Biological Psychiatry

A Journal of Psychiatric Neuroscience and Therapeutics

In this Issue - November 15th

Alzheimer's Disease Pathology

Inflammation may be an important contributor to the progression of Alzheimer's disease (AD). The peripheral benzodiazepine receptor (PBR) may be an important marker of brain inflammation because it is expressed by activated microglia, brain cells involved in immunity and inflammation. **Yasuno *et al.*** (pages 835–841) quantified PBR in AD using positron emission tomography (PET) and a new PBR ligand, [^{11}C]DAA1106. They found the widespread increase of PBR binding in the brains of AD patients, suggesting a broad existence of cellular reactions with PBR in relatively early-stage AD.

Parkinson's disease with dementia (PDD) and dementia with Lewy bodies (DLB) represent two conditions with unknown relative contributions of AD pathology to dementia. **Parnetti *et al.*** (pages 850–855) measured the cerebrospinal fluid biomarkers of AD pathology - Aβ42, total tau and phosphorylated tau - in PDD and DLB and compared them to Alzheimer's and Parkinson's patients, and normal controls. The results suggest that features of AD pathology are present more commonly than one might expect in DLB.

Review: Functional Magnetic Resonance Imaging in Clinical Research

In this review, **Carter *et al.*** (pages 842–849) discuss a number of conceptual and methodological challenges that confront the implementation of functional magnetic resonance imaging (fMRI) in clinical and translational research. In addition, they offer a set of recommendations intended to enhance the interpretability and reproducibility of results in clinical fMRI and highlight areas where further development is needed.

Hippocampal Physiology and Morphology

Stern *et al.* (pages 856–862) confirm that a functional polymorphism in the gene that codes for brain-derived neurotrophic factor (BDNF) influences hippocampal N-acetylaspartate (NAA) levels. In particular, the Met allele of this gene was associated with lower NAA levels, as measured by magnetic resonance spectroscopy (MRS). NAA is a marker of the metabolic integrity of nerve cells in the brain. Thus, these data provide evidence that the BDNF gene polymorphism is related to the volume or activity of nerve cells in the hippocampus, a brain region implicated in learning and memory.

Few morphometric studies have examined whether hippocampal volume is associated with clinically meaningful outcomes such as response to treatment. **MacQueen *et al.*** (pages 880–883) examined regional hippocampal volumes in both remitted and unremitted depressed patients following 8 weeks of initial treatment. Patients who remitted had larger pre-treatment hippocampal volumes bilaterally compared to those who were not in remission, but this difference was apparent only in the body/tail region of the hippocampus.

In cancer research, it is common knowledge that the invasiveness of particular tumors depends on their ability to stimulate the local growth of the blood supply feeding the tumor. A critical factor in this process is vascular endothelial growth factor (VEGF), now a target of some cancer chemotherapies. Perhaps building on the need for local control of blood supply to feed the development and function of the brain, **Blumberg *et al.*** (pages 901–903) now provide some evidence that a polymorphism in the VEGF gene is associated with hippocampal volume. These data may hold clues to the neurobiology of depression and cognition as well as to the cognitive and behavioral side effects of chemotherapies that interfere with VEGF action in the body.

Expression of Depressive Symptoms Evaluated via Animal Models

Banasr and Duman (pages 863–870) demonstrate that animals subjected to chronic unpredictable stress (CUS) show decreased number of astrocytes in the prefrontal cortex, similar to the decreases observed in postmortem tissue from depressed subjects. Using a pharmacological strategy, the authors also demonstrate that selective glial ablation in the prefrontal cortex results in deficits in four depressive-like behaviors that are also observed in animals exposed to CUS. The present data demonstrate that chronic stress affects glial function and suggest that cortical glial loss and dysfunction plays a direct role in the expression of depressive symptoms, possibly via altered function of neurons.

Gourley *et al.* (pages 884–890) evaluated the persistent effects of corticosterone exposure in a novel stress-related mouse model of depression. They found that direct hippocampal BDNF infusion reversed the corticosterone-induced behavioral deficits. The authors suggest that this model may provide a powerful tool for future investigation into the neurobiology of complex stress-associated depressive symptoms that persist long after stress exposure itself.

Alzheimer's Disease: Risk Factors

Devanand *et al.* (pages 871–879) followed 126 patients with mild cognitive impairment for 3 years to evaluate the utility of combining a series of eight early markers to potentially predict their conversion to AD. A five-predictor combination showed 85.2% sensitivity for 10% false positives, and was markedly superior to combining age and Mini-Mental State Examination scores.

A family history of AD and the ϵ4 version of the apolipoprotein E gene are risk factors for the development of AD. **Bloss**

0006-3223/08/$34.00

BIOL PSYCHIATRY 2008;64:831–832

et al. (pages 904–906) report that possession of both risk factors was associated with lower cognitive test performance among a sample of school-aged children. These results suggest that risk factors for a disorder of pathological aging may have implications for the etiology of certain types of learning difficulties in children.

Inflammatory Cytokines in Alzheimer's and Depression

To reveal the inflammatory response of lymphocytes to Alzheimer's neuro-toxic β-amyloid peptide, **Teixeira *et al.*** (pages 891–895) evaluated the release of several cytokines from peripheral blood mononuclear cells with immuno-assays. The observed changes in the profile of inflammatory cytokines may serve as diagnostic and predictive factors of the development and progression of AD.

Capuron *et al.* (pages 896–900) sought to examine the involvement of inflammation in the relationship between metabolic syndrome and depressive symptoms. They found that subjects with metabolic syndrome had more depressive symptoms, characterized primarily by neurovegetative features such as reduced level of activity, than those without.

Cizza *et al.* (pages 907–911) found increased immune activity and changes in stress system-related nerve chemicals in the sweat of women with depression in remission. These changes could pre-dispose to medical conditions, such as cardiovascular disease, osteoporosis and diabetes. The sweat patch can be used to collect stress and immune molecules without pain or distress.

Higher Risk of Stroke for Depressed Patients

Lee *et al.* (pages 912–915) followed 18-44 year old patients hospitalized for depressive disorders for five years, along with non-depressed age- and gender-matched subjects to evaluate their risk of stroke. The adjusted hazard of stroke was 5.43 times greater for depressed patients than for non-depressed subjects.