As the American Psychiatric Association committees begin formal work on DSM-5, we welcome brief editorials on issues that should be considered in its formulation.

Issues for DSM-5: Whither Melancholia? The Case for Its Classification as a Distinct Mood Disorder

Melancholia, a syndrome with a long history and distinctly specific psychopathological features, is inadequately differentiated from major depression by the DSM-IV specifier. It is neglected in clinical assessment (e.g., in STAR*D [1]) and treatment selection (e.g., in the Texas Medication Algorithm Project [2]). Nevertheless, it possesses a distinctive biological homogeneity in clinical experience and laboratory test markers, and it is differentially responsive to specific treatment interventions. It therefore deserves recognition as a separate identifiable mood disorder.

Melancholia has been variously described as "endogenous," "endogenomorphic," "autonomous," "type A," "psychotic," and "typical" depression (3–6). In contrast to the current DSM criteria for the melancholia specifier (features of which are often shared with major depression), it has characteristic clinical features (5–7).

Clinical Features

1. *Disturbances in affect* disproportionate to stressors, marked by unremitting apprehension and morbid statements, blunted emotional response, nonreactive mood, and pervasive anhedonia—with such features continuing autonomously despite any improved circumstances. The risks for recurrence and for suicide are high.
2. *Psychomotor disturbance* expressed as retardation (i.e., slowed thought, movement, and speech, anergia) or as spontaneous agitation (i.e., motor restlessness and stereotypic movements and speech).
3. *Cognitive impairment* with reduced concentration and working memory.
4. *Vegetative dysfunction* manifested as interrupted sleep, loss of appetite and weight, reduced libido, and diurnal variation—with mood and energy generally worse in the morning.
5. Although *psychosis* is not necessarily a feature, it is often present. Nihilistic convictions of hopelessness, guilt, sin, ruin, or disease are common psychotic themes.

"Melancholia's features cluster with greater consistency than the broad heterogeneity of the disorders and conditions included in major depression and bipolar disorder."

Biological Changes

Several biological changes occur more frequently in melancholia than in other forms of depressive illness. Three indicative markers are known.

1. *Hypercortisolemia,* reflected in the dexamethasone suppression test (DST). It is common in melancholia and relatively uncommon in nonmelancholic mood disorders (6).
2. *Psychomotor disturbance* measurable by the CORE scale (5), with CORE scores demonstrating a linear relationship with DST nonsuppression rates (8).
3. Characteristic *disturbances in sleep architecture,* with reduced REM latency, increased REM time, and reduced deep sleep (9).

Treatment

Melancholic patients respond better to broad-action tricyclic antidepressants than to narrow-action antidepressants (e.g., serotonin uptake inhibitors) (10). They respond well to ECT (11). In comparison to those with nonmelancholic mood disorders, melancholic patients rarely respond to placebos, psychotherapies, or social interventions (12).

Conclusions

Melancholia is a lifetime diagnosis, typically with recurrent episodes (5, 6, 13, 14). Within the present classification it is frequently seen in severely ill patients with major depression and with bipolar disorder. Melancholia's features cluster with greater consistency than the broad heterogeneity of the disorders and conditions included in major depression and bipolar disorder. The melancholia diagnosis has superior predictive validity for prognosis and treatment, and it represents a more homogeneous category for research study.

We therefore advocate that melancholia be positioned as a distinct, identifiable and specifically treatable affective syndrome in the DSM-5 classification.

References

1. Gaynes BN, Warden D, Trivedi MH, Wisniewski SR, Fava M, Rush AJ: What did STAR*D teach us? results from a large-scale, practical, clinical trial for patients with depression. Psychiatr Serv 2009; 60:1439–1445
2. Crismon ML, Trivedi M, Pigott TA, Rush AJ, Hirschfeld RM, Kahn DA, DeBattista C, Nelson JC, Nierenberg AA, Sackeim HA, Thase ME: The Texas Medication Algorithm Project: report of the Texas Consensus Conference Panel on Medication Treatment of Major Depressive Disorder. J Clin Psychiatry 1999; 60:142–156
3. Kendell RE: The classification of depression: a review of contemporary confusion. Br J Psychiatry 1976; 129:15–28
4. Klein DF: Endogenomorphic depression: a conceptual and terminological revision. Arch Gen Psychiatry 1974; 31:447–454
5. Parker G, Hadzi-Pavlovic D (eds): Melancholia: A Disorder of Movement and Mood. Cambridge, UK, Cambridge University Press, 1996
6. Taylor MA, Fink M: Melancholia: The Diagnosis, Pathophysiology and Treatment of Depressive Illness. Cambridge, UK, Cambridge University Press, 2006
7. Bolwig TG, Shorter E (eds): Melancholia: Beyond DSM, Beyond Neurotransmitters. Acta Psychiatr Scand Suppl 2007; 115
8. Mitchell P: Validity of the CORE, I: a neuroendocrinological strategy, in Melancholia: A Disorder of Movement and Mood. Edited by Parker G, Hadzi-Pavlovic D. Cambridge, UK, Cambridge University Press, 1996, pp 138–148
9. Armitage R: Sleep and circadian rhythms in mood disorders. Acta Psychiatr Scand Suppl 2007; 115:104–115
10. Perry PJ: Pharmacotherapy for major depression with melancholic features: relative efficacy of tricyclic versus selective serotonin reuptake inhibitor antidepressants. J Affect Disord 1996; 39:1–6
11. Petrides G, Fink M, Husain MM, Knapp RG, Rush AJ, Mueller M, Rummans TA, O'Connor KM, Rasmussen KG Jr, Bernstein HJ, Biggs M, Bailine SH, Kellner CH: ECT remission rates in psychotic versus non-psychotic depressed patients: a report from CORE. J ECT 2001; 17:244–253
12. Brown WA: Treatment response in melancholia. Acta Psychiatr Scand Suppl 2007; 115:130–135
13. Goodwin FK, Jamison KR: Manic-Depressive Illness. New York, Oxford University Press, 1990
14. Swartz CM, Shorter E: Psychotic Depression. New York, Cambridge University Press, 2007

GORDON PARKER, M.D.
MAX FINK, M.D.
EDWARD SHORTER, PH.D.
MICHAEL ALAN TAYLOR, M.D.
HAGOP AKISKAL, M.D.
GERMAN BERRIOS, M.D.
TOM BOLWIG, M.D.
WALTER A. BROWN, M.D.
BERNARD CARROLL, M.B.B.S.
DAVID HEALY, M.D.
DONALD F. KLEIN, M.D.
ATHANASIOS KOUKOPOULOS, M.D.
ROBERT MICHELS, M.D.

JOEL PARIS, M.D.
ROBERT T. RUBIN, M.D.
ROBERT SPITZER, M.D.
CONRAD SWARTZ, M.D.

Address correspondence and reprint requests to Dr. Parker, Black Dog Institute, Prince of Wales Hospital, Hospital Road, Randwick, N.S.W., Australia; g.parker@unsw.edu.au (e-mail). *Editorial accepted for publication January 2010 (doi: 10.1176/appi.ajp.2010.09101525).*

Dr. Parker is an advisory board member for AstraZeneca, Eli Lilly, and Lundbeck; he has also spoken at and chaired meetings for and received financial sponsorship from AstraZeneca, Eli Lilly, GlaxoSmithKline, Pfizer, Servier, and Wyeth in recent years. Dr. Akiskal has served on speakers or advisory boards for Abbott, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, and Janssen. During 2008–2009 and extending into 2010, Dr. Healy has been, continues to be, and will be an expert witness in legal actions against companies producing sertraline and paroxetine; the cases involve suicide linked to treatment, physical dependence on treatment, and birth defects consequent on treatment with these drugs. Dr. Swartz has equity ownership in Novartis, Somatics, and Sanofi-Aventis and is a director of Somatics. Dr. Freedman has reviewed this editorial and found no evidence of influence from these relationships. The other authors report no financial relationships with commercial interests.