

This intriguing result represents one of the few biomarkers of antidepressant response in adolescent depression.

Exciting new approaches to investigating reward function in adolescent depression include examining brain-behavior associations and employing personally relevant social stimuli. When combined with experience sampling, functional neuroimaging can identify regions of the striatum whose response distinguishes adolescents with depression from healthy adolescents and is also correlated with higher levels of positive affect experienced in natural environments (Forbes *et al*, 2009). Assessing neural response to social rewards, which are postulated to be critical for triggering adolescent depression (Davey *et al*, 2008), can provide a more meaningful understanding of altered reward function. In addition, future work will benefit from attention to clinical characteristics such as anhedonia, comorbid anxiety and clinical course.

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#### DISCLOSURE

The author declares no conflict of interest.

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## Dorsal vs Ventral Hippocampal Neurogenesis: Implications for Cognition and Mood

An emerging view of the hippocampus is that of a functionally heterogeneous structure along its longitudinal axis. Lesion studies reveal that the dorsal (septal pole) hippocampus is involved in learning and spatial memory, whereas the ventral (temporal pole) hippocampus regulates emotional and motivated behaviors (Fanselow and Dong, 2010). Anatomical connectivity and gene expression analyses support this functional dissociation. For example, serotonergic fibers provide denser input to the ventral hippocampus with a concomitant enrichment of 5-HT1A and 2C receptors ventrally (KF Tanaka and R Hen, unpublished). Efferent connectivity indicates that ventral hippocampus can modulate reward circuitry and emotional behavior through projections to nucleus accumbens, prefrontal cortex and amygdala, and stress responses by regulating the hypothalamic–pituitary–adrenal axis (Sahay and Hen, 2007). In both regions, the subgranular zone of the dentate gyrus (DG) continues to produce new neurons in adulthood. These adult-born granule cells (GCs) functionally integrate into the DG circuit, exhibit enhanced excitability, and have a significant impact on both learning and emotional behavior (Sahay and Hen, 2007). As adult

neurogenesis has been implicated in both learning and mood, an exciting possibility is that adult-born GCs in the dorsal and ventral hippocampus may be functionally dissociated.

Chronic antidepressant treatment increases neurogenesis in the DG, a requirement for some of their behavioral effects (Santarelli *et al*, 2003). Recent studies suggest that antidepressants regulate behavior by selectively increasing ventral hippocampal neurogenesis. Chronic treatment with agomelatine, a melatonin receptor agonist, and 5-HT2C receptor antagonist with robust effects in animal models as well as efficacy in human major depressive disorder increases neurogenesis selectively in the ventral DG (Banasr *et al*, 2006). In humans, selective serotonin reuptake inhibitors and tricyclic antidepressants increase proliferating and neuronal precursor cells more prominently in the anterior portion of the DG of patients with MDD as compared to controls and untreated MDD subjects (Boldrini *et al*, 2009). These two studies, although correlational, provide exciting preliminary evidence that warrants future studies aimed at selectively blocking or stimulating neurogenesis in the ventral hippocampus.

In the cognitive realm, adult neurogenesis has recently been implicated in pattern separation, the ability to distinguish between similar contexts (Deng *et al*, 2010). Owing to their unique physiological properties, adult-born GCs may contribute to pattern separation by modulation of sparse coding in the DG. A recent report indicates that ablation of adult-born GCs increases the magnitude of spontaneous gamma bursts in the dorsal DG and enhances modulation of single unit firing by these bursts (Lacefield *et al*, 2010). This increase in spontaneous activity suggests that adult-born GCs may modulate network inhibition of mature GCs through either feedback inhibition or synaptic competition. Thus, young GCs may contribute to sparse coding and pattern separation by modulating inhibitory control of the mature GCs in the DG. Deficits

in pattern separation may not only impact cognition, but may also contribute to anxiety disorders by impairing the ability to discriminate between safe and fearful contexts. The resulting inability to respond appropriately to similar situations that have differing emotional valence may lead to the generalization observed in certain anxiety disorders such as PTSD. As adult-born GCs have a role in sparse coding in the DG and pattern separation, it will be of great interest to examine how blocking or stimulating ventral hippocampal neurogenesis may influence emotional behavior by modulating pattern separation.

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