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Review: Moving Borderline Personality Disorder to Axis I

Borderline personality disorder (BPD) is a prevalent and disabling condition, yet the empirical research into its nature and treatment has not been commensurate with the seriousness of the illness. In this review, **New *et al.*** (pages 653–659) present their case for a reconceptualization of BPD, and for its placement on Axis I. They address fundamental misconceptions that have contributed to a misunderstanding of this disease, review what is known from empirical evidence, and propose an approach for future research.

Hypermethylation in the Suicide Brain

A new report by **Poulter *et al.*** (pages 645–652) indicates that epigenetic control of gene expression may be different in the brains of depressed suicides versus controls. They found altered expression in a number of suicide brain areas that are related to depressive illness, including a change in the frontopolar cortex that was associated with increased methylation of the γ-aminobutyric acid $(GABA)_A$ receptor α1 subunit gene, whose mRNA expression has previously been shown to be reduced.

Timing of Depression Vital to Cardiac-Related Risks

Previous research indicates that those with depression following hospitalization for an acute coronary syndrome have an elevated risk of cardiac death or readmission over the following year. In the current study, **Parker *et al.*** (pages 660–666) found that only episodes of depression that commenced after the coronary event, not lifetime or existing depression, were associated with increased cardiac-related morbidity and mortality but that this increased risk was substantial.

Altered Visual Perception in Depressed Patients

Depression is a disorder that affects cognitive functions such as memory and attention, and **Zomet *et al.*** (pages 667–671) sought to evaluate whether perception is also affected. They found that depressed patients do not fill-in missing targets and therefore display a lack of standard perceptual illusions known as illusory contours, suggesting that there may be reduced neural excitation, a key factor in the neural processing involved in memory and decision making.

Anxiety Disorder Candidate Genes

Cross-species approaches are potentially useful for identifying genes influencing complex traits, including susceptibility to human psychiatric disorders. **Donner *et al.*** (pages 672–680) tested 13 genes previously shown to be differentially expressed between anxious and non-anxious mouse strains as candidate genes for human anxiety disorders with a genetic association study. The results revealed some evidence for association of *ALAD* with risk for social phobia, *DYNLL2* with risk for generalized anxiety disorder, and *PSAP* with risk for panic disorder.

Impact of Stress on Pathophysiology

Simmons *et al.* (pages 681–690) report differences in brain activation between women with posttraumatic stress disorder (PTSD) as a result of intimate partner violence (IPV) and non-traumatized control women during an affective anticipation task. The data revealed increased activation in the anterior/middle insula during negative anticipation in women with IPV-related PTSD, which suggests that these groups differ in the way that affectively relevant physiological information is processed and how this is subsequently integrated in an affective network.

Adversity and stressful life events produce psychopathological changes in only a minority of stress-exposed individuals. The neurobiological mechanisms that mediate vulnerability to conditions such as depression and PTSD are poorly understood. **Krishnan *et al.*** (pages 691–700) employ a mouse model of chronic social stress to demonstrate an important role for AKT (thymoma viral proto-oncogene) signaling within the ventral tegmental area (VTA) in manifesting features of a vulnerable phenotype. The authors use a multidisciplinary approach to illustrate how decrements in AKT activation in the VTA affect the physiology of the mesolimbic dopamine circuit.

Cognitive Coping and Sense of Control Influence Stress Response

Stress influences many types of illness, so finding ways in which to reduce its biological consequences should enhance health. An intervention that reduces novelty and enhances cognitive coping and sense of control can reduce the hypothalamic-pituitary-adrenal (HPA) axis response to pharmacological activation. **Abelson *et al.*** (pages 701–707) replicate this finding and show that novelty reduction and cognitive coping alone are as effective as a more complex intervention. Sense of control alone may also be able to reduce stress system activation. Coping and control may be key factors in protection from stress.

Corticosteroids: Influence on Memory & Behavior

Cohen *et al.* (pages 708–717) examined the long-term effects of a single course of corticosterone or saline on behavioral responses to a potentially traumatic experience and to further stress in a prospective animal model for PTSD. They found that early treatment with high-dose corticosterone reduced the prevalence of PTSD-like behavioral responses relative to saline treatment, whereas lower doses of corticosterone increased the prevalence of PTSD-like behavioral disruptions. This finding suggests that corticosterone levels may influence both vulnera-

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bility and resilience in a dose-dependent manner through its involvement in memory processes.

Brown *et al.* (pages 727–729) found that people receiving long-term corticosteroid therapy had a greater improvement in memory with the *N*-methyl-D-aspartate (NMDA) glutamate receptor antagonist, memantine, than with placebo. Memantine is prescribed to preserve or enhance cognitive function in patients with dementia. These data provide support for the hypothesis that blocking NMDA receptors may protect against some negative effects of corticosteroid treatment.

Abnormalities in the Bipolar Brain

Following synaptic release, the major neurotransmitter in the brain, glutamate, is taken up by glial cells, converted to glutamine, and cycled back to neurons for glutamate synthesis. **Öngür *et al.*** (pages 718–726) used magnetic resonance spectroscopy to measure the glutamine/glutamate ratio as an index of neuronal-glial coupling in acutely ill medicated patients with bipolar mania and schizophrenia. They found significantly elevated glutamine/glutamate in bipolar mania but not schizophrenia, consistent with reports of glial cell abnormalities in bipolar disorder in postmortem studies.

Abnormalities in the anterior interhemispheric connections provided by the corpus callosum have been implicated in bipolar disorder. Using complementary diffusion tensor imaging methods, **Wang *et al.*** (pages 730–733) provide new evidence for abnormalities in the structural integrity of the anterior corpus callosum in bipolar disorder patients.