

CLOZAPINE AND THE NEUROPSYCHOLOGY OF SCHIZOPHRENIA

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There is some evidence that the syndromes of schizophrenia may be secondary to the specific neuropsychological deficits which have been characterised in this disease. Clozapine's (CLOZ) superior antipsychotic efficacy may lie in the amelioration of such deficits, which may not be susceptible to conventional treatment. This is an ongoing naturalistic prospective study recruiting treatment resistant inpatients who commence CLOZ or continue treatment as usual (TAU). Group membership is decided on clinical grounds, e.g. felt reasonable to await further 24 months for CLOZ, refusal of/unfit for CLOZ. Some patients have crossed over groups, acting as their own controls. Very detailed assessments take place at baