Conclusions: This study has shown that *Nedd4* and *Kcna1*, genes encoding proteins either forming ion channels or modulating their activity, showed dysregulation following treatment with antipsychotics, which may provide important clues to the pathogenesis of schizophrenia.

The Australian Biomarkers Lifestyle and Imaging flagship study of ageing

K Ellis[1], D Ames[1], R Martins[2], P Hudson[3], C Masters[1]

[1]The University of Melbourne, Melbourne, Australia; [2]Edith Cowan University; and [3]CSIRO, Australia

Background: The potential to optimize treatment and preventative strategies in the delay and prevention of Alzheimer's disease (AD) relies in part on the capacity to make early diagnoses and monitor disease progression. The Australian Biomarkers Lifestyle and Imaging (AIBL) study is a 3-year longitudinal cohort study that aims to improve understanding of the pathogenesis and diagnosis of AD using neuropsychological, neuroimaging and biomarker techniques, and to examine lifestyle and dietary factors associated with AD and healthy aging.
Methods: A total of 1000 volunteers (minimum age 65 years) were recruited, comprising 200 participants from the following groups: 1) AD, 2) mild cognitive impairments, 3) healthy volunteers (ApoE4+), 4) healthy volunteers (ApoE4–) and 5) 'memory complainers' (ie healthy volunteers reporting subjective memory complaints). At baseline and 18 months, all participants received a clinical/neuropsychological assessment and blood biomarker analysis, with a subgroup also receiving [C-11]PIB-PET and magnetic resonance imaging scans. Participants also completed questionnaires assessing diet and exercise patterns, with a subgroup receiving actigraph accelerometer measurement of activity levels and dual-energy X-ray absorptiometry measures of body composition.
Results: Patterns of change in individual measures (neuropsychology, neuroimaging and biomarkers) were examined within each population group. Changes in neuropsychological measures were correlated with neuroimaging and biomarker measures to establish convergent validity.
Conclusions: This forms the largest study of its kind ever undertaken in Australia. The current study identified neuroimaging, biomarker and neuropsychological measurements of longitudinal changes in a large cohort and enhanced knowledge of lifestyle and dietary factors associated with AD and healthy aging.

Clozapine – fatal constipation more common than fatal agranulocytosis

P Ellis[1], M Harrison-Woolrych[2], R McLean[2]

[1]Department of Psychological Medicine, Wellington School of Medicine, University of Otago; and [2]Department Preventative and Social Medicine, University of Otago, New Zealand

Background: Premarketing evaluation of side-effects of medication is too small to evaluate rarer side-effects. This requires effective postmarketing pharmacovigilance. While spontaneous reporting to a national center is encouraged, more active methods are required to recruit larger cohorts of known size so rates of rare adverse events can be estimated.
Methods: The New Zealand Intensive Medicines Monitoring Programme (IMMP) prospectively examines the safety of marketed medicines using prescription-event monitoring methodology. Cohorts of patients are established using prescription data from pharmacies throughout the country. The IMMP obtains reports of adverse events from multiple sources, including from follow-up questionnaires sent to patients' doctors, spontaneous reports from health professionals, pharmaceutical company reports and linkage to national mortality and morbidity databases. An evaluation of atypical antipsychotics using this approach indicated high levels of GI side-effects with clozapine.
Results: A large number of cases of constipation were identified, some severe. Two subjects suffered toxic megacolon, one paralytic ileus, one bowel ischemia requiring resection and one bowel perforation. The latter two subjects died of complications of surgery. Two other subjects were shown to suffer esophageal dysmotility, one requiring surgical intervention.
Conclusions: Clozapine interacts with a range of muscarinic, serotonergic and other receptors to have particularly marked effects on the GI tract. These effects are predictable and can be managed provided adequate inquiry is made into symptoms. Only one New Zealander had died of clozapine agranulocytosis – at least three had died of consequences of constipation.

Age differences in mental health literacy

L Farrer[1], H Christensen[1], LS Leach[1], KM Griffiths[1], AF Jorm[2]

[1]Centre for Mental Health Research, The Australian National University, Canberra, Australia; and [2]ORYGEN Research Centre, The University of Melbourne, Melbourne, Australia

Background: The community's understanding of mental health problems, their risk factors, treatments and sources of help may vary as a function of age.

