

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



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

DR. BRODIE

chairman of the university's psychiatry department this summer.

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.

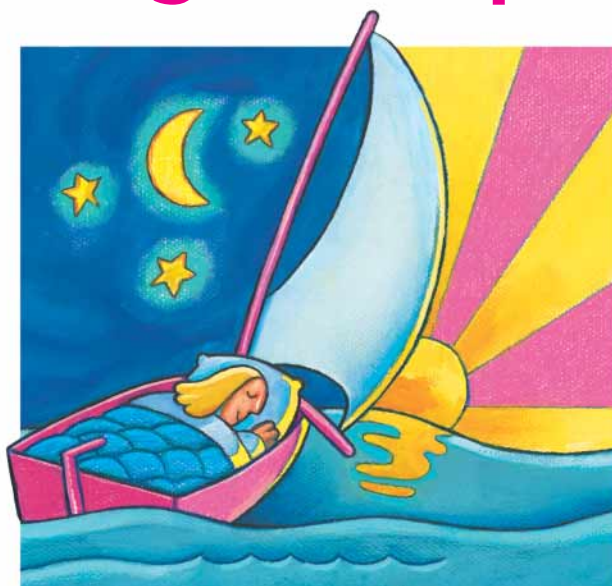
Right now, Dr. Brodie and his research team are looking into a possible breakthrough for cocaine and methamphetamine addiction through the use of gamma-vinyl gamma-aminobutyric acid (GVG or vigabatrin), a drug used to treat pedi-

atric 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." ■

In managing insomnia

A good
night's sleep...



...on course
toward better days



Patients wake up refreshed the next day so they're ready to perform

- 2.5-hour half-life¹
 - Long enough to provide restful nights
 - Short enough to provide refreshed awakenings
- Minimal drug effect on next-day functioning^{2*}
- Low abuse potential at recommended doses^{3,4}
- The #1 prescribed sleep agent in the US⁵



¹Zolpidem tartrate worldwide.

*Next-day residual effects were evaluated in 7 studies involving normal volunteers. In 3 studies in adults (including 1 study in a phase-advance model of transient insomnia) and 1 study in elderly subjects, a small but statistically significant decrease in performance was observed in the Digit Symbol Substitution Test (DSST) when compared with placebo. Studies in nonelderly patients with insomnia did not detect evidence of next-day residual effects using the DSST, the Multiple Sleep Latency Test (MSLT), and patient ratings of alertness.¹

AMBIEN is indicated for the short-term treatment of insomnia. In elderly or debilitated patients, or patients with hepatic dysfunction, treatment should be initiated with a 5-mg dose and patients closely monitored. Due to its rapid onset of action, patients should take AMBIEN right before going to bed and when ready for sleep. Patients should not take AMBIEN unless they are prepared to get a full night's sleep (7 to 8 hours) to avoid residual effects. Until they know how it will affect their physical or mental performance upon awakening, patients should not drive or operate hazardous machinery after taking AMBIEN or any other sleep medication. During short-term treatment with AMBIEN, the most commonly observed adverse effects in controlled clinical trials were drowsiness (2%), dizziness (1%), and diarrhea (1%). Because individuals with a history of addiction or substance abuse are at increased risk of habituation and dependence, they should be under careful surveillance when receiving AMBIEN or any other hypnotic. AMBIEN is classified as a Schedule IV controlled substance. Sedative hypnotics have produced withdrawal signs and symptoms following abrupt discontinuation. Hypnotics should generally be limited to 7 to 10 days of use, and reevaluation of the patient is recommended if they are taken for more than 2 to 3 weeks. Prescriptions for AMBIEN should not exceed a 1-month supply.

Please see brief summary of prescribing information on back.

sanofi aventis

Sanofi-Synthelabo Inc., a member of the sanofi-aventis Group

©2005 Sanofi-Synthelabo Inc.
57-050005

Visit our Web site at www.ambien.com

AMBIEN[®]
(ZOLPIDEM TARTRATE)[®]
5-MG & 10-MG TABLETS

Restful nights, refreshed awakenings