

Editorial

Rewards and Challenges of Cognitive Neuroscience Studies of Persons With Intellectual and Developmental Disabilities

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It is with great pleasure that I write an editorial for this special issue of the *American Journal on Intellectual and Developmental Disabilities (AJIDD)* on Cognitive Neuroscience Studies of Persons With Intellectual and Developmental Disabilities, just as it was to accept Len Abbeduto's invitation to join the journal as an associate editor. His charge to me, as part of that invitation, was to increase the representation in the *Journal* of first class cognitive neuroscience studies of children and adults with intellectual and developmental disabilities. I accepted both invitations enthusiastically for two reasons. One was that as a developmental cognitive neuroscientist studying children with neurodevelopmental disorders, I know firsthand how few really appropriate journals exist for this rather young and emerging field of clinical and translational research. The other reason was that it was obvious to me how appropriate it is that *AJIDD*, with its long history of communicating the cutting edge of research and practice about individuals with intellectual impairments and cognitive disability, should become a leader in this discipline. I hope that, as Abbeduto stated in a recent editorial, the appearance of this special issue does indeed mark the beginning of "a whole new era for *AJIDD*" (Editorial, 2010, p. 2).

To explain the motivation for this special issue, I think it is worth reprising some of the main points made in our Call for Papers (2008). There we made the following statements.

The now well-established field of cognitive neuroscience has made significant progress in elucidating the neural substrates and cognitive processing underpinnings of a wide range of cognitive functions. However, its focus has been predominantly on typical adult function; much less attention has been given to typical and atypical development. (p. 322)

We also stated that

cognitive neuroscientific methods hold considerable promise for significantly advancing explanations for the basis for many

conditions that produce intellectual and developmental disabilities. Also, because of their neurobiological and mechanistic strengths, these methods are likely to lead to rapid progress towards a range of interventions. (p. 322)

However, the application of cognitive neuroscience methods to the study of atypically developing individuals is not one of simple translation of established techniques to a new study population. In general, in cognitive neuroscience studies of typical adults and, more recently, children, researchers tend to focus on identifying the mental representation and algorithmic processing and/or neural underpinnings of a particular cognitive function or domain. Although these are also crucial goals in cognitive neuroscience studies of atypical development, investigators generally aim to go further by generating causal mechanistic explanations for particular domains of impairment, and they also try to account for the etiology and developmental progression of the observed disorder. Frequently, this is done because a longer term goal is to develop therapeutic interventions.

These goals make the task more difficult because one must interpret atypical development (whether in children or adults) entirely differently from typical development. This is especially true when attempting to make mappings of impaired cognitive functions and their underlying substrate in the atypically developing brain. This is not only because they change over the course of development, as in the typical case, but also because, in the atypical brain, the mappings are likely to be different from typical ones and change in atypical ways. These methodological concerns have been discussed in detail, most particularly by Karmiloff-Smith and her colleagues (Johnson, Halit, Grice, & Karmiloff-Smith, 2002; Karmiloff-Smith, 1998; Scerif & Karmiloff-Smith, 2005). In brief, the issue can be understood as follows.

All other things being equal, most typically developing people experience a somewhat similar neurodevelopmental environment throughout their lives. Thus, in Westernized cultures at least, one would expect, and can observe, a good deal of convergence in the mental representations and processes individuals acquire and the neural substrates that are gradually specialized for those functions even while significant individual differences exist. However, in atypically developing individuals, especially those with congenital rather than acquired disorders, there is quite likely to be an entirely different developmental trajectory towards a mature, if not ever stable, neurocognitive state that begins even before birth. The genetic and associated environmental impact created by such disorders will significantly influence the nature of the developing neurocognitive machinery so that what information can be acquired, represented, processed, and transformed is atypical throughout these individuals' entire lives. One could argue, then, that the least reasonable assumption one might make is that their neurocognitive state, at any point during development, would or even should be the same as that of a typically developing person of similar chronological or even mental age. This makes hypothesizing, predicting, and interpreting the nature and course of neurocognitive functioning and growth, particularly challenging and prone to significant error if one makes the oversimplistic assumption that the minds and brains of these individuals should be generally like those of their typical counterparts but are "damaged" or "altered" in some way (Johnson et al., 2002). In reality, the challenge is more one of trying to determine just what entirely different neurocognitive solution such individuals have created in response to their altered world and how that is structurally and functionally configured.

