What are the most pressing challenges in psychiatry clinical trials? How are scientists addressing them?

In conversation with... Scott J. Hunter, PhD

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Dr. Opler: Dr. Hunter, could you give us a brief personal introduction, how you got into the field, what your research focus is and why development of new treatments for neurodevelopmental disorders matters?

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Dr. Hunter: I am a pediatric neuropsychologist who, over the course of my career, has emphasized understanding the development of both cognitive and behavioral capacities in individuals with a range of neurodevelopmental challenges. This includes both those tied to likely, and even known, genetic considerations that emerge very early in development, and those that appear to be more readily acquired as a result of the different medical illnesses or conditions that unfold across childhood and into adolescence and emerging adulthood.

I got into this area because I found that, through my training on the clinical side, the work I was doing with individuals who had complex neurodevelopmental challenges both engaged and excited me. But I also saw some stagnation in understanding how to move forward in the way that we treat these individuals and provide opportunities for them. And looking at where the advances were taking place in pharmacological and genetic-based interventions, it became clear that those advances hadn't necessarily been well applied to my area.

This gave me opportunity to think about how to support and encourage families and the groups that work with individuals with neurodevelopmental challenges to help them become more effective members of their families and their communities, and to move forward towards a greater level of independence.

Scott J. Hunter, PhD, *a member of WCG's Scientific Leadership Team, shared his insights during a recent conversation with Mark Opler, PhD, MPH, chief research officer at WCG's MedAvante-ProPhase. Dr. Hunter is a professor of psychiatry and behavioral neuroscience, as well as pediatrics, at the University of Chicago.*

The interview has been edited for clarity and length.

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Dr. Opler: One of the things that I've noticed, that I think is very exciting for the field, is a certain level of optimism about moving these advances from theory into practice. With that in mind, what do you think are the top three challenges today in our current trial methodologies and trial conduct?

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Dr. Hunter: That's a great question. I think that first, one of the most significant issues I have been thinking about and seeing at play is recruitment of the participants for these studies, and the diversity of the populations that we're getting into the studies in terms of racial, cultural and linguistic factors. I think this has been an area where we have needed, and are needing to put, a much greater level of focus. Given that there is hesitancy amongst some communities to become engaged in clinical trials research, this is something that needs a much greater degree of thought, considering that we live in a highly multicultural country and society.

Second, I think that the specificity and reliability of the measures we are choosing for assessing symptom presence and severity, as well as their efficacy with regards to the populations that we are assessing, remain concerns. We often find that the profile of behavioral concern may not be a direct match to what the measure had been originally developed to assess. We need to consider ways of adapting current measures and ultimately, developing new ones.

Third is adherence. One of the greatest challenges I find in any type of clinical trial is the willingness of the family not only to engage, but to sustain their involvement. We know that some of these interventions will lead to certain types of side effects; we need to make sense of those side effect and then then determine when and how they resolve. For a lot of families that's especially tough.

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Dr. Opler: If you were in the process of starting a trial today, what should the individual or a team running that study be cautious about as they embark?

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Dr. Hunter: I think that, without a doubt, having a better understanding of the lay of the land for the different sites that are being recruited to participate in the trial, and the communities that exist in those areas where the sites are, so we can have a better understanding of both the population to draw from, and the diversity of that population, but also the concerns about agency and capacity to understand what participation means, and what may or may not be gained from participating. I think that that's one of the first things that a team really needs to be paying close attention to.

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I think the second is, following up on my response about challenges, perhaps spending more time thinking about the measures for assessing behaviors and capacities of interest–and their sensitivity to variability that may play out based on a developmental level. We need to understand those measures and whether they are sensitive enough to help us understand if change is taking place.

Those are ones that really stand at the top of the list for me.

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Dr. Opler: Thank you. That really gives us a very good sense of the lay of the land. Moving on from there, could you tell us about a few of the developments in clinical research in 2018 that you are most excited about?

