Prefrontal N-acetylaspartate:creatine ratio predicts functional outcome eighteen months after a first psychotic episode

S. J. Wood[1,2], G. Berger[3], D. Velakoulis[1], P. Conus[3], G. W. Stuart[1], M. Lambert[3], P. D. McGorry[3], P. Desmond[4], C. Pantelis[1]

[1]Melbourne Neuropsychiatry Centre, University of Melbourne, Melbourne, VIC, Australia, [2]Brain Research Institute, Melbourne, VIC, Australia, [3]Orygen Research Centre, Department of Psychiatry, University of Melbourne, Melbourne, VIC, Australia, [4]Department of Radiology, Royal Melbourne Hospital, Melbourne, VIC, Australia

Introduction

Psychotic illnesses such as schizophrenia often cause significant psychosocial impairment. However, the long-term outcome of these disorders is not uniform, and prognostic indicators are required which allow treatment to be tailored to the individual. Previous research has identified a number of demographic or symptom-based predictors, such as age of onset, gender, and symptoms at onset (with an emphasis on negative symptoms). By comparison, there are few studies that use data from brain imaging to predict outcome, despite the fact that structural brain abnormalities have been consistently demonstrated in patients with chronic schizophrenia, and associated with severity of symptoms. Those that do exist generally fail to demonstrate predictive value of baseline volumetric data (eg Milev et al, 2003). One possibility is that structural imaging fails to capture information about underlying neuronal integrity. To this end, we have used magnetic resonance spectroscopy to obtain data about the biochemical nature of the medial temporal and prefrontal regions in first episode psychosis, and then utilised this data to predict functional outcome 18-months after first admission.

Methods

Thirty-nine first-episode psychosis patients (61.5% male; mean age = 21.3 ± 3.1 years) were recruited from the Early Psychosis Prevention and Intervention Centre (EPPIC), ORYGEN Youth Health, Melbourne, Australia. Symptoms were rated using the Positive and Negative Symptom Scale (PANSS) and scores computed according to the five factor model comprising Negative Symptoms, Cognitive Disturbance, Antisocial Tendency, Delusions and Hallucinations, and Affective Symptoms (Stuart et al, 2001).

Proton spectra were acquired using a 1.5T scanner (GE, Milwaukee) at the Royal Melbourne Hospital. Two volumes of interest (dimensions 15 x 15 x 15 mm) were obtained from the left hemisphere in each subject, one in the left medial temporal lobe and one in the left middle frontal gyrus. Shimming was performed by an automated global shim, and water suppressed spectra acquired using a point-resolved spectroscopy sequence (PRESS; TR = 1500ms, TE = 135ms, NEX = 128). Spectra were analysed using LCModel (Provencher, 1993), and data are reported as the ratio of N-acetylaspartate (NAA; 2.01 ppm) over the creatine/phosphocreatine peak (Cr; 3.02 ppm).

Outcome data (remission of psychosis, number of inpatient admissions and Global Assessment of Function (GAF)) were obtained by file review as part of the FEPOS study (Lambert et al, 2002) in which the files of all the patients treated in EPPIC between 1998 and 2000 (n=786) were reviewed by two experienced psychiatrist. Validity of the data was established by comparison of ratings on a subset of patients who were included in prospective studies. Inter rater reliability was established by independent rating of 40 files randomly selected and stratified for time with kappa ranging from 0.80 to 0.90.

Results

Three regression models were constructed. For remission from psychosis, binary logistic regression was conducted, which indicated that only Negative Symptoms were predictive of outcome ($p=0.03$). For number of admissions over the follow-up period, the linear regression model incorporated prefrontal NAA/Cr ($p=0.007$) and Age at Onset ($p=0.013$), such that lower values for both variable were associated with more admissions. Finally for the GAF score, the linear regression model incorporated prefrontal NAA/Cr ($p=0.031$), Negative Symptoms ($p=0.001$), Premorbid GAF ($p=0.002$) and Antisocial Tendency ($p=0.021$).

Discussion

These data indicate that psychotic remission *per se* is predicted by the baseline level of negative symptoms. However, more descriptive measures such as the number of inpatient admissions and the GAF score after 18 months are predicted by baseline spectroscopic measures of prefrontal neuronal integrity, along with other demographic and symptomatic variables. This suggests that patients at increased risk for poor outcome are those with greater prefrontal pathology at first presentation.

References

Lambert M et al. Acta Psychiatrica Scandinavica 2002; 413: 45
Milev P et al. Biological Psychiatry 2003; 54: 608
Provencher SW. Magnetic Resonance in Medicine 1993; 30: 672
Stuart GW et al. Schizophrenia Research 2001; 49: 23