

OPINION, Q&A

Questions for James McPartland: Biomarkers for better trials

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22 SEPTEMBER 2015



Most measures used for assessing social skills in people with autism are highly subjective, relying on the **observations of clinicians or parents**. Without more objective ways to track social deficits, clinical trials may **come up short** in finding answers for treating this core symptom of autism.

In July, multiple government and nonprofit funding groups launched an initiative that aims to identify the right combination of objective measures for social functioning.

Researchers involved in the \$28 million initiative, called the **Autism Biomarkers Consortium for Clinical Trials**, plan to monitor a meticulously characterized sample of 200 children with autism for six months. They aim to compare traditional measures for social skills, including parent interviews, with more objective tools, such as software that tracks a child's speech patterns during real-life interactions.

Teams from five sites across the country also plan to test other biological markers, using electroencephalography (EEG) and **eye-tracking technology**, to help predict and track how children with autism respond to treatment.

We asked lead researcher **James McPartland**, associate professor of child psychiatry and psychology at the Yale Child Study Center, to expand on the consortium's scope and goals.

Spectrum: What is unique about the consortium?

James McPartland: What we're doing here in the context of autism is something that hasn't really been done in an organized way at this scale. We're going to get a clear sense of how measures of brain activity, visual attention and behavior blend together with a person's social performance, which is scientifically interesting.

Another special feature of this project is its scale. It brings together five major autism research centers. But it also focuses on rigorous standardization across sites, allowing us to regulate hardware, software and data analysis protocols. That is something that I think is rare, and the reason for this level of investment.

S: What is the consortium's main goal?

JM: The thrust of this kind of research is to move us toward being more effective at conducting clinical trials. We want to understand who is going to get better with treatment, how they're getting better and how quickly. To do this, we need ways of measuring autism symptoms that are sensitive to change and can be reliably applied across sites in multisite studies.

The idea here is to take a really broad array of potential **biomarkers** and a large sample of people that is extremely well-characterized so that we can say, "Okay, once and for all, what works and what doesn't?" The more we can precisely identify these biomarkers, the more incentive there is for industry to help us develop new treatments for children with autism.

S: Why is it so hard to identify biomarkers for autism?

JM: Probably a lot of it has to do with heterogeneity. Most of the information we have about potential biomarkers is from studies of 20 or 30 children. For example, if you look at brain activity while a child looks at another person's face, there's a pattern of results that emerges across studies, but not a perfect replication.

There are promising studies with respectable sample sizes, but it's hard to know how they generalize. And when we see failures of replication from study to study, it's hard to know whether that's telling us it isn't a viable biomarker or simply that we didn't have similar participants in these studies. What we're going to be able to do here is really limit and control for heterogeneity.

S: What do EEG and eye tracking bring to the table as potential biomarkers for autism?

JM: What is compelling about them is their potential for use in large-scale clinical trials. They're economical, scalable and accessible.

We want something that can be used in as wide and diverse a group as possible. Both EEG and eye tracking are strong in that regard.

S: What tools will you use to assess social behavior?

JM: Most of the tools available to measure behavior in autism rely on observations by a clinician or a parent. We plan to use these also but focus on methods that are less reliant on human interpretation.

For example, a tool called **LENA** (Language Environment Analysis) automatically records the vocalizations that a child either makes or hears. It lets us **study a child's language abilities objectively**. Similarly, a camera that charts a child's movement in a room can automatically measure the amount of time that child chooses to spend near other people versus alone.

S: What are the advantages of the public-private partnership at the core of this project?

JM: It lets you bring together different kinds of expertise: scientists in academic settings, in the government and in industry. Each group has a different take on things. The hope here is that bringing these people together will make for a much richer discussion and, I think, will result in a more comprehensive and more effective study. It's also really fun getting to collaborate with people whom I would never run into at a faculty meeting at Yale.