Clinical characterization of brain tissue for neuroscience research: a comparison of antemortem and postmortem diagnoses

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Background: The validity of postmortem human brain research relies upon accurate clinical and psychopathological diagnosis. Current literature shows few instances where standardized diagnostic assessment tools such as the Diagnostic Instrument for Brain Studies (DIBS) have been used. The present study investigates the degree of concordance between predominant antemortem psychiatric diagnoses indicated in medical records and postmortem diagnoses derived through structured diagnostic instruments such as the DIBS and the Item Group Checklist (IGCL) of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN).

Methods: Fifty-eight subjects from the New South Wales Tissue Resource Centre with a recorded diagnosis of mental illness during their lifetime were included in the study. The predominant antemortem psychiatric diagnosis of each case was compared with its corresponding postmortem diagnosis obtained through structured case reviews to which either the DIBS or the IGCL of the SCAN were applied. Demographic variables such as age of illness onset, and alcohol or other drug use were also examined.

Results: Comparison of diagnoses obtained from these two approaches produced an overall kappa coefficient of 0.66. Kappa coefficients for the schizophrenia cohort were 0.61, 0.35 for the schizoaffective cohort, 0.95 for the major depressive disorder cohort and 0.70 for the bipolar disorder cohort.

Conclusions: These results indicate moderate to excellent interrater reliability for most cohorts in this sample. There is sufficient disagreement, however, particularly in the schizoaffective cohort, to suggest the value of applying standardized and structured assessment to enhance both the accuracy of diagnosis and the prospective validity of tissue-based research.

Delirium outcomes: is this a time-limited disorder?

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Background: Delirium has classically been defined in relation to dementia, at least in its temporal dimension, delirium being a short-term condition, dementia long term. From the earliest accounts in the ancient medical literature to the contemporary DSM-IV-TR definition, it has been conceptualized as a time-limited process. It is also firmly established in the literature that delirium is underrecognized.

Methods: A literature search was undertaken using PubMed database covering the years 1966–2006 and using search terms that included delirium, organic brain syndrome, outcome, subsyndromal and identification.

Results: When compared with patients who did not suffer from delirium, delirium is associated with significantly greater mortality, higher rates of long-term cognitive impairment, greater length of stay and increased rates of institutional placement. These poor outcomes appear to hold for subsyndromal delirium as well as frank delirium. It is plausible to suggest that unrecognized delirium is associated *a fortiori* with poor outcomes, but as yet there is no firm evidence that early detection results in better outcomes.

Conclusions: The definition of delirium as a short-term condition needs to be reevaluated. It could be speculated that its conceptualization as time limited may contribute to it's underrecognition because there may a little risk associated with missing a condition that is expected to resolve. In this case, it is expected that improved education for health professionals about the serious consequences and long-term course of delirium may result in improved detection and management of this disorder.

Mismatch negativity in schizophrenia: effect of probability, deviant type and duration of illness

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Background: A reduced amplitude mismatch negativity (MMN) component of the auditory event-related potential (ERP) is repeatedly observed in individuals with schizophrenia. MMN amplitude also declines significantly with age in healthy adults. Our group is endeavoring to understand whether the factors underlying MMN reduction are common or unique. In this study, we explored the effect of deviant probability on group differences.

Methods: ERPs were recorded from 43 individuals diagnosed with schizophrenia and 42 age-matched

controls. Sound sequences containing duration, intensity and frequency deviant sounds at low (6%) or high (20%) probability were presented while participants viewed a movie with low-level soundtrack.

Results: A repeated-measures ANOVA was used to compare MMN amplitude across groups (patients/controls) and deviant type (duration/frequency/intensity) and probability (low/high) with age as a covariate. There were significant main effects of probability and deviant type both modified by age and a main effect of group modified by probability. Patients produced significantly smaller MMN responses to low- but not high-probability deviants. Age was a significant covariate in the low-probability but not the high-probability condition with the differences being more pronounced for frequency and intensity MMN than duration MMN.

Conclusions: MMN amplitude was significantly reduced in schizophrenia vs. controls for the low-probability condition only (ie when under conditions of increased repetition of the standard sound). The age-related decline in MMN was also most pronounced under these conditions. The results are discussed with respect to current research into memory-based and discrimination-based conceptualizations of the MMN.

Depression and anxiety in cardiac rehabilitation patients: characteristics, treatment and outcome

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Background: The past decade has seen a growing body of evidence to support independent links between depression and coronary heart disease. Despite this evidence, depression is rarely assessed in cardiac rehabilitation programs and there are few published studies of psychological interventions for depression with this population. The aim of the present evaluation was to first determine levels of depression and anxiety symptoms among cardiac rehabilitation patients in John Hunter Hospital (JHH), Newcastle, and second to link those scores with demographic, lifestyle and medical variables. Additionally, it was aimed to evaluate a group cognitive behaviour therapy intervention (BraveHeart), specialized for treatment of depression in people with cardiac disease.

Methods and Results: The Hospital Anxiety and Depression Scale is being used to screen cardiac rehabilitation patients at JHH at week 4 of their program. Over 650 patients have been screened with this tool, with results suggesting that around a third are experiencing significant levels of anxiety and/or depression. These scores have been linked with available patient information kept on an epidemiological database, the Heart and Stroke Register, to determine the characteristics and medical outcome of those with high vs. low symptom scores. A randomized controlled trial of BraveHeart has commenced and preliminary data from the study will be presented.

Conclusions: Results from screening support prior research suggesting that significant levels of emotional distress exist among cardiac rehabilitation participants. Depression is known to lead to worse outcomes among this patient population, and development of efficacious psychological treatments is indicated.

Differential effects of antipsychotic drugs on serotonin-1A receptor-mediated disruption of prepulse inhibition

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Background and Methods: Serotonin-1A (5-HT1A) receptors have been implicated in the symptoms of schizophrenia. However, there is limited *in vivo* evidence for an interaction of antipsychotic drugs with 5-HT1A receptor-mediated behavioural effects. We therefore investigated in rats the action of several antipsychotic drugs on prepulse inhibition (PPI), a measure of sensorimotor gating, which is deficient in schizophrenia. Disruption of PPI was induced by treatment with 0.5 mg/kg of the 5-HT1A receptor agonist, 8-hydroxy-di-propyl-aminotetralin (8-OH-DPAT).

Results: In rats pretreated with 0.25 mg/kg of haloperidol or raclopride, the disruption of PPI was no longer significant. Of the atypical antipsychotic drugs clozapine, olanzapine, risperidone, amisulpride and aripiprazole, only aripiprazole significantly reduced the effect of 8-OH-DPAT on PPI. This effect was mimicked by pretreatment with the 5-HT1A receptor partial agonist, buspirone. On the other hand, some of the antipsychotic drugs and other pretreatments showed complex, prepulse-dependent effects on their own, both on PPI and prepulse facilitation at the 30 ms ISI (clozapine, risperidone, amisulpride) and PPI at the 100 ms ISI (olanzapine, risperidone, MDL 73,005EF).

Conclusions: These data show little *in vivo* interaction of several atypical antipsychotic drugs with the