

illness and an external locus of control, or a belief that events in their lives are controlled by external forces. “The greatest potential to further increase patient benefit in the future will be realized by keeping dropouts in treatment,” the researchers concluded. “There is reason for hope: eating disorders do actually respond to treatment, outcome benefits can be measured, as demonstrated in our study.”

## Psychotic and Mood Disorders – Pathophysiology and Imaging

Psychotic and mood disorders are often diagnostically complicated. They affect various regions of the brain, and diagnostic criteria can be inconsistent. Additionally, these disorders are often progressive in nature, so signs and symptoms may change over time. Stephen M. Lawrie, MD, University of Edinburgh, Edinburgh, Scotland, discussed the challenges and possible diagnostic strategies that are specifically related to schizophrenia and psychosis.

Psychotic symptoms are unreliably elicited and are diagnostically nonspecific. Therefore, the use of DSM-IV schizophrenia criteria alone is not always the most viable method of diagnosis. According to Dr. Lawrie, the “gold standard” of schizophrenia diagnosis needs to be augmented with more reliable clinical data. He suggests a variety of diagnostic aids to ensure consistency throughout the clinical community.

Creating a reliable clinical profile of psychosis should begin in the clinical trial environment. Studies should be designed and analyzed with the real world in mind. The study population should include cohorts that will appropriately translate into clinical practice. The trial setting also should be considered when reporting clinically relevant statistics, such as sensitivity and specificity, positive and negative predictive value, and effect size.

Developmental abnormalities may also assist clinicians in identifying patients with schizophrenia. Early social, sensory-motor, and intellectual deficits and anomalies may predict schizophrenia and merit further evaluation as diagnostic tools. However, it is important to note that they may simply be trait effects and that predictability may be age-dependent [Tarbox et al. *Psychol Bull* 2008; Lawrie SM et al. *B J Psych* 2001; Pukrop R et al. *Neurotox Res* 2010].

Using imaging as a diagnostic aid may be the most reliable tool to date. Structural imaging, functional imaging, and the identification of imaging biomarkers show promise

as diagnostic tools. Advances are being made in this area of technology, making early detection of psychosis more attainable. However, Dr. Lawrie cautions that technology with higher sensitivity tends to be more expensive and technically demanding. Furthermore, as more biomarkers and disease-predicting genotypes become available, false negative results may also be introduced and tend to compound the diagnostic burden.

Stephen M. Strakowski, MD, University of Cincinnati, Cincinnati, OH, detailed various imaging approaches in bipolar disorder (BPD). Amygdala and striatal enlargement has been associated with BPD in several imaging studies. However, there is some inconsistency across studies with regard to the amygdala findings [Strakowski SM et al. *Mol Psychiatry* 2005; Noga et al. 2001; Altschuler L et al. *Arch Gen Psychiatry* 1998; DelBello et al. *Bipolar Disorders* 2004].

BPD is a progressive disorder, and structural changes within the anterior limbic network (ALN) of the brain have been suggested in relation to disease progression. In fact, frequent episodes may alter brain structure. However, there also appears to be a developmental component to these structural modifications [Strakowski SM et al. *Mol Psychiatry* 2005]. Some observed structural changes include decreased cerebellar vermis volume, occurring in patients who have experienced multiepisodes; age-related fluctuations in amygdala volume; and increased ventricular volume, correlating with the number of episodes [Delbello et al. 1999; Chen et al. 2004; Strakowski et al 2002; Brambilla et al. 2001; Strakowski SM et al. *Mol Psychiatry* 2005].

Aggressive psychopharmacological treatment may help prevent disease progression. The use of proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) has elucidated some metabolic processes that are associated with drug treatment and suggests contributing factors in BPD, such as abnormalities in mitochondrial metabolism, membrane metabolism, and second messenger systems [Stork & Renshaw. *Mol Psychiatry* 2003]. Glutamatergic excitotoxicity may also contribute to observed progressive brain changes.

According to <sup>1</sup>H-MRS studies, there is considerable neurochemical variability that is associated with different drug therapies. For example, while lithium decreases glutamate, glutamine, and gamma-aminobutyric acid (Glx) concentration, valproate does not [Friedman SD et al. *Biol Psychiatry* 2004]. Lithium also increases N-acetyl-aspartate (NAA) in the brain [Moore GJ et al. *Biol Psychiatry* 2000]. These factors suggest that lithium may be neuroprotective. In an <sup>1</sup>H-MRS study by Delbello

and colleagues that investigated the effects of olanzapine on neurochemistry in manic adolescents, NAA levels increased in treatment remitters ( $p=0.05$ ) and decreased in nonremitters ( $p=0.03$ ). Additionally, investigators suggested that olanzapine-induced increases in choline may lead to abnormalities in cell membrane metabolism or second messenger pathways that are thought to play a role in BPD pathology [Delbello MP et al. *Neuropsychopharmacol* 2005].

Functional magnetic resonance imaging (fMRI) may also reveal how treatment impacts brain function. Overactivation of the ALN has been implicated in disease progression, according to fMRI studies, specifically related to increased amygdala activation and decreased prefrontal modulation [Eliassen et al. *Biol Psychiatry* 2006; Olson et al. *Biol Psychiatry* 2006].

Advances in technology and psychopharmacology have increased our understanding of the pathophysiology of psychotic and mood disorders, such as schizophrenia and BPD. While definitive diagnoses are not always feasible, we are now able to identify potential biomarkers and may be able to use imaging to predict treatment success and disease risk. Metabolic abnormalities and structural changes within the brain have also provided insight into disease pathology. Established protocols are still being developed concerning optimal treatment strategies for psychosis and mood disorders, but clinical practice is beginning to move toward an imaging-based approach to diagnosis and treatment.

## New Research Looks at Internet Dependency and the Impact of Violent Video Games

Internet and computer game dependency is not just a symptom of other psychiatric conditions, but should be a diagnostic entity in itself, according to new research presented at the American Psychiatric Association's Annual Meeting. Computer games played on the Internet seem to contain an addictive potential comparable to substance abuse disorders, the authors said.

The research poster, *Diagnostic Aspects of Pathological Internet use: A Prospective Study on Psychiatric Phenomenology and Comorbidity of Internet Dependency* (NR7-02), was presented by Bert T. te Wildt, MD, Hanover Medical School, Hanover, Germany and suggests that this new diagnostic entity might best be labeled as Internet dependency or a more encompassing, media dependency.

Patients seeking psychiatric assistance and fulfilling the criteria for pathological Internet use were compared to a group of healthy controls. The average time spent in Cyberspace was 6 ½ hours per day, mostly in multiplayer online role-playing games and online first-person shooter games. Similar to other studies, they found mostly depressive, anxiety, and personality disorders exist alongside Internet dependency. The study however, cannot explain whether a depression or anxiety disorder is a cause or effect of the pathological Internet use.

According to most previous studies, the average patient presenting with pathological Internet use is a young male who has withdrawn himself from real life and escapes into a virtual parallel world, mostly to alleviate his lack of self-esteem and self-confidence by playing the hero he could not be in real life. The addictive potential of Internet and online games may be especially relevant for children and adolescents, who ever more often seem to develop a dependency on the Internet and computer games without a distinct comorbid pathology the researchers argue.

Researchers concluded, "against the background of an ever increasing number of young and adult Internet dependent individuals ... it has become undisputable that Internet dependency has to be taken seriously from a medical point of view."

In the meantime, however, the researchers suggest that psychiatrists "must not forget to examine the patients for comorbid psychopathology, in order to provide a comprehensive treatment regimen. Yet, to sufficiently understand and treat those patients, psychiatrists also have to be empathically interested in the parallel virtual lives of their patients." Some patients, the researchers note, may need an antidepressant to treat depression or anxiety, and psychotherapeutic approaches to address the media dependency to help them re-establish real life as an attractive and fulfilling existence.

Players of violent video games have significantly higher feelings of aggression and differences in brain activity during both cognitive motor activity and resting periods, according to research results to be presented by at the American Psychiatric Association's Annual Meeting in New Orleans.

There has been increased interest in the influence of violent video games on the behavior of players, and recent research shows an increase in aggression due to the intensive use of first-person shooter games (FPSG) but little is known about the influence of the games on the brain activity.

Researchers led by Gregor R. Szycik, PhD, Hannover Medical School, Hannover, Germany, investigated