2007 in Review

The editors are pleased to offer a brief personal selection of some of the articles that they found particularly interesting and important in this year's *Journal*.

Clinical Treatment Trials in Schizophrenia

Until only recently treatment trials in schizophrenia were directed wholly toward symptoms of psychosis. Previously, the domains of symptomatology in schizophrenia were not well distinguished and certainly were not developed as treatment targets. Schizophrenia was conceptualized as an illness which required a single antipsychotic medication. Psychosocial outcome was almost ignored. Fortunately, this situation has changed with reasonable speed and has produced illness constructs with greater face validity. Symptomatic domains of dysfunction (e.g., psychosis, cognitive dysfunction, and negative symptoms) are understood as pathophysiologically distinct and deserving of independent inquiry. Not only are these concepts being discussed, written about, and used as the basis for disease formulations, but they have already become the basis for clinical treatment trials. Such a treatment trial, albeit with negative findings, was conducted by Sergi et al. (1). The clinical target of this treatment trial was social cognition, i.e., the ability to construct mental representations of others and oneself and the relations between others and oneself. It is a treatment target which is distinct even from basic cognition. Because deficits in social cognition critically interfere with psychosocial recovery, it is an important impairment in schizophrenia. Sergi et al. used social cognition as the treatment target, comparing the actions of three different antipsychotic drugs on its outcome in "Social Cognition and Neurocognition: Effects of Risperidone, Olanzapine, and Haloperidol." Even though none of the treatments improved the outcome measure, the methodology models the design for the segregation of symptom domains in future treatment trials. This "clinical target" treatment approach represents a new strategy for schizophrenia therapeutics.

CAROL A. TAMMINGA, M.D.

Risk Taking as a Reaction to Terrorism

Risk-taking behavior such as dangerous driving, drug and alcohol use, and engaging in unprotected sex is characteristic of adolescents, particularly adolescent boys. There are genetic, developmental, cognitive, and psychosocial determinants of such behavior. In their article, Pat-Horenczyk and colleagues (2) focused on the latter, specifically prior exposure to severe trauma, in "Risk-Taking Behaviors Among Israeli Adolescents Exposed to Recurrent Terrorism: Provoking Danger Under Continuous Threat?" The authors studied Israeli high school students (N=409) who had been exposed to terrorist attacks (40% of whom had been personally present at such attacks or had someone close to them wounded or killed). Serious risk-taking behavior was common among these adolescents (18% drove dangerously and 8% played Russian roulette). Increased exposure to terrorism was associated with increased risk taking, as was the presence of posttraumatic symptoms. Adolescent boys took more risks than adolescent girls. The study leads to several interesting conclusions. For researchers, the study demonstrates that it is possible to conduct important, methodologically sound, socially valuable, and ethical research—the authors obtained 100% participation, trained teachers in trauma management and preventive intervention, provided counselors for students with posttraumatic symptoms, and completed the entire study in a single day. For mental health clinicians, it underscores the important relationship between trauma and risk taking

and the value of screening adolescents exposed to trauma. For the rest of us, especially political leaders, it points out yet another social cost of war, and the burdens that adults place upon children when waging it.

ROBERT MICHELS, M.D.

Developmental Perspectives on Psychopathology

Developmental perspectives on cognition and behavior have emerged as a dominant theme in clinical and basic thinking. Longitudinal studies represent the pillar on which these perspectives rest. Recent work in the *Journal* solidified prior knowledge while extending well-worn longitudinal design into the fields of genetics and imaging. In fact, refined melding of longitudinal, genetic, and imaging methods may offer the best hope for expanding current developmental perspectives beyond the theoretical realm to influence daily practice. In their articles, Colman et al. (3) and Waldinger et al. (4) built upon prior longitudinal observations by demonstrating childhood predictors of emotional psychopathology that are manifested as much as four decades later. Two other articles this year introduced an unusually high level of precision to the measurement of relevant clinical indices by utilizing rigorously maintained prospective cohorts. Gregory et al. (5) charted broad associations among specific mood and anxiety disorders in individuals followed from childhood into their thirties; Storr et al. (6) showed that early childhood behavior influences risk for posttraumatic stress disorder later in life through both direct and indirect means. Finally, two articles this year joined classic longitudinal design with genetics or imaging methodology. Gothelf and colleagues (7) used the 22q11.2 deletion syndrome as a model to illustrate the manner in which genes might shape longitudinal developmental trajectories in thoughts and behavior through transducing effects on the brain. Similarly, Mackie and colleagues (8) focused specifically on cerebellar development and demonstrated how knowledge of brain function might inform predictions for symptom trajectories in attention deficit hyperactivity disorder. Taken together, these six longitudinal studies contribute to the foundation of developmental perspectives while providing glimpses of future advances.

DANIEL S. PINE, M.D.

Medication Access and Continuity Under Medicare Part D

An unprecedented upheaval has recently occurred in prescription drug coverage for disabled mentally ill patients who receive Medicare and Medicaid benefits. In January of 2006, Medicare Part D went into effect for dual-eligible psychiatric patients who were previously covered by state Medicaid. At that time, these patients underwent random auto-assignment to one of many new drug plans and had to initiate switching plans themselves if their needs were not met. This was not necessarily an easy task for individuals with severe mental illness. The West et al. study (9), "Medication Access and Continuity: The Experiences of Dual-Eligible Psychiatric Patients During the First 4 Months of the Medicare Prescription Drug Benefit," anticipated the importance of monitoring such an upheaval. The authors surveyed practicing psychiatrists regarding medication access problems as well as adverse events during the first 4 months of coverage under Medicare Part D. The results were astonishing: 53.4% of dual-eligible patients had at least one medication access problem. Among these patients, 27.3% experienced a significant adverse clinical event and 19.8% visited the emergency room. The authors aptly suggest that further refinements in the system may be needed.

We have our work cut out for us in ensuring that all of our patients maintain continuous access to essential medications, including the larger group of adults over the age of

65 who are not dual-eligible but rely on Medicare Part D for medication coverage. It is critical that we continue to monitor this process and advocate for our patients of all ages.

SUSAN K. SCHULTZ, M.D.

Adverse Life Events and Depression

The *Journal's* pages this year have informed us of the many advances in understanding the role of genetic factors in the liability for various psychiatric disorders and the differences across individuals in the effectiveness (and adverse effects) of pharmacological interventions. However, it has also become clear that the contribution of genetic factors is both quite complex and insufficient to account for the clinical features of most psychiatric disorders. The study by Keller and colleagues (10), "Association of Different Adverse Life Events With Distinct Patterns of Depressive Symptoms," clearly illustrates the latter with regard to depressive symptoms. The authors found that different types of life events are associated with particular patterns of depressive symptoms, both across and within individuals. These findings suggest that even if a given person carries a genetic risk for depression, the clinical manifestations of that liability may be strongly influenced by the specific types of life experiences that precede a depressive episode. The authors conclude that the potentially causal relationship between environmental factors and profiles of depressive symptoms has important implications for the diagnostic criteria for depression, in that some symptoms currently considered core features of depression may be particular to certain types of life events. Their findings also suggest that the development of novel pharmacological treatments for depression may need to consider not only the underlying genetic and molecular neurobiology of the illness, but also the ways in which that neurobiology might be differentially shaped by experiences at different times in life.

DAVID A. LEWIS, M.D.

Patient Detection of Dopamine Receptor Blockade

"Effectiveness of Olanzapine, Quetiapine, and Risperidone in Patients With Chronic Schizophrenia After Discontinuing Perphenazine: A CATIE Study" by Stroup et al. (11) was a favorite because the study had unexpected results with implications for patient treatment. A unique feature of the CATIE study was that like in actual practice, both patients and doctors could decide when to switch medication. The doctors in the study felt that the patients did well on any of the three second-generation antipsychotic medications offered after discontinuation of perphenazine (a first-generation antipsychotic), both in therapeutic response and for side effects. The unexpected result was that patients did not feel the same. Nearly all patients disliked taking risperidone, and most decided to switch to a different medication. In hindsight, these patients probably detected the effects of the dopamine D_2 receptor blockade, which is more prominent with risperidone than with other second-generation antipsychotics, and felt that the side effects were too similar to what they had previously experienced with perphenazine, whose mechanism of action is also the dopamine D_2 receptor blockade. The article shows us that patients are more sensitive to extrapyramidal side effects than physicians sometimes perceive and that patient drug preference is, as always, important in assuring adherence to treatment. Because detection of subtle movement disorders such as akathisia may be a lost art for psychiatrists more familiar with second-generation antipsychotics, Elaine Bratti, Stephen Marder, and John Kane were subsequently asked to write on restlessness during antipsychotic drug treatment for our Treatment in Psychiatry series (12).

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