

## Patterns and predictors of aggressive incidents in children and adolescents admitted to a mental health in-patient unit

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**Background:** Aggression is a common clinical issue arising during treatment of young people with mental health problems. Poorly managed aggressive behaviours can compromise the therapeutic environment and pose a safety risk to patients and staff. The aim of this study was to understand patterns and predictors of aggressive behaviour in young people admitted to an in-patient psychiatric unit.

**Methods:** All patients admitted to the Mater Child & Youth Mental Health Service Inpatient Unit between October 2004 and December 2005 were monitored for aggressive behaviours. Incidents were documented prospectively by clinical staff. Documentation incorporated nature of the incident, time, location and response. Demographic and clinical characteristics were collected from charts for all patients.

**Results:** During this time, 377 incidents were documented involving 40 patients (range 1–88 incidents per patient). About 23% of admissions were associated with aggressive behaviour. Thirty-six per cent of incidents involved violence toward staff. Compared with nonaggressive patients, aggressive patients were younger ( $P < 0.001$ ), were more likely to be men ( $P < 0.01$ ), have a history of aggression ( $P < 0.05$ ) and were more likely to be receiving psychotropic medications at admission ( $P < 0.001$ ). Aggression patients were more likely to have a diagnosis of mental retardation, pervasive development disorders and attention deficit hyperactivity disorder (ADHD), and less likely to have a mood disorder ( $P < 0.001$ ).

**Conclusions:** Young people most at risk of aggression appear to be younger men, with a diagnosis of mental retardation, development disorders or ADHD, and a history of aggressive behaviours. Further research is required to optimize prevention and management of these behaviours.

## Antidepressants in children and adolescents – changes in utilization after safety warnings

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**Background:** Antidepressants, in particular selective serotonin reuptake inhibitors (SSRIs), are one of the most commonly used classes of psychotropic drug in children and adolescents. In 2003, emerging evidence suggested that antidepressants may increase risk of suicidal behaviour in young people. This evidence was accompanied by national and international guidelines cautioning against use of many antidepressants in young people. This study aimed to assess whether these safety warnings have impacted upon antidepressant utilization rates.

**Methods:** This study was based at a metropolitan health service incorporating children's and adult hospitals. Total service utilization of antidepressants was extracted from pharmacy software for the period January 2002 to December 2005. Monthly utilization rates were computed for adults and children's services as defined daily doses per occupied bed days. Changes in utilization over time were compared for children and adults.

**Results:** There was a significant relationship between time and antidepressant utilization in children and adolescents, where antidepressant use decreased over time ( $R = 0.416$ ,  $t = -3.11$ ,  $P < 0.01$ ). In contrast, there was a trend suggesting a minor increase in use of antidepressants over time in adults ( $R = 0.262$ ,  $t = 1.84$ ,  $P = 0.072$ ). In children, there was a reduction in use of all SSRIs, except for fluoxetine, which exhibited a small increase in use.

**Conclusions:** National and international warnings about safety of antidepressants in children and adolescent appear to have influenced utilization of these medications. Further research is required to determine optimal utilization rates.

## Orbitofrontal dysfunction and aggression in war veterans with post-traumatic stress disorder

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**Objectives:** To examine olfactory identification (OI) ability in war veterans with post-traumatic stress disorder (PTSD) as a probe of putative orbitofrontal dysfunction and to explore the utility of OI ability in predicting aggressive and impulsive behaviour in this clinical population.

**Methods:** Participants comprised 31 out-patient male war veterans with PTSD (mean = 58.23 years, SD = 2.56) recruited from a Melbourne Veterans Psychiatry Unit, and 31 healthy age- and gender-matched controls (mean = 56.84 years, SD = 7.24). All

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 orbitofrontal 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.

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## 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.

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## 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*).