Guest Editorial / Misafir Editoryal

Staging Bipolar Disorder: Theoretical Exercise or Clinical Reality?

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In an optimistic view, bipolar mood disorders are seen as episodic illnesses with complete remission after each episode that respond well to lithium. This clinical picture exists; however, among patients diagnosed with bipolar disorder there is a vast variety of clinical presentations, with differences in previous illness and treatment histories, treatment responses, and degrees of interepisode residual symptoms and cognitive or functional impairment. Some patients have an illness course somewhere in between schizophrenia and bipolar disorder, conveniently classified as schizo-affective disorder. Moreover, patients may or may not have a family history of mood disorders, a personal biography complicated by traumatic life events, a comorbid anxiety disorder, substance abuse disorder, or personality disorder. Still, treatment practice, treatment guidelines, and clinical trials tend to disregard this heterogeneity, lumping patients together under the shared diagnosis of bipolar disorder, only to be differentiated into large subcategories such as bipolar I or bipolar II. Although the cross-sectional clinical syndromes of mania, hypomania, and depression may have many similarities among patients, it is in the longitudinal illness course where the individual differences become apparent. Some patients continue to thrive, even after repeated and sometimes severe mood episodes, while others show a gradual decline in psychosocial and cognitive functioning. It is therefore not surprising that treatment response and outcome may differ considerably within a group of bipolar patients, be it in an outpatient treatment program or in a formal clinical trial. In an era where early intervention and personalized treatment have become issues of growing interest, clinical staging of psychiatric disorders is one approach to deal with individual differences in illness progression, complementing current classification.

In general medicine, the staging of progressive disorders is well established in areas such as oncology, cardiovascular disease, and kidney disease. Staging has prognostic significance and helps the clinician to decide which treatment is the most appropriate in an individual patient.

Staging systems in psychiatry have been introduced some decades ago (1) but are hampered by the fact that the pathophysiology of psychiatric illness is still largely unknown and recognition of biomarkers is currently in its infancy. Disorders are entirely defined by their

clinical symptomatology and, albeit to a lesser extent, by their longitudinal clinical course. For bipolar disorder, several complementary staging models have been proposed. Berk et al. (2) described a staging system largely based on the occurrence and recurrence of mood episodes, from being at risk to having a final chronic unremitting illness. Kapczinski et al. (3) took a different approach, using the interepisodic functional state as a proxy of illness progression, finally leading to the inability to live autonomously. Both models are based on the concept of neuroprogression, an assumed process of progressive structural, functional, and neurochemical brain changes, reflected by cognitive and functional decline, poorer treatment response, and an increasing vulnerability to relapse with chronicity. Both models also suggest one-directional linearity. A third model, proposed by Duffy, assumes that there are different illness trajectories from the outset: one in the direction of a classical episodic illness, the other heading more towards bipolar spectrum disorders with mixed and or even predominant psychotic features that come close to schizophrenia (4). These various models underline the different dimensions of the longitudinal illness course: recurrence of episodes, quality of remission, and multi-directional evolution of clinical syndromes. The missing link is our limited knowledge of the biological mechanisms underlying these illnesses. Some have even called for restraint when developing staging further, until more of the pathophysiology has been revealed (5). Even though for now, staging is still largely a theoretical concept, it is a next step towards personalized treatment to include the concept of illness progression, and hence to allow for intervention as early as possible.

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