Editorial: Sharpening the Focus in Mood Disorders: From Disease Models to Individualized Measurement-based Care

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Mood disorders are highly prevalent syndromes associated with high rates of nonrecovery, relapse, and inter-episodic dysfunction. Mounting evidence indicates that mood disorders are a leading cause of disability and premature mortality (1,2). Cost of illness studies indicate that mood disorders impart staggering direct and indirect costs in both developed and developing nations (3). During the past decade, there has been an intensified effort to refine the phenomenology of mood disorders (notably bipolar disorders), elucidate factors which predict outcome and treatment response, unravel the complex pathophysiology of mood disorders, and define valid and measurable clinical endpoints in the therapeutic environment. We are only beginning to understand the genetic and environmental interactions that result in the symptomatic state. Genes “load the gun” and the environmental events “pull the trigger.” In clinical practice, differential diagnosis remains a challenge for many clinicians as bipolar disorder often masquerades as depression often leading to antidepressant usage in the absence of a concomitant mood stabilizer.

A sobering and puzzling paradox regarding mood disorders is that despite the development of multiple pharmacological strategies, as well as manual-based psychosocial treatments (e.g., cognitive behavioral therapy), symptomatic and functional outcomes for individuals with mood disorders remain rather disappointing. Several broad-based (e.g., health systems) and specific factors (e.g., insufficient characterization of the disease pathophysiology) additionally conspire in this process. For example, despite federally and privately funded public health initiatives, as well as widespread educational fora regarding mood disorders at medical professional meetings, most affected individuals remain undetected with an even smaller percentage receiving guideline-concordant care (4,5). With some incredulity, six decades after the modern psychopharmacological revolution began, there remains a pressing need for innovative treatments capable of not only suppressing “surface-based” symptomatology, but also reversing the underlying injurious disease process.

Results from the Sequenced Treatment Alternatives to Relieve Depression Study (STAR-D) indicate that the provision of measurement-based care was an important moderating variable contributing to enhanced outcomes in “real-world” patients treated with citalopram monotherapy (6). Nevertheless, optimal pharmacotherapy, including augmentation/combination/switching strategies and psychosocial interventions, delivered as part of a larger best practices chronic disease management model, failed to achieve remission in a large percentage of affected individuals. Similarly, results from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) provide important effectiveness data indicating that most
individuals with bipolar disorder, despite receiving evidence-based algorithmic care, fail to achieve and sustain remission with full functional restoration (7).

The results of the pragmatic STAR-D and STEP-BD trials, as well as numerous efficacy studies, provide the basis for emphasizing individualized treatment selection in mood disorders. Toward this aim, elucidating demographic, clinical, and treatment factors which increase (or reduce) the probability of achieving remission are needed.

During the past decade, data has emerged that mood disorders are neurodegenerative syndromes. For example, postmortem and preclinical studies of brain tissue samples have documented abnormalities in cellular plasticity, cellular resilience and intracellular signaling. Regional and layer-specific alterations in the size, shape, and density of neurons and glia are also documented (8). In addition, neuroimaging studies have reported progressive regional abnormalities in brain structure and function (e.g., hippocampus) (9–11). Alterations in insulin-glucose homeostasis, inflammatory networks, cellular metabolism, glutamate signaling, and glucocorticoid function are proposed as possible neurotoxic mediators (12–14). In keeping with this view, treatments which normalize aberrant functioning within these interacting biological networks constitute possibly novel, hypothesis-driven (and disease-modifying) treatment avenues.

In this special issue of *Annals of Clinical Psychiatry*, contributors were selected based on their recognized expertise in the research, diagnoses, and treatment of mood disorders. Contributors have provided manuscripts regarding the symptomatic interface between bipolar disorder and major depressive disorder with an emphasis on differentiating features. Special populations commonly encountered in clinical practice such as seasonal depression, gender issues in depression, depression in older adults, managing the medically comorbid patient, and approaches to treatment-resistant depression are reviewed. This special issue also provides a brief and clinically accessible review of neuroimaging technology and its implications for everyday practice as well as an emerging heuristics that mood disorders are progressive neurotoxic syndromes mediated by aberrant energy homeostasis (i.e., metabolic syndrome type II). As clinicians and practitioners are increasingly relying on self-educational endeavors as part of maintenance of certification programs, a special article by Dr. Norman Sussman providing a pragmatic approach to interpreting research articles is also provided.

**REFERENCES**