

Seeking to end the 'drug-discovery recession' for mental illness

November 4 2014, by Meredith Cohn, The Baltimore Sun

There is little doctors can do for those suffering serious brain injuries from car crashes, athletics and battle, other than wait and treat the symptoms, but a unique collaboration between those who study mental illness and those who treat the disorders offers hope for new therapies.

The first goal of the new Towson, Md-based institute formed by researchers at the Lieber Institute for Brain Development and doctors at Sheppard Pratt Health System is to reformulate an old Parkinson's drug to soothe aggression and aid memory in people suffering from such brain injuries.

Officials expect the new institute to eventually translate discoveries of their own and others in genetics and brain functioning into better treatments for those suffering not just head injuries but schizophrenia, bipolar disorder, autism and other <u>mental illnesses</u> affecting millions of Americans.

"Care has gotten better over the years, and patients are better but not well by a long shot," said Dr. Steven S. Sharfstein, president and CEO of Sheppard Pratt, a century-old mental health system based in Towson that treated more than 60,000 patients in the region last year. "We need breakthroughs."

Sharfstein reached out to the Lieber Institute about two years ago to discuss a collaboration that culminated with each committing \$1 million to launch the nonprofit Sheppard Pratt-Lieber Research Institute Inc.,



which will launch in January on Sheppard Pratt's campus.

Officials hope the new venture will accelerate the pace of advancements in mental health, where researchers struggle even to explain the underpinnings of disorders. The pace of discoveries and new therapies in mental illness lags far behind advances for cancer and other diseases in recent decades. They also aim to develop "personalized medicine," treating patients based on their own genetic makeup.

While researchers around the world have begun linking gene mutations and specific pathways in the brain to mental illness in the last 10 years, what makes the new institute unique is the partnership with a treatment facility, which can provide the electronic records, including DNA and brain images, of thousands of patients, as well as people to participate in studies and benefit more immediately from new and re-purposed medications.

"It's a unique effort to walk the walk everyone talks about, translating science into treatment," said Dr. Daniel R. Weinberger, director and CEO of Lieber, a private center formed four years ago with donations from two philanthropic families and housed in the Johns Hopkins Science and Technology Park in East Baltimore.

Making discoveries and turning them into new treatments has been difficult because the brain is the body's most complex organ, said Dr. Ken Duckworth, medical director for the advocacy group National Alliance on Mental Illness.

There aren't one or two, but possibly hundreds or thousands of genes linked to mental illnesses, making for many targets for therapy, he said. That offers lots of opportunities, but also lots of chances to fail.

Duckworth welcomed the new partnership between Sheppard Pratt and



Lieber because it means "smart people" are working on both understanding the neuroscience and trying to do something with it.

"We've been in a drug-discovery recession for the better part of a decade," Duckworth said. "Patients and families welcome any effort to translate the science into better treatments. There is a crying need for more treatment."

The National Institutes for Mental Health, which funds much of the nation's research into mental illness, has taken steps to promote sharing of data to advance research.

And in recent years, scientists have discovered many genes and brain processes linked to schizophrenia, autism and other mental illnesses. There are now government-sponsored databases that researchers can tap for their own work.

There is also a Psychiatric Genomics Consortium, maintained at the University of North Carolina School of Medicine, created in 2007 by researchers in the field who wanted to encourage more collaboration. It's now the largest confederation dedicated to psychiatric study, with more than 500 investigators and more than 80 institutions in 25 countries.

Dr. Thomas Insel, director of the National Institutes of Mental Health, credited the consortium with the recent identification of the location of 108 genes linked to schizophrenia.

He wrote in a September blog post that "combining data from multiple projects allows scientists to find significant associations that cannot be detected by any individual lab."

Still, researchers know that turning their findings into new blockbuster drugs could be slow and painstaking.



In Baltimore, officials from Lieber and Sheppard Pratt said they expect their Parkinson's drug could take years to prove effective and become standard care for serious brain injuries. Over time, they plan to look for more ways large and small to improve treatments of those suffering mental illness.

Another early project will focus on adults with autism spectrum disorder. Researchers want to discover the genetic components of the disorder to develop innovative treatments for Sheppard Pratt's patients, but also for more recently diagnosed children.

Those on the autism spectrum have many different outcomes later in life, some people becoming more productive than others; yet there is little research after age 10, Sharfstein and Weinberger said. Their findings could help doctors better structure rehabilitation programs and help families understand what to expect.

The findings could also mean less waste of time and money on treatments that won't help, Weinberger said. Lieber has developed an algorithm that can help predict who will respond well to certain drugs and plans to expand on such work, he said.

The new institute also will help develop drugs for mental illness, or new uses for old drugs, a process that historically has happened mostly by accident. The common psychiatric medication lithium, for example, was initially studied for use on high blood pressure. Researchers discovered patients with bi-polar disorder were benefiting.

"We fell into treatment," Sharfstein said. "We'd like less serendipity and more tailored treatments."

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Citation: Seeking to end the 'drug-discovery recession' for mental illness (2014, November 4) retrieved 11 May 2024 from https://medicalxpress.com/news/2014-11-drug-discovery-recession-mental-illness.html

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