antipsychotics as an adjunctive therapy to mood stabilizers (Yatham Bipolar Disord 2003, 5 7–19), reawakening interest in neurotransmitter dysfunction as a potential basis of the disorder. Morphological studies indicate that there is an apparent disruption in cortical neuronal/glial balance in subjects with bipolar disorder (Rajkowska et al. Biol Psychiatry 2001, 49 741–752; Cotter et al. Cereb Cortex 2002, 12 386–394). Furthermore, impaired executive function suggests that functionality of the dorsolateral prefrontal cortex may be compromised (Martinez-Aran et al. Psychother and Psychosom 2002, 71 39–46). Studies in our laboratory have shown that in the dorsolateral prefrontal cortex, Brodmann's area 9, there is little sign of alterations in neurotransmission as defined by receptor number. However, there are quite profound changes in some of the molecules involved in mediating normal synaptic function. Together, these data suggest that the functionality of this brain region may be disrupted in bipolar disorder.

03-04

Genetic and genomic approaches to better understanding bipolar disorder

PR Schofield[1,2,3,4], IP Blair[2,3], A Chetcuti[1,2,4], EZ McAuley[1,2,3], JM Fullerton[1,2,3], JA Donald[4], PB Mitchell[5,6,7]

[1]Prince of Wales Medical Research Institute, Sydney, New South Wales, Australia; [2]Neuroscience Research Program, Garvan Institute of Medical Research, Sydney, New South Wales, Australia; [3]Faculty of Medicine, University of New South Wales, Sydney, New South Wales, Australia; [4]Neuroscience Institute for Schizophrenia and Allied Disorders, Sydney, NSW, Australia; [5]Department of Biological Sciences, Macquarie University, Sydney, New South Wales, Australia; [6]School of Psychiatry, University of New South Wales, Sydney, New South Wales, Australia; and [7]Black Dog Institute, Prince of Wales Hospital, Sydney, New South Wales, Australia

Background: Bipolar affective disorder (BP) is a severe mood disorder characterized by alternating periods of mania and depression, with estimates of lifetime prevalence up to 4%.
Methods: Studying BP families, genetic linkage analysis has been used to identify susceptibility loci. Positional cloning and association analysis was used to identify the susceptibility gene. Microarray analysis of gene expression profiles of mice treated with antimanic drugs was performed.
Results: The cadherin gene FAT was identified by positional cloning. Association with bipolar disorder was seen in two case-control cohorts with a family history of psychiatric illness, and in two cohorts of parent-proband trios where association was identified among bipolar cases who had exhibited psychosis. Pooled analysis further supported association ($P = 0.0002$, odds ratio = 2.31, 95% confidence interval: 1.49–3.59). Expression of FAT, and putative interacting proteins beta-catenin and the Ena/VASP proteins were investigated in mice following administration of the mood-stabilizing drugs, lithium and valproate. FAT was significantly downregulated ($P = 0.027$), and Catnb and Enah were significantly upregulated ($P = 0.0003$ and 0.005), in response to lithium. Expression of genes encoding murine homologs of the FAT-interacting proteins was investigated by microarray analysis, with eight genes showing significantly altered expression in response to lithium (binomial $P = 0.004$).
Conclusions: Together, these data provide convergent evidence that FAT and its protein partners may be components of a molecular pathway involved in susceptibility to bipolar disorder. Genetic and genomics approaches may provide a means to better understanding the genes involved in BP onset and progression.

03-05

Treatments and outcomes in bipolar disorder

P Joyce

Christchurch School of Medicine and Health Sciences, Christchurch, New Zealand

The treatment of bipolar disorder remains a major challenge. A wide variety of psychopharmacological treatments are available, which are usually considered under the groupings of antimanic drugs, antidepressant drugs and mood stabilizers. In real-life clinical practice, monotherapy is the exception, and the challenge is to obtain rational polypharmacy. Even, with a wide range of available drugs, and a high likelihood of being able to achieve remission from any particular mood episode, the probability of recurrence and/or chronic residual symptoms is high. The greatest therapeutic challenges are in the areas of depressive and mixed symptom states.

PTSD and Neuroimaging: Neural Correlates of Affective, Cognitive and Clinical Response

K Felmingham

The Brain Dynamics Centre, Westmead Millennium Institute, Westmead Hospital and Western Clinical School, University of Sydney, Australia

https://doi.org/10.1017/S0924270800032038 Published online by Cambridge University Press