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DIAGNOSING AND TREATING MOOD DISORDERED PATIENTS

To the Editor:

With the recent press release regarding the changes we can expect to see in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition,[1] I think it is timely to comment on the rationale for making diagnoses in mood disordered patients. Few would argue that unipolar and bipolar disorders are likely heterogeneous conditions that are often difficult to differentiate in the clinical setting.[2] I believe that clinicians would benefit from having a practical model of the pathogenesis of mood disorders that can be applied in the clinical setting that may yield more accurate diagnoses and possibly more effective treatments.

Saggese and colleagues[3] suggested that the current *DSM-IV-TR*[4] classification of mood disorders places too great an emphasis on polarity to the detriment of cyclicity in the diagnosis and treatment of mood disorders. They base their conclusions on epidemiologic data and treatment outcomes. Additionally, many would argue that over the decades patients with so called "treatment refractory depression" appear to respond only marginally well to treatments such as medication switching or augmentation strategies. This implies that better diagnostic accuracy might lead to better treatment decisions and hence better outcomes.[5]

I wish to propose that a well-known pathogenic model might explain cycle frequency and nicely seperates autonomous, cycling from non-cycling mood disorders.[6] I believe that non-cycling mood disorders represent true unipolar depressive illness. Such patients meet the *DSM-IV-TR* criteria for major depressive disorder (MDD). They tend to lack the features of bipolar spectrum disorders as defined by Ghaemi and colleagues.[7] Their onset tends to be later in life and characterized by low recurrence rates, partial remission, or a chronic, indolent course. Even when "recovered," these patients often appear to need more sleep, tolerate work less well, have diminished exercise tolerance, and appear to suffer various types of medical conditions including neurocardiogenic syncope, fibromyalgia, migraine, and chronic fatigue syndrome.[8] For such patients, relatively minor emotional stressors may trigger recurrent episodes of depressions. When examined closely, most true unipolar recurrences are not autonomous. In true unipolar depression, antidepressant monotherapy or combinations of antidepressants with psychotherapy or therapy alone may relieve the depression and reduce recurrences. Mood stabilizers may be used but are not essential to prevent relapse. In summary, the onset, family history, course of illness, and response to treatment of true unipolar depression varies substantially from cycling mood disorders.[9]

The pathogenesis of autonomous, recurrent, or cycling mood disorders appears to be best described by Post's[6] "kindling theory" of bipolar disorder. Kindling theory suggests that patients are born with a stable, balanced neuroendocrine and nervous system. In essence, their limbic system acts as a natural "emotional thermostat." From birth this "emotional thermostat" is programmed to maintain a reasonably constant emotional tone. When normal and appropriate variations in the environment occur, a normal emotional reaction may follow. These emotional reactions are culturally appropriate in intensity and duration. However, in the genetically vulnerable individual, when a traumatic life event occurs such as abuse or neglect, the stability of the "emotional thermostat" is disrupted. With the severest of traumas, that sense of security, stability, and predictability may be permanently disturbed. The individual may recover, but only partially. Physiologic data from childhood trauma show persistently elevated heart rates, dysregulated cortisol levels, and other changes as a sign of permanently disturbed neuroendocrine function. Subsequent traumas, disappointments, failures to be validated, or significant experiences of neglect can further disrupt the "emotional thermostat" until a sufficient allostatic load finally "breaks" the mechanism altogether. When this occurs, even at rest, the "emotional thermostat" can no longer maintain a reasonable, steady emotional tone. Instead, it perpetually over-shoots or under-shoots the mark. These are the patients that present to our clinics and hospitals as individuals suffering from bipolar disorder, personality disorders, substance abuse disorder, and, commonly, with highly recurrent MDD with or without psychosis. These cases I propose are the end result of "kindling" phenomenon. I propose that autonomous, highly recurrent mood disorders are the result of kindling and should be diagnosed as such based on the concepts set forth by Saggasse and colleagues,[3] Post,[6] and Ghaemi and colleagues.[7]

Thase,[10] in his article on treatment-resistant depression and the bipolar spectrum, concludes by reiterating that recent evidence indicates that up to 50% of those seeking treatment for depression may have a bipolar spectrum disorder. Therefore, when we see this pattern of high frequency, autonomous mood recurrences, we should consider the addition of mood stabilizing agents and atypical antipsychotics to re-stabilize the "emotional thermostat."

Sincerely,

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Disclosures: Dr. Rapport reports no affiliation with or financial interest in any organization that may pose a conflict of interest.

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