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Dr. Hunter: As a member and vice chair of the institutional review board, I get a chance to see a lot of research that's in development and being considered. There are two areas I'm increasingly excited about. First and foremost is the movement into big data and the ability to glean not only specific kinds of biological response data, but also a greater degree of information about the individuals and their lives. That allows for a much better examination of the intersection of environment, person and disease.

I think that we have seen some substantial movements in some specific diseases, particularly cancers, in that domain. And understanding not only the genetics of the disease in a more effective and nuanced manner, but also how the lives individuals lead and both the strengths and the areas of challenge that they bring, contribute to risk, resilience and response.

In tandem with that I have to say something that's really surprised me is the movement to studying the microbiome and understanding the interplay between the internal and the external environment for individuals. This provides a much greater understanding about how bodies, in environments, lead to having different types of responses to interventions–particularly pharmacological interventions–that are being developed and tested. I think that probably, in tandem, big data and microbiome are a key shift in where the focus lies for a lot of different research studies that are coming out now. I think it will propel us into a fascinating and exciting new domain.

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Dr. Opler: I would absolutely agree with you, Dr. Hunter, that the past year has forced us to examine a number of our assumptions. With that in mind, what do you think are the top three opportunities for clinical development, in neurodevelopment? In other words, where can we make the biggest impact?

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Dr. Hunter: Well, I think that one area in particular is in better balancing our investigations of rare and more common neurodevelopmental disorder conditions.

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We should approach studies more integratively in a way that allows us to make sense of the genetic relationships between multiple neurodevelopmental disorders. How what we're learning about the more common types of presentation, let's say Fragile X, and some of the rarer ones, and where the intersection is in terms of risk, as well as potential areas for support.

I also think that wider recruitment is key. The current emphasis on international studies is an important advance. We recognize that this complicates some of the ways that we have to think about assessment, but recruiting individuals from a much wider set of communities across the world gives us a much better understanding of what the possibilities are for the treatments we're looking to develop.

Last, I think a key area for impact moving forward is the integration of social and biological scientists in the work that's being done. Our field will be incredibly enhanced by the opportunity to better understand environmental influences–both in the ways in which we can take advantage of environments, and in understanding where environments may lead to greater risk.

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Dr. Opler: My last question for you today involves a little fortune telling: Tell us what you think 2019 will look like.

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Dr. Hunter: The first prediction I'm excited about is that we have a number of very interesting new medications in the pipeline–medications that are being developed directly in response to our growing understanding of genetic profiles, allowing for more targeted approaches.

One of the things that we're seeing as a big issue–and a big topic of conversation– is the use of gene interventions. But I have to say that I think that what might be even more important is, based on what we're learning both from big data studies as well as ongoing molecular studies, that we have these new compounds, new medicines, that could very well work in particular subsets of individuals. We have a better way of assessing and understanding that. And I think 2019 will be an incredibly important year in promoting and pushing that forward. That's going to be key for being able to address some neurodevelopmental disorders–both rare ones and those that are more common.

Interviewee

Scott J. Hunter, PhD is a Professor of Psychiatry and Behavioral Neuroscience, as well as Pediatrics, at the University of Chicago. He is also the University's Director of Neuropsychology and Coordinator of its Child Psychology Training Program. Dr. Hunter is an expert in the neuropsychological and psychosocial aspects of many childhood-onset conditions, including learning disabilities, epilepsy, childhood cancers, hydrocephalus, neurofibromatosis and autism, and on the impact environmental and socioeconomic factors have on neuropsychological development.

Interviewer

Mark Opler, PhD, MPH, serves as Chief Research Officer, directing scientific research and development at WCG's MedAvante-ProPhase. Dr. Opler was the founder of ProPhase and served as its CEO and Chief Scientific Officer among other positions. He holds the titles of Adjunct Assistant Professor of Psychiatry at New York University and Assistant Professor of Clinical Neuroscience at Columbia University's College of Physicians and Surgeons.