Dozen young Yale scientists honored for promising mental health research

Yale UniversityYale University

Twelve Yale investigators were among 202 researchers to receive Young Investigator Grants from the Brain & Behavior Research Foundation (formerly NARSAD). The $11.9 million program helps support researchers with promising ideas about how to understand and treat mental illness.

Receiving up to $60,000 over two years, the investigators pursue brain and behavior research related to depression, bipolar disorder, schizophrenia, autism, attention-deficit hyperactivity disorder, and anxiety disorders like obsessive-compulsive and post-traumatic stress disorders.

“The NARSAD Young Investigator Grants have led to groundbreaking and important new research that has improved the lives of people living with mental illness through enhanced treatments and therapies and a better understanding of the causes of mental illness,” said Benita Shobe, president and CEO of the Brain & Behavior Research Foundation.

NARSAD Young Investigator Grants have proven to be catalysts for additional funding once the Young Investigators have “proof of concept” for their hypotheses.

The Yale Young Investigators and the focus of their research follow:

Dr. Chadi Abdallah, Department of Psychiatry
Abdallah will use a brain imaging method called magnetic resonance spectroscopy on a small group of patients with severe treatment-resistant depression to examine the effect of ketamine. Ketamine is an anesthetic medication that provides rapid antidepressant effects on glutamate. This work may facilitate the development of medications similar to ketamine, but with reduced adverse side effects.

Alan Anticevic, Department of Psychiatry
To gain a multi-level mechanistic understanding of the cellular mechanisms involved in cognitive dysfunction of working memory in schizophrenia, Anticevic will combine brain scanning with a mathematical model of working memory, and will align its predictions with cognitive tests, an approach that may provide a more focused framework for developing treatments for cognitive dysfunction.

Irina Esterlis, Department of Psychiatry
Esterlis will give MRI brain scans to bipolar disorder patients and healthy controls to determine differences in magnitude and distribution of metabotropic glutamate receptors 5 (mGluR5) — a site in the brain where glutamate binds — and how these differences relate to mood and cognitive symptoms.

Dr. Michael J. Higley, Department of Neurobiology
Using optogenetics, Higley will measure the actions of interneurons on their synaptic targets to find out how synaptic inhibition is modulated by dopamine and how its dysregulation may be an important factor in schizophrenia. He will also examine dopamine and inhibition in synaptic plasticity — a disruption of which likely represents a key pathology associated with schizophrenia.

Ulf Knoblich, Department of Neurobiology
Converging evidence suggests that inhibitory interneurons underlie the ability to function under continuously varying conditions. Knoblich seeks to understand the specific roles of interneurons in fast and slow perceptual processes, and thus provide a direct link between the physiological and cognitive symptoms of schizophrenia.

Dr. Nandakumar Narayanan, Department of Neurology
The prefrontal cortex receives dopamine signals mainly from the ventral tegmental area. By recording, disrupting and stimulating neurons in the ventral tegmental area and in the prefrontal cortex, Narayanan will explore how dopamine affects prefrontal networks in great detail with several cutting-edge techniques. This could lead to new approaches to treating schizophrenia.

Dr. R. Andrew Sewell, Department of Psychiatry
In all types of animals tested so far, activating cannabinoid receptors enhances fear extinction, but this has never before been attempted in humans. Sewell aims to increase our understanding of the neurobiology of fear and anxiety by testing whether enhancing cannabinoid function can enhance extinction learning in healthy human subjects, providing a first step towards development of new treatments for PTSD.

Akio Sumioka, Department of Cellular and Molecular Physiology
Sumioka has established a new type of genome-wide screening for regulatory genes of the NMDA-type glutamate receptor (NMDAR) activity, and has identified several genes as NMDAR modulators. This research will examine roles of these genes and identify auxiliary subunits of the NMDAR protein, providing a fundamental understanding of NMDAR regulation which may contribute to the development of new therapeutic approaches for schizophrenia.

Dr. Toral S. Surti, Department of Psychiatry
Surti seeks to develop a cognitive training exercise for improving visual processing in schizophrenia. She chose a model visual processing task called visual backward masking, success at which demands better social and cognitive abilities and greater functioning. Surti will compare how healthy people and those with schizophrenia learn to improve on this task, and she will examine whether, at the end of the training, people with schizophrenia are better able to learn visual information and identify facial expressions.

Sarah I. Tarbox, Department of Psychiatry
In an effort to develop more effective means of identifying risk for psychosis early in life and develop interventions, Tarbox will study high-risk individuals and normal-

risk siblings. Her goals are to determine whether social functioning deficits across development as well as the association between social functioning deficits and psychosis risk symptoms are more strongly influenced by within-family effects compared to unique environmental effects.

Fei Wang, Department of Psychiatry
Wang will compare the white matter integrity and functional connectivity of medication-naïve adolescents and young adults experiencing their first episode of Bipolar Disorder versus those experiencing their first episode of schizophrenia. This will provide unique opportunities for understanding the development of both illnesses, their neuropathophysiological differences and potentially the identification of markers that differentiate them. This information will be key in the development of early identification, treatment and prevention strategies.

Yang Yang, Department of Neurobiology
The proposed research will help reveal how dopamine D1 receptors influence prefrontal cortex (PFC) neurons through actions at ion channels that reduce PFC cell firing. Dr. Yang's thesis is that ion channels contribute to D1 gating actions, and that these ion channels may provide a novel therapeutic target for cognitive disorders.

NARSAD Grants support research across disciplines in four main categories:

- basic research — to understand what happens in the brain to cause mental illness
- new technologies —to advance or create new ways of studying and understanding the brain
- diagnostic tools / early intervention — to recognize early signs of mental illness and treat it as early as possible
- next generation therapies — to reduce symptoms and retrain the brain

For more information, visit the **foundation's website** [1].

Links:
[1] http://bbrfoundation.org/press-releases/brain-behavior-research-foundation-invests-in-narsad-grants-for-a-new