All of this means that, more than anything, it is critical for researchers conducting studies of atypical development to focus on the delineation of an endophenotype of the domain of function of interest. An endophenotype, according to Gottesman and Gould (2003), consists of "measurable components unseen by the unaided eye along the pathway between disease and distal genotype [that] may be neurophysiological, biochemical, endocrinological, neuroanatomical ... in nature" (p. 636). An endophenotype need not be genetically heritable in the sense that Gottesman and Gould envisaged, but it should

aid the process of explicating genotype–phenotype relationships by identifying tractable levels of analyses at which scientists can explain not just how but also why the behavior and abilities of atypically developing children or adults differs from their typically developing peers. Once such explanations exist, it is likely that scientists will begin to identify targeted questions about how substrates or processes might be changed by a range of interventions such that different outcomes may be possible.

In this special issue, we present a set of articles that begin that process by identifying atypicalities in a range of cognitive functions and in several neurodevelopmental disorders. Some characterize differences in genetic type and expression; others focus on changes affecting cognitive processing and the mental representations on which it depends. Another set characterizes differences in terms of neural responses to cognitive task demands. In each case the authors seek to explain how atypically developing individuals differ from their typical peers and expect that, if their hypotheses are supported by replications in their own labs and those of others, these differences could one day become targets for interventions that may vary as widely as gene therapy to pharmacological agents to cognitive and behavioral training.

In all six papers in this issue, the authors approach the endophenotyping issue in slightly different but related ways. Four papers are focused on two very heavily studied neurodevelopmental disorders of known genetic etiology, namely Williams and Down syndromes. Elsabbagh et al. explored how (mostly) adults with Williams syndrome represent and computationally process auditory information by examining how it is structured in mental representations and then processed for coherence and relationships among units. Their research was motivated in part by attempting to explain how and why individuals with Williams syndrome have apparent strengths in domains involving auditory information, such as music and language. For them, the key to these strengths lies in the fact that for both kinds of information, accessing and working with internal structure of the auditory information are necessary to comprehend its content.

In other words, there may be common underlying processes neither explicitly musical or linguistic in nature that explain how these higher level competencies work. In a series of

experiments, Elsabbagh et al. required participants to determine which elements in a stream of auditory input should be grouped together to make meaningful units and which should be segregated from one another to create boundaries between those units. They found that adults with Williams syndrome could segment unfamiliar melodies as effectively as could typical controls on the basis of pitch. These authors also reported that despite their often vaunted linguistic and musical strengths, individuals with Williams syndrome could not take advantage of further cues involving the contour of the elements in the auditory stream to more effectively segment them, whereas typical controls were able to use the extra information. In this way, Elsabbagh et al. discovered the different ways in which those with Williams syndrome can perform as well as typical individuals and how and why they fail to do so in different kinds of tasks. The timeliness of this topic is shown by the fact that it is accompanied by a second paper on auditory processing in individuals with Williams syndrome by Thorton-Wells and colleagues, who focused more on musical aspects. Their results, obtained using functional MRI (fMRI), offer a further insight into how and why such individuals so often show a relative strength for musical cognition. Using musical and nonmusical stimuli, in a series of experiments, they found that adults with Williams syndrome differed from similarly aged typical controls in that they tended to activate brain areas typically associated with visual and emotional information processing much more than did control participants. These results represent novel information about the possible cross modal manner in which those with Williams syndrome represent and process auditory information that might bear some resemblance to the phenomenon of synesthesia or the blending of multiple senses when processing sensory or even conceptual information. Of course, bearing in mind the interpretive caveats mentioned earlier, the results might also indicate that for those with Williams syndrome, some parts of visual cortex come to process different kinds of information than do typically developing brains or that they are able to process the same information in a different way. They may even operate more flexibly to process, and possibly then blend, a wider range of sensory information. A series of future experiments is clearly indicated to clarify these fascinating and important questions.

In another functional imaging study, Virji-Babul and colleagues examined the neural correlates of action execution and observation in individuals with Down syndrome because understanding of the physical and social world requires the ability to perceive and interpret the actions of others. Furthermore, in recent studies of what has been termed the *mirror neuron system* (Cattaneo & Rizzolatti, 2009), researchers have pointed to the role of mental and physical imitation in both comprehension and learning. Understanding the functioning of such a system may help us understand as well as remediate common motor and perceptual impairments seen in people with Down syndrome. Using magnetoencephalography to measure electrical signaling in the brain, Virji-Babul and her colleagues found that, unlike their typically developing peers, adults with Down syndrome did not show strongly lateralized neural activations when executing motor movements and that when observing the movements of others, they did not appear to activate the areas of motor cortex that were seen in the typical participants in the same condition. The authors interpreted the apparent discontinuity in their findings between execution and observation in the Down syndrome group as evidence that the mirror neuron system is dysfunctional in the individuals whom they studied. Such findings might lead to an explanation of why motor learning can be hard for individuals with Down syndrome and could point to interventions to improve that weakness either by finding ways to strengthen the functioning of the mirror neuron system or to discover methods of teaching and learning that compensates for its weakness.

In a very different paper, Rachidi and colleagues reviewed work on the molecular and cellular basis of cognitive impairments in Down syndrome, much of it in the form of studies carried out with mouse models that allow genes in the critical regions of chromosome 21 associated with Down syndrome to be directly manipulated. Identification of possible explanations for cognitive dysfunctions in terms of anomalies in the Calcineurin and NFATc pathways and the regulation and expression of neurotransmitters such as NMDA and GABA may lead in the future to pharmacological and genetic therapies that could significantly alter the neurodevelopmental trajectory of those with Down syndrome and enhance their intellectual, functional, and adaptive outcomes.

Beaton and colleagues also used fMRI to determine whether girls with Turner syndrome process spatiotemporal information differently from typically developing controls, primarily because this information could help us understand their problems when processing information about space, time and numbers, and learning arithmetic. Using a dynamic object tracking task, Beaton et al. found that, girls with Turner syndrome activated some of the same areas seen in the typically developing group in response to the task but also activated many different parts of their brains that did not respond compared with typically developing girls. This was true even when performance between the two groups was held constant and, therefore, could not be explained by errors, suggesting that girls with Turner syndrome cannot develop the same neurocognitive solution to the problem of spatiotemporal information processing. This information points to methods of remediation and measurement of therapeutic impact.

Willner and his colleagues, like Elsabbagh et al., took an entirely experimental approach to investigate an important problem called *temporal discounting* in adults with developmental disabilities. The phenomenon, mostly studied in individuals with ADHD, is used to examine the ability to represent and process the value of an available reward along with the relative costs and benefits of either delaying in order to increase the value of the reward or accept a smaller reward immediately. Willner et al. found temporal discounting to be very difficult for adults with intellectual and developmental disability mainly due to impulsiveness. This inability was strongly related to the specific domain of executive function and not general intellectual function as measured by IQ. Executive function competence also mediated the extent to which affected adults could benefit from training. These findings have implications for understanding the ways in which adaptive functioning might be limited for adults with intellectual and developmental disability. They also, importantly, pointed to executive functioning as the underlying competence that could be a key target for any effective intervention to increase a wider range of abilities.

I believe that in this strong set of articles, the researchers have very clearly “elucidat[ed] the neural substrates and cognitive processing underpinnings of a wide range of cognitive functions related to intellectual and developmental disability” and that “their neurobiological and mechanistic strengths ... lead to rapid progress towards a range of interventions” (Call for papers, 2008, p. 322). I hope that they mark the start of a regular acceptance of such articles to be published in the *Journal*, and I look forward to editing many more of them as they are submitted in the future to be considered for publication in the regular editions of the *American Journal on Intellectual and Developmental Disabilities*.

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