Genetics, Imaging Will Change Drug Treatments

BY MARIA LEVENTIS
Contributing Writer

Medications tailored to individuals based on genetics will probably play a key role in future psychiatric care, predicts Jonathan Brodie, M.D.

"There will be no one-drug-fits-all treatments," Dr. Brodie, professor of psychiatry at New York University Medical Center, told this newspaper in an interview. He expects genetic subtyping will offer insights into illness prevention as well as better treatments of identified psychiatric disorders when used with biomarkers to predict treatment response and resistance.

Dr. Brodie also thinks treatment breakthroughs are on the horizon for schizophrenia, bipolar disorder, neurodegenerative illnesses such as Alzheimer's disease, and addictions. "We will move our thinking to a model of mental illness involving understandable, and hopefully, treatable alterations in brain functioning," said Dr. Brodie, who is slated to become interim chairman of the university's psychiatry department this summer.

Advances in imaging will make it possible to determine when drugs are, or aren't, working.

DR. BRODIE

For the last 25 years, Dr. Brodie has investigated the use of PET technology in psychiatry and neuroscience. He thinks advancements in PET and functional MRI will make it possible not only to see how drugs work but also to be able to determine when they are working—or aren't. Using functional imaging, physicians are able to "photograph" the brain in action with neurochemical as well as physiological and behavioral filters.

In the case of new medications, Dr. Brodie said there will be increased emphasis on treatments that target the presynaptic modulation of the physiological reserve rather than simply targeting widespread receptor types. He believes drugs will be classified based on their downstream pharmacologic activity, as opposed to where they initially bind, as in the present system.

This is important, because typically, psychotropic drugs occupy their initial target receptors in a matter of minutes to hours. Yet for many drugs, the behavioral effects take from hours to days and sometimes weeks to manifest themselves. Most of these drugs would have as a final common path the return of neurochemical plasticity and behavioral elasticity. "So the superficially attractive but naive notion that newer, cleaner drugs with a single binding site should be the pharmacologic holy grail actually supports the argument that all effective psychotropics are likely to be dirty drugs," he said, referring to drugs with more than one site of action.

"Drugs with specific and multiple sites of action either directly or indirectly will prove efficacious in modulating moods, thoughts, and behaviors," he said.

As genetic subtyping grows, so, too, will psychiatry's understanding of which treatments are more effective. Just as oncologists use trastuzumab (Herceptin) to treat certain types of breast cancers, knowing they will respond, but don't use the drug to treat other types, psychiatrists will be able to pick out the most effective antidepressant for a particular patient, he said.

As the mechanisms of addiction become better understood through imaging and subtyping, Dr. Brodie predicted that psychiatry will have a major role in treatment. But in order for advancements to be made in this area, psychosocial treatments must become more frequent and more intense.

Right now, Dr. Brodie and his research team are looking into a possible breakthrough for cocaine and methamphetamine addiction through the use of gamma-vinyl gamma-aminobutyric acid (GVG or vigabatrin), a drug used to treat pediatric epilepsy in Europe and most of the world except for the United States. Clinical trials for the treatment of addiction with GVG—known as Sabril in Europe—are now underway in this country.

"I expect with future medications for addictions, there will be the elimination of craving and reward," he said. "As a result, the psychosocial treatments will be more fruitful, providing a psychosocial milieu for achievement and progress—rather than punishment and maintenance." ■