Biological Psychiatry

A Journal of Psychiatric Neuroscience and Therapeutics

In this Issue-July 1st

Abnormal brain structure in mood disorders: treatment effects

Using a magnetic resonance imaging (MRI) technique, **Bearden *et al.*** (pages 7–16) found significantly increased gray matter in lithium-treated patients with bipolar disorder relative to a group of healthy people, particularly in brain regions involved in the control of attention and emotion. In contrast, patients who were not taking lithium did not differ from the healthy group. These data are consistent with other recent findings suggesting that lithium treatment may increase brain volume in several regions, an effect that may be related to its effectiveness in treating bipolar disorder.

McNamara *et al.* (pages 17–24) present new evidence of deficits in the levels of omega-3 fatty acid docosahexaenoic acid (DHA) in post-mortem orbital frontal cortex tissue from patients with major depressive disorder. DHA deficits were greater in female patients.

The link between depression and cardiac disease

Depression and coronary artery disease appear to contribute to the risk for the other disease, accounting for their common comorbidity. But the nature of this interplay is not well understood. In a large, population-based case-control study, **Janszky *et al.*** (pages 25–32) found that hospitalization for clinical depression was a risk factor for first acute myocardial infarction (MI) and death, even after adjusting for other factors that might have contributed to their coronary artery disease. Further, a history of hospitalization for a depression episode contributed to the risk for MI even when the episode occurred over 15 years prior to the MI. These data strengthen the view that depression may contribute to disease progression or be a very early marker of coronary artery disease.

Cortisol and neural mechanisms of learning

Is cortisol released during the retrieval of traumatic memories contributing to the persistence of post-traumatic stress disorder (PTSD)? Using an animal model, **Tronel and Alberini** (pages 33–39) report that a previously established fear memory can be weakened if cortisol (glucocorticoid) receptors are blocked in the amygdala immediately after the retrieval of the memory. The effect is persistent and the memory remains weakened even after reminders of the traumatic event. These data highlight the malleability of traumatic memories when they are retrieved and the potential opportunity, at those moments of memory retrieval, of targeting the neurobiological processes that appear to contribute to the persistent intrusiveness of traumatic memories.

Cortisol, depression risk, and treatment response

Offspring of depressed parents are at elevated risk of depression themselves. **Halligan *et al.*** (pages 40–46) investigated the mechanisms by which this risk is transmitted. In a longitudinal study of the offspring of postnatally depressed mothers and non-depressed mothers, they found that elevated morning salivary cortisol levels in the at-risk group at 13-years predicted subsequent depressive symptomatology at 16-years.

Ising *et al.* (pages 47–54) show that, during antidepressant treatment, improved stress hormone regulation, as measured by the hormonal (ACTH, cortisol) responses to the combined administration of dexamethasone and corticotrophin releasing hormone (DEX/CRH test), precedes improvement in symptoms and predicts the subsequent extent of clinical response. This finding raises the possibility that biological tests might be developed to estimate the likelihood of medication response in patients early in the course of treatment.

Antidepressant effects via inhibition of histone deacetylase

The secondary structure of DNA, the folding patterns that influence DNA function, is regulated in part by supporting proteins called histones. One enzyme involved in regulating the function of histone proteins, histone deacetylase (HDAC), removes acetyl groups. In their study, **Schroeder *et al.*** (pages 55–64) report that an HDAC inhibitor, sodium butyrate, exerts antidepressant-like behavioral and biochemical effects in mice. Further treatment with sodium butyrate and the serotonin reuptake inhibitor (SSRI), fluoxetine, was more effective than either drug alone.

Would antidepressants appear to be more effective if more severely ill patients were studied?

Shortcomings in study design may contribute to the high rate of antidepressant treatment studies that fail to show efficacy, even with medications widely believed to be effective. **Khan *et al.*** (pages 65–71) provide compelling evidence against the widely held belief that antidepressant trials that study patients with high levels of symptom severity are more likely to benefit from antidepressant drugs and less likely to benefit from placebos. Among 51 antidepressant trials that showed a relationship between severity of depressive symptoms and outcome, the authors found no relationship between entry criteria and trial outcome.

0006-3223/07/$32.00

BIOL PSYCHIATRY 2007;62:A5–A6

Heritable risk for depression

Heritable differences in the regulation of serotonin function appear to influence the risk for depression and suicide. **Lopez de Lara *et al.*** (pages 72–80) report that variation in the gene coding for the enzyme that controls the rate of serotonin synthesis, tryptophan hydroxlase-2 (*TPH2*), moderates the risk for suicide among depressed individuals. However, the *TPH2* effect does not appear to be mediated by an increase in impulsive or aggressive behavior, generally.

Animal models for depression

Liu *et al.* (pages 81–91) report progress in identifying the genes that are related to depression risk and treatment response in an animal model of depression, the tail suspension test (TST). The TST is widely used as a tool to screen agents that are being developed as potential antidepressant treatments. Using an animal genetics testing approach, several DNA regions were identified that might be involved in the vulnerability to stress and the response to the tricyclic antidepressant, imipramine.

Holderbach *et al.* (pages 92–100) provide new evidence that chronic mild stress, in an animal model of depression, suppresses the birth of new neurons and depresses neural function in the hippocampus, a brain region implicated in mood and memory. They also showed that these effects of stress were prevented by antidepressant treatment.