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Methods: Data are taken from an epidemiological survey conducted with a national clustered sample of 3998 Australian adults. Following the presentation of a vignette describing depression or schizophrenia, respondents were asked a series of questions relating to their knowledge and recognition of the disorder, beliefs about the helpfulness and harmfulness of helping professionals and treatments, likely outcomes and causes, and personal and perceived stigma.
Results: Participant age was coded into five categories and cross-tabulated with mental health literacy variables. Multiple comparisons between the youngest age group (18–24) and all other groups showed that although young adults were better than those aged 70+ at correctly recognizing depression and schizophrenia, they were more likely to misidentify schizophrenia as depression. For those who received the depression vignette, younger adults differed from older age groups in terms of their beliefs about the helpfulness and harmfulness of certain treatments, and personal stigma. Differences were also observed between younger and older adults who received the schizophrenia vignette, specifically for helpfulness and harmfulness ratings, and beliefs about causes.
Conclusions: Differences in mental health literacy across the adult life span suggest that more specific, age-appropriate messages about mental health are required to inform different age groups. The tendency for young adults to 'overidentify' depression perhaps signals the need for awareness campaigns to focus on differentiation between mental disorders.

A randomized double-blind trial of right prefrontal cortex low-frequency transcranial magnetic stimulation in major depression

P Fitzgerald[1], ZJ Daskalakis[2], S Huntsman[3], R Gunewardene[4], J Kulkarni[1]

[1]Alfred Psychiatry Research Centre and Monash University Department of Psychological Medicine; [2]Centre for Addiction and Mental Health, Toronto, Ontario, Canada; [3]Palm Beach Currumbin Clinic, Gold Coast, Queensland, Australia; and [4]Mosman Private Hospital, Mosman, New South Wales, Australia

Background: Low-frequency right prefrontal repetitive transcranial magnetic stimulation (rTMS) appears to have antidepressant properties although the effectiveness of this treatment in clinical practice has not been assessed and the optimal stimulation parameters defined. The boundaries of 'low-frequency' stimulation are not clear.
Methods: A total of 122 patients with treatment-resistant depression were randomized to either 1- or 2-Hz stimulation over right prefrontal cortex (PFC) (one single 15-min train) for 2 weeks. A second 2-week period of treatment was provided for patients showing initial response (>20% reduction in HAMD score).
Results: One hundred eighteen patients received a full 2 weeks of treatment (63 – 1 Hz, 55 – 2 Hz). There was a mean reduction in HAMD scores of 30.1 ± 29.8% in the 1-Hz group and 33.2 ± 31.7% in the 2-Hz group ($P > 0.05$). Seventy-eight patients received a further 2 weeks of treatment. Over the full 4 weeks, there was a reduction in HAMD scores of 62.2 ± 25.1 (1-Hz group) and 61.3 ± 25.2% (2-Hz group) ($P > 0.05$). Thirty of 63 (48%) patients in the 1-Hz group and 29 of 55 (53%) patients in 2-Hz group met response criteria (>50% reduction HAMD score) at study end. There was no difference in clinical response between groups.
Conclusions: Despite a heterogeneous sample, a significant proportion (~50%) of patients met clinical response criteria following treatment. There was no difference in clinical response to 1- or 2-Hz rTMS applied to right dorsolateral PFC. This suggests that 2-Hz right PFC rTMS has antidepressant properties but offers no advantage over 1-Hz stimulation despite a twofold increase in pulse number.

A meta-analytic study of changes in brain activation in depression

P Fitzgerald[1,2], J Maller[1,2], K Hoy[1,2], T Oxley[1,2], Z Daskalakis[3], A Laird[4]

[1]Alfred Psychiatry Research Centre, The Alfred; [2]Monash University Department of Psychological Medicine, Melbourne, Australia; [3]Centre for Addiction and Mental Health, College Street Site, Toronto, Ontario, Canada; and [4]Research Imaging Centre, The University of Texas Health Science Centre San Antonio, USA

Introduction: A large number of studies with considerably variable methods have been performed to investigate brain regions involved in the pathophysiology of major depressive disorder. The aim of this study was to use a quantitative meta-analytic technique to synthesize the results of much of this research.
Methods: Three separate quantitative meta-analytical studies were conducted using the activation likelihood estimation technique. Analysis was performed of studies conducted at rest comparing brain activation in patients with depression and controls, studies conducted of brain changes associated with antidepressant medication treatment and studies comparing brain activation patterns induced by the induction of positive or negative emotion in patients with depression compared with controls.
Results: The results of the study indicated a complex series of areas of the brain implicated in the pathophysiology depression. This included a network of dorsal regions that are hypoactive in depressed subjects and increase in activity with treatment and a corresponding

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