participants were assessed for PTSD, depression, anxiety and alcohol misuse; OI; performed neurocognitive measures of dorsolateral prefrontal, lateral prefrontal and mesial temporal functioning; and completed a self-report assessment of aggression.
**Results:** War veterans with PTSD exhibited significant OI deficits (OID) compared with controls, despite uncompromised performance on tests of verbal fluency, verbal paired associate learning, visuospatial planning and construction, and attention and motor inhibition. OIDs remained after covaring for IQ, anxiety, depression and alcohol misuse. No significant smoking or medication effects were observed. OIDs were significant predictors of aggressive and impulsive behaviour.
**Conclusions:** This research contributes to emerging evidence of orbitoprefrontal dysfunction in the pathophysiology underlying PTSD. This is the first study to report OID as a strong predictor of impulsive and aggressive behaviour in this clinical population. It prompts research to further explore the potential diagnostic utility of OIDs in the assessment of PTSD. Such measures may help delineate the complexity of PTSD symptom presentation and support the targeted interventions for impulsive aggressive behaviour.

## Converging evidence from taxometric analyses confirms a cognitive subtype of schizophrenia with distinct genetic basis

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**Background:** Two distinct schizophrenia subtypes have recently been identified by the Western Australian Family Study of Schizophrenia by grade of membership (GoM) analysis of the phenotype (Hallmayer et al. 2005; Jablensky 2006): one characterized by pervasive cognitive deficit (CD) and low scores on personality trait measures and one featuring significant personality deviations but with relatively intact cognitive performance [cognitively spared (CS)]. Whole-genome scan of 93 families discovered significant linkage to 6p25-22 for the CD subtype, while the linkage for CS subtype was definitively excluded for that region. The aim of this study was to investigate by another method whether differences between these subtypes are qualitative or quantitative.
**Methods:** Several taxometric procedures, originally proposed by P. Meehl (1994, 1996, 1998), were used to analyze taxonicity of schizophrenia subtypes: mean-above-mean-below-a-cut, maximum-eigenvalue and latent mode analyses in a sample of 138 individuals with schizophrenia and schizophrenia spectrum disorders.
**Results:** Three independent taxometric procedures showed consistently a latent taxonomic structure in our sample of patients with schizophrenia. Estimated mean base rates for CD taxon ranged from 0.37 to 0.43, suggesting that about 40% of patients with schizophrenia belong to this taxon.
**Conclusions:** CD schizophrenia subtype is discrete, that is, taxonic. Taxometric analyses have further corroborated the existence of an etiologically discrete schizophrenia subtype.

## Coregulation of genes in the mouse brain following antipsychotic drug treatment

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**Background:** Schizophrenia is a major psychiatric disorder that affects approximately 1% of people during their lifetimes. Antipsychotic drugs are the most effective treatment for the psychotic phase of schizophrenia, although their mechanism of action remains largely unknown.
**Methods:** We have treated mice with one of three antipsychotics to create animal models of antipsychotic drug action. Control mice were treated with saline. Drug treatment was performed by means of daily intraperitoneal injections for 1 and 4 weeks. RNA was extracted from the brains of these mice and hybridized to whole-genome microarray chips. Validation of mRNA expression changes in selected genes was undertaken using quantitative polymerase chain reaction (PCR) and protein expression was investigated using Western blot analysis.
**Results:** Data analysis showed that many genes were dysregulated by antipsychotic drug treatment, including those involved in signal transduction, synaptic transmission and neurogenesis. Genes were selected for further analysis based upon their coregulation by different antipsychotics, chromosomal location or known molecular function. Changes in gene expression were confirmed for 13 of 19 genes thus far analyzed by quantitative PCR. Western blot analysis indicated that these changes in mRNA levels are translated into protein expression changes in at least two genes; neural precursor cell developmentally downregulated gene 4 (*Nedd4*) and potassium voltage-gated channel, shaker-related subfamily, member 1 (*Kcna1*).



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**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

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**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

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**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

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**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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