CROSS TALK

How do we begin to treat autism's most severe cases?

BY **GREG BOUSTEAD**

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In a **news article last month**, we covered the challenges of studying severe, intractable autism that is further complicated by other serious medical conditions. A consortium of scientists has launched a new network of specialized research hospitals to help meet this need.

The article raises important questions about how best to understand and treat an under-served population of individuals whose very deficits make them challenging to serve. In fact, considering the dramatic differences in the deficits of people with severe versus high-functioning forms of autism, these issues invite the thornier question about whether we're even looking at the same disorder.

For this **Cross Talk**, we turned to clinicians who study and specialize in treating the most severe forms of autism to get their outlook on this new project.

What do you think? Share your reactions and follow-up questions in the comments section below.

Helen Tager-Flusberg

Director,Research on Autism & Developmental Disorders, Boston University

What is this work likely to accomplish?

Taking up the challenge: “The new program of research will start to fill a gap in both science and practice. It is clear that this most severe end of the spectrum is highly heterogeneous, and this group of investigators is to be commended for taking up the challenge to move this area of research forward at a more accelerated pace. For this reason, I am delighted to serve on the external scientific advisory board for this consortium.”
Critical samples: “Among all the planned aims of this work, perhaps the most important component of the research is the collection of DNA samples. Given our current technology, analyses of these data will likely demonstrate the high percentage of very severe cases for which there is some definable genomic etiology. Importantly, however, it is not autism per se that defines this end of the spectrum as so severe. It is the comorbid conditions that travel with autism that increase the likelihood of hospitalization.”
Matching genes to comorbidities: “These conditions include significant intellectual disability, absence of language and severe psychopathology that is manifest in aggressive self-injury and other challenging behaviors. So it is likely that as the genomic data are analyzed, it will be possible to begin highlighting some key associations to these comorbid conditions. The extent to which these data will parallel what is emerging from research on less severe cases remains to be seen.”

James McPartland

Assistant Professor of Child Psychiatry and Psychology,Yale School of Medicine

Severe irony

Limits of understanding: “It is ironic that, in some respects, our field knows the least about individuals with the most severe autism. Our limited understanding of how to intervene in these cases reflects several biases in clinical practice and research. Although behavioral disruption is common in autism, it is neither a diagnostic feature nor a unique facet of autism. Early childhood interventions may focus primarily on language, academic skills or social behavior instead of tantrums or aggression, placing children with severe autism and their families at longer-term risk for significant behavioral challenges.”

‘Listening’ to behavior: “A review published last year by Carla Mazefsky and Susan White highlights the importance of improving emotion regulation in autism. As my colleagues in speech and language pathology say, behavior, including disruptive behavior, is communication. People with strong preferences or insistence on sameness may encounter more sources of frustration in daily life. Providing functional communication strategies is vital.”

New support: “Fortunately, touch-screen tablets and smartphones are readily transportable and support an increasing number of applications to augment communication. Onboard cameras capture immediate, concrete representations of people and objects in the environment, enabling parents and providers to create communicative tools ‘on the fly.’ It is an added bonus that tablets are intrinsically interesting and reinforcing to many people (on and off the spectrum). Especially in contrast to the cumbersome and costly devices of the previous generation, they may afford social caché, rather than stigma.”

Difficult completion: “Historically, individuals with intellectual disability, minimal language, and behavioral dysregulation have often been excluded from research. The study of individuals with autism and intellectual disability requires a more complex experimental design, incorporating additional clinical control groups to extricate the influence of autism symptoms per se from intellectual disability. While this complexity increases the quality and generalizability of a study, it also increases its difficulty to complete.”

Trends and applications: “More research on severely affected, minimally verbal individuals is emerging. In 2012, the National Institutes of Health funded an Autism Center of Excellence at Boston University, specifically focused on individuals with autism who do not develop language. In our lab, we are attempting to develop brain imaging methods that are more easily applied to this population by decreasing reliance on language and making experiments naturally directed by participant behavior. By pairing an eye-tracker with an electroencephalography system, we can create brain-imaging tasks that are controlled by a participant’s gaze.

“Such technologies may offer insight into the distinct neural characteristics of an understudied group. This approach may also yield therapeutic applications. Paradigms controlled by eye gaze can be used to shape behavior. Together, studies like Matthew Siegel’s, along with increasingly innovative approaches to basic science, hold promise for deeper understanding and more effective treatments for this population.”

Alexander Kolevzon

Associate Professor of Psychiatry and Pediatrics, Clinical Director,Seaver Autism Center, Icahn School of Medicine at Mount Sinai

A uniquely positioned approach

Challenging treatment: “Aggression and self-injury are extremely challenging for people affected by autism and their families. Inpatient admissions are often required in order to better understand antecedents to disruptive behavior and to develop effective treatment plans, including medicine. Often, these individuals are also on complicated pharmacological regimens, obscuring the distinction between underlying symptoms versus the medications’ side effects. This new consortium will fill a crucial gap because not only are such units woefully lacking resources, but most inpatient psychiatric units try to avoid admitting severely affected and intellectually disabled patients because of their complexity and intensive needs.”

Distinct disorders? “It is possible that severe autism with intellectual disability represents a genetic subtype, because there is significant overlap among genes known to cause autism and those that cause intellectual disability (even without autism). Protein-interaction studies also suggest that some of these autism/intellectual disability genes, including SHANK3, TSC1, TSC2 and FMR1, converge on common molecular pathways to cause syndromes associated with both autism and intellectual disability. As such, collecting biological samples will be critical for the project, creating opportunities to discover new genes or uncover new molecular pathways that are disrupted in autism, and potentially leading to novel treatment approaches.”

Better measures: “On everyone’s wish list is the creation of better objective measures to capture clinical outcomes in the context of autism treatment trials, especially in nonverbal, intellectually disabled individuals who are unable to reliably follow instructions. With the establishment of this consortium, the field may be better poised to develop and test new instruments.”

Putting it together: “A consortium of specialized psychiatric centers is uniquely positioned to collaborate in refining the clinical phenotype, collecting genetic data, and developing much-needed assessment tools for severe autism and intellectual disability. Eventually, these centers may also serve as a clinical trial network to test treatments for the most severely affected patients who may otherwise be unable to participate in research.”