Biological Psychiatry

A Journal of Psychiatric Neuroscience and Therapeutics

In this Issue-August 15th

Heritability and Risk and Resilience Mechanisms

As the population ages, it is becoming more critical to understand what factors help some individuals age more successfully than others. Based on their review of the published literature, **Glatt *et al.*** (pages 282–293) suggest that approximately 25% of individual variability in successful aging is heritable. They discuss several candidate genes that may contribute to this process.

The serotonin transporter (5-HTT) linked polymorphic region (5-HTTLPR) has been implicated in the risk for depression and other psychiatric disorders. Here, **Praschak-Rieder *et al.*** (pages 327–331) use [^{11}C] DASB positron emission tomography (PET) to show that the 5-HTTLPR long (A/G) polymorphism influences an index of 5-HTT density in putamen, such that the density of these transporters is increased in L_A/L_A carriers of Caucasian ancestry.

Fowler *et al.* (pages 355–358) measured brain levels of activity of the enzyme monoamine oxidase-A (MAO-A) using PET. They did not find that individuals who differ in their genotype for the gene that codes for MAO-A differ in the level of MAO-A activity in their brains. These data raise important questions as to the mechanisms that MAO-A genotypes might influence the risk for psychiatric disorders.

Inflammation, Depression, and Cardiovascular Disease

Frasure-Smith *et al*. (pages 302–308) assessed depression symptoms and markers of inflammation in 602 men with stable coronary artery disease. Both elevated depression symptoms and elevated levels of C reactive protein (CRP) significantly predicted major adverse cardiac events over two years. However, there was a ceiling effect of risk. Men with both elevated depression symptoms and elevated CRP levels experienced about the same increase in risk as those with only one of the two factors.

Kling *et al.* (pages 309–313) found elevated serum levels of the acute phase proteins CRP and serum amyloid A in 18 remitted, unmedicated women with recurrent Major Depressive Disorder (MDD). These findings suggest the persistence of a pro-inflammatory state following symptomatic recovery from depression and discontinuation of antidepressants, which may help account for the increased risk of cardiovascular disease associated with MDD.

Whooley *et al.* (pages 314–320) question the role of inflammatory processes in the adverse cardiovascular outcomes associated with depression in patients with cardiovascular disease. The authors found no evidence that current major depression was associated with elevated levels of six inflammatory markers in 984 outpatients with stable coronary heart disease. Instead, depression was associated with lower plasma levels of CRP, fibrinogen, and interleukin-6.

Kloiber *et al.* (pages 321–326) investigated the impact of weight on psychopathology, attention, neuroendocrinology, weight change, and treatment response in 408 inpatients with major depression. Overweight and obese patients showed significantly slower clinical response, less improvement in neuroendocrinology and attention, and less weight gain during antidepressant treatment compared to normal weight patients.

Depression and Traumatic Brain Injury

Jorge *et al.* (pages 332–338) report that patients with moderate to severe traumatic brain injury who developed mood disorders had significantly smaller hippocampal volumes than patients with equivalent severe brain injury who did not develop mood disturbance. These data raise the possibility that more severe hippocampal injury may increase risk for depression or that depression itself increases the hippocampal damage associated with traumatic brain injury.

Cardiovascular Disease and Dementia

Patients with dementia or coronary artery disease may shower their brain with small blood clots that can block small brain blood vessels without producing signs of a stroke. **Purandare *et al.*** (pages 339–344) now show that spontaneous cerebral emboli are associated with a more rapid worsening of cognition and daily functioning in both Alzheimer's disease and vascular dementia. These data highlight the importance of identifying individuals with these emboli and preventing further brain damage.

Medications and Seizures

Alper *et al*. (pages 345–354) reviewed available public domain data regarding the incidence of seizures in clinical trials of psychotropic drugs approved in the United States between 1985 and 2004. They present evidence that clozapine, olanzapine, chlomipramine, and alprazolam increased seizure risk, while other antidepressants reduced seizure risk.

Novel Mechanisms of Synaptic Plasticity

Okulski *et al.* (pages 359–362) present data suggesting that an endogenous inhibitor of a class of enzymes implicated in the functional remodeling of synapses, matrix metalloproteinases, may influence the capacity to learn. This finding is based on the capacity of this inhibitory enzyme, TIMP-1, to interfere with a form of a cellular process implicated in learning, long-term potentiation, in the prefrontal cortex.

0006-3223/07/$32.00