SPEAKER NOTES

Genetic Research on Autism

Summarized by Thomas T. Thomas

Our members and support group participants are hearing more and more people using the word "autism" in the context of mental illness. The speaker at our October 28 informational meeting was **Susan Kuo, PhD,** instructor in psychiatry at the Center for Genomic Medicine, Massachusetts General Hospital and the Stanley Center for Psychiatric Research, and at the Broad Institute of MIT and Harvard.

Kuo said she works on the differences in genetic effects and the experiences of individuals. Autism is influenced by genetic factors—both those that are inherited from the parents and those that occur "de novo," or new changes in the person's DNA—as well as by environmental factors. Examples of environmental factors are the mother's illness during pregnancy or not getting enough folic acid or valproic acid during pregnancy.

Genetic influences are diverse. For example, everyone carries some de novo changes, and they can occur anywhere in the genome. It's estimated that 20% to 30% of individuals with autism traits have de novo genetic changes.

The likelihood of a person getting an autism diagnosis is 1% to 3% in the general population. However, that likelihood is about 28 times greater if an older biological sibling has autism, and it's about twice as great if a biological cousin has the diagnosis. So inheritance plays a part.

Common inherited variations appear in about 1% of the population, and an example would be a change in a single nucleotide (the A's, T's, C's, and G's) of the DNA code. Complex traits often involve several common variations working together. Rare variants are often de novo, not inherited, and appear in less than 1% of the population. These rare variants often have large effects. A diagnosis of autism or a mental illness like schizophrenia is influenced by both common and rare variants. And some can be diagnosed by clinical genetic testing.

One type of rare variant is the neurodevelopmental disability associated variants (NDAV). Many of these are diagnosable through clinical genetic testing, usually after the individual fails to attain developmental milestones such as smiling, communication abilities, or potential for self-care. These milestones vary according to the age at which autism is diagnosed. Generally, the earlier the diagnosis is made, the more variability of effects the individual will display going forward. We now have greater awareness of autism, and the condition is being diagnosed later in life.

With these variants there is increased likelihood of other, co-occurring psychiatric diagnoses, such as attention-deficit/hyperactivity disorder (ADHD), impulse control and conduct disorders, anxiety, depression, sleep disorders, obsessive-compulsive disorder (OCD), and to a lesser extent schizophrenia and bipolar disorder. Autistic children might also experience mental health disorders without cognitive impairment. This could be attributable to having higher than average common variant burdens with psychiatric disorders. And the likelihood is higher with cognitive impairments. Autism and psychiatric conditions can overlap due to genetic

differences. Common variants with small effects can overlap with other variants affecting areas such as cognition and psychosis.

"The autistic experience can be extremely diverse," Kuo said. Support for autistic individuals starts with listening, she said. "Ask what they are experiencing."

Kuo concluded by saying that current genetic research into autistic conditions is focused on rare brain developments which can be life threatening, such as seizures.

Q. How common is genetic testing for autism?

A. Clinical genetic testing is not used to diagnose autistic traits in an individual, but it can be used to identify if a person is carrying a disruptive rare variant. That can lead to more support and monitoring. But we're not at the stage of genetic testing for other psychiatric conditions.

Q. Is the term "schizoaffective" used when the condition is not specified.

A. Schizoaffective disorder straddles the line between schizophrenia and bipolar disorder. Rates of diagnosing schizoaffective disorder would be higher because its symptoms are seen in both psychiatric conditions. Variability within diagnoses and across diagnoses can be challenging.