Journal & Proceedings of the Royal Society of New South Wales, vol. 157, part 1, 2024, pp. 35–37. ISSN 0035-9173/24/01035-03

Keynote presentation

Lessons from developmental and cognitive neuroscience

Joshua Gordon

Director, National Institute of Mental Health, USA[1]

joshua.gordon@nih.gov.au

I'm Joshua Gordon, director of the National Institute of Mental Health, which is one of the 27 institutes and centres that make up the US National Institutes of Health, the largest biomedical research agency in the world. Our mission is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. In order to achieve that mission, we support thousands of grants, contracts, and other research-funding opportunities throughout the United States and indeed around the globe. This research over the past 75 years since the NIMH was founded has played a pivotal role in our understanding of the brain, in developing groundbreaking treatments and therapies, and improving the quality and availability of mental-health care. NIMH-supported researchers have made tremendous progress in neuroscience, in translational medicine, and in improving healthcare systems, including in approaches to personalised medicine which I want to focus on today.

In order to improve mental-health care we need novel therapies and we need to understand how best to use the therapies that we already have. NIMH research is building on findings from basic and applied science to develop and improve interventions for people with mental illnesses, based on the premise that knowing more about our patients can help us treat them better. One major initiative is in rapidly acting treatments for treatment-resistant depression, or RAPID, an NIMH-funded research project that supports the development of speedier therapies for severe treatment-resistant depression. RAPID aims to translate evidence into practical treatments by evaluating interventions with proof-of-concept trials, and then following on that with randomised clinical studies. Study findings so far have suggested that standard and high doses of ketamine can rapidly produce antidepressant effects, but lower doses are ineffective.

With this evidence in 2019 the FDA approved a relative of ketamine, S ketamine in the form of a nasal-spray medication, as an intervention for treatment-resistant depression. Today NIMH-funded researchers are testing the safety, efficacy, and feasibility of therapies, including ketamine and S ketamine, but also other modalities such as transcranial magnetic stimulation, to rapidly reduce suicidal thoughts and behaviours in youth and adult adults.

We continue to lead the research field in establishing effective neuromodulatory treatments for effective disorders via evidence-based clinical exploration. Specifically, we've conducted research to

1 This is an edited transcript of the address [Ed.]

understand how best to use image-guided transcranial magnetic stimulation to provide more precision to our stimulation, which can allow for personalised stimulation in the future. Deep-brain stimulation, another modality of treatment, also shows promise for treatment-resistant depression, and NIMH-funded research is examining how to use deep brain stimulation on a very personal basis by first recording the activity of individuals with anxiety and mood disorders and then stimulating to reduce abnormal patterns of activity that have been identified in those particular individuals.

Moving beyond depression and into other areas, NIMH has launched a broader precision psychiatry initiative that really aims to understand how best to apply the medications that we have now to the individuals who will best respond to them. As you know, treatment in psychiatry can be a hit-or-miss effort, where the first treatment for someone may not work: they may need two or three or four clinical trials with medication or other therapies before they respond. This process for someone with depression or bipolar disorder or psychosis can last weeks or months, leaving individuals with the burden of their illnesses for extended periods of time. NIMH precision psychiatry initiative — especially the biomarker development piece of this — aims to reduce those waiting times and to improve care for individuals.

In the biomarker space, NIMH is applying an innovation funnel approach to support stage-gated milestone-based projects to develop highly sensitive and specific biomarkers that can help physicians and their patients understand how best to intervene, what treatments that are available are most likely to benefit each individual patient. This approach starts with a number of ideas, asks for pilot projects to prove their potential, and then a few of those ideas will move on to the second stage where they will be engaged in a prospective laboratory-based clinical trial, with the eventual aim to support large phase-three type clinical trials of biomarkers in community settings to show that they can improve outcomes in individuals when applied to their cases.

Another project that we have is the Individually Measured Phenotypes to Advance Computational Translation in Mental Health, or IMPACT MH initiative. This initiative seeks to gather a large database of information on individuals with mental illness, including their clinical records but also other information that may help us understand the course of their illness — this could include behavioural and physiological methods, digital data etc., and then to apply machine learning and other techniques to understand how these data relate to those diagnoses and whether those data can improve our ability to make predictions about individual patients. These studies — the ones aimed at biomarker development and the one aimed at the larger constellation of manifestations of mental illness — are meant to improve our ability to treat patients and to improve outcomes by targeting therapies to their needs.

Of course, the best therapies and approaches won't work if services aren't available for people and if those services don't use the evidence-based approaches that we've been developing. Therefore, NIMH supports research to evaluate the effectiveness of interventions, improve the quality and outcomes of care-enhanced service delivery, and communicate and implement evidence-based treatments

across a variety of care settings. In this vein we are funding several projects to test strategies that increase the reach, efficacy, and quality, for example, of digital mental health interventions.

A large project that seeks to use evidence-based approaches to improve care in the here and now is the Early Psychosis Intervention Network, or EPINET. This research initiative is aimed at enhancing effective, coordinated specialty care delivery to people with symptoms of early psychosis. We funded eight regional scientific hubs that aim to study the fidelity, quality, and treatment effectiveness of coordinated specialty care in real-world clinics distributed throughout the United States. These hubs will collect data on diagnosis, interventions, and outcomes in thousands of individuals with early psychosis, and contribute that data to a national data coordinating centre that will then feed the data back to those very same clinics so they can understand what is working for whom, and where they need to make efforts to improve their care delivery. This project involves more than 100 community clinics in 17 states throughout the United States and really hopes to set a standard for how we can use data to provide continuous quality improvement for individuals with serious mental illness. I should mention of course that coordinated specialty care is a model of care delivery that's based upon work that's been done here in Australia for early intervention in psychosis.

Another effort is our collection of Advanced Laboratories for Accelerating the Reach and Impact of Treatments for Youth and Adults with Mental Illness, or ALACRITY. The ALACRITY centre's program supports the advancement of clinical research and practice by accelerating the translation of research findings, and serving as incubators for innovative research ideas and new transdisciplinary collaborations. For example, one of our centres explores the intersection of behavioural economics and implementation science in the pursuit of improving mental health service delivery. Others, for example, look at improving early detection of mental illness with digital measures in order to prevent adverse outcomes, particularly for youth and (particularly in the United States) for racial and ethnic minority youth. We have similar centres that are focused on suicide prevention. These practice-based suicide prevention centres are modelled after the ALACRITY centre program. They incorporate features intended to speed the translation of research into practice. This program is focused on developing testing and refining effective and scalable interventions at key intercepts in the chain of care, to reduce suicide deaths in the United States, a problem that has been increasing over the last 20 years.

Hopefully you see from what I've talked about that NIMH research is doing a lot to try to help to develop novel therapies and to ensure that those evidence-based therapies are applied in real-world settings. We feel that NIMH research is more important now than ever before. Innovative research is needed to generate new knowledge methods and technologies that can be applied to achieve near-term improvement in mental-health outcomes across diverse illnesses, disorders, age groups, backgrounds, and settings. Despite our scientific accomplishments, there is much more work that we need to do and so it's been my pleasure to introduce NIMH to you today and I hope that you have a wonderful meeting.