informed the development of modern physical treatments for psychiatric disorders, in particular depression (Malhi et al. Neuropsychiatric Dis Treatment 2006, 2 165–179). We describe a study of direct current stimulation for the clinical treatment of depression and its neurobiological effects as measured electrophysiologically, in a pilot study conducted at the Black Dog Institute. Transcranial direct current stimulation (tDCS) is a noninvasive technique in which a weak direct current is applied across the scalp to alter the excitability of juxtaposed cortical tissue. The effects on neuronal membranes and neurotransmission persist beyond the periods of stimulation and can be measured using quantitative EEG. Preliminary findings from seven subjects will be presented and the putative mechanism of action discussed. In addition, the literature pertaining to this field will be reviewed with reference to current research in tDCS and emergent findings from modern deep brain stimulation and neurosurgical interventions (Dalgleish et al. Am J Psychiatry 2004, 161 1913–1916).

Different Approaches to Endophenotypes in Schizophrenia

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Overview

The concept that schizophrenia is a grouping of, rather than a single illness, is well accepted. However, it is seldom explored and rarely taken into account when investigating the disorder. This symposium is structured to give a snapshot of different concepts of endophenotypes, starting with those arising from basic research, progressing to an endophenotype associated with a purported risk factor for schizophrenia. We then move into the clinical setting, addressing whether or not testing paradigms define discrete groupings of altered functionality. The symposium ends with a presentation on endophenotypes defined by cognitive testing and the genetic aspect of such deficits.

08-01

Neurochemical endophenotypes of schizophrenia

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A major problem for investigators in the field of schizophrenia research is the difficulty of producing unambiguous results because, at least in part, of schizophrenia being a syndrome comprising of a number of disorders, which all present clinically with similar clusters of symptoms. The symptoms of schizophrenia can be categorized into three clusters: 1) positive symptoms (an excess or distortion of normal functions), 2) negative symptoms (the diminution or loss of normal functions) and 3) cognitive symptoms (deficits in attention, concentration and memory) (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders 2000). The heterogeneity of the schizophrenia syndrome ordains that studies on the disorder generate data that have a 'decreased signal to noise ratio' (Hallmayer et al. Am J Hum Genet 2005, 77 468–476). That is to say, studying the biochemical indexes of a group of disorders gives a less clear outcome than would be obtained by studying a single disorder. It has now been shown that investigating specific phenotypes in the schizophrenia syndrome and comparing results across phenotypes within the syndrome, as well as to those from control subjects, enhances the potential of identifying specific pathogenetic mechanisms (Hallmayer et al. Am J Hum Genet 2005, 77 468–476). We now use this approach of using endophenotypes to increase the capacity of our postmortem research to detect the biological abnormalities that underlie the schizophrenia syndrome.

08-02

Identifying Disease-specific Protein Expression Patterns Within the Syndrome of Schizophrenia

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While schizophrenia has long been recognized as a syndrome, no strong biological basis for segregating the diseases within that syndrome has been elucidated. One of the defining outcomes of disease is changes in the biochemical pathways affected by the disorder. Such changes would be predicted to alter levels of critical proteins in these disease-specific pathway changes. Two-dimensional (2D) electrophoresis now provides the opportunity to identify changes in the levels of multiple proteins in complex biological symptoms and therefore offers the opportunity to identify disease-specific protein footprints in tissue affected by different diseases. This approach has

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