Annaz, D., Humphreys, K., Ewing, S., Brace, N., et al. (2004). Exploring the Williams syndrome face processing debate: The importance of building developmental trajectories. *Journal of Child Psychology and Psychiatry, 45*(7), 1258–1274.

This article is aimed at investigating face processing abilities of people with WS. By building developmental trajectories of normal children's performance across a wide age range, the authors found that people with WS showed both delay and deviance in processing faces, with particular problems in configural processing. The authors argued against matching and in favor of theory-neutral developmental trajectories on which to plot atypical development.

Johnson, M. H. (2001). Functional brain development in humans. *Nature Reviews Neuroscience, 2*, 475–483.

This article argues against innately specified brain functions and takes the interactive specialization perspective of progressive brain development as a function of postnatal experience. The author argued that the human infant is well adapted through primitive biases to attend to relevant stimuli in its environment. The infant's interaction with its environment helps to sculpt inter- and intraregional connections within the cortex, eventually resulting in the highly specialized adult brain.

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