In This Issue

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A brief summary of the articles appearing in this issue of *Biological Psychiatry*.

Review of Mesolimbic BDNF in Depression

Brain-derived neurotrophic factor (BDNF) in the brain's dopaminergic reward circuitry is crucial to the development of depressive-like behavioral abnormalities following stress exposure in animal models. While BDNF modulates the influence of dopamine signaling in the response to acute stress, evidence is discrepant for different forms of chronic stress, with BDNF signaling or dopamine signaling appearing to be primarily responsible for the behavioral effects. In this review, **Koo *et al.*** (pages 738–748) discuss the molecular, cellular, and circuit basis of this discrepancy, which appears to involve the nature of the stress, its severity and duration, and its effects on distinct cell types within the mesolimbic circuit.

Lesion Network Mapping of Depression

Discovery of the association between frontal brain lesions and depression has led to vital neuroanatomical insights into depression, but work related to lesion location has yielded inconsistent results. Using 5 independent lesion datasets with different lesion etiologies and measures of depression, **Padmanabhan *et al.*** (pages 749–758) report that lesion locations associated with depression failed to map to a specific brain region, but did map to a specific brain circuit, centered on the left dorsolateral prefrontal cortex. These results are consistent with brain stimulation sites that have shown success in treating depression and may help further refine treatment targets in depression.

White Matter Microstructure and Depressive Symptoms

White matter microstructure is altered in depression, but data that can inform on the impact of dynamic depressive symptoms over time has been lacking. In this study, **Shen *et al.*** (pages 759–768) investigated associations between white matter microstructure and the longitudinal trajectory of depressive symptoms in a large neuroimaging cohort. Results revealed different regional patterns of decreased microstructural integrity in the brain related to severity, course, and intrasubject variability of depressive symptoms, providing insight into the neurobiology of varying trajectories of depression.

Stress, Morphometry, and Depression

Stress affects brain development and can induce depression, yet the impact of common life stressors during adolescence, a period of vital neurodevelopment and the emergence of mood disorders, remains unclear. Using magnetic resonance imaging in a community sample of adolescent girls, **Bartlett *et al.*** (pages 769–778) found reduced cortical thickness and volume in adolescents with a greater burden of recent stress. Further, cortical thickness in the precuneus prospectively predicted new onset of depressive symptomatology for 27 months. These data provide a link between recent stressful life events and cortical structure in adolescence, and suggest that precuneus thickness may represent a biomarker of adolescent depression.

Transdiagnostic Sensory Dysconnectivity

Transdiagnostic initiatives aim to address the substantial overlap in clinical symptoms, cognitive deficits, brain abnormalities, and genetic risk factors that are present across psychiatric disorders. Using a dimensional data-driven approach, **Kebets *et al.*** (pages 779–791) identified 3 transdiagnostic components (general psychopathology, cognitive dysfunction, and impulsivity) with dissociable whole-brain resting-state functional connectivity signatures across healthy individuals and individuals with psychiatric illness. All 3 components featured altered connectivity within the somatosensory-motor network and in its connections to subcortical and cortical executive networks. These findings advance our understanding of brain-behavior associations that span psychiatric boundaries.

LSD Microdosing Effects in Healthy Adults

Anecdotal reports suggest that repeated ingestion of very low "microdoses" of lysergic acid diethylamide (LSD) improve mood and cognition, but these claims have not yet been investigated in a laboratory setting. Here, **Bershad *et al.*** (pages 792–800) conducted a randomized, double-blind, within-subject, placebo-controlled study examining the acute effects of low doses of LSD (6.5, 13, and 26 μg) on subjective states and cognition in healthy adults. The authors report that LSD produced dose-related effects on subjective ratings without impairing cognitive performance. These data indicate that LSD might be used safely in a repeated dosing regimen to investigate its effects in clinical populations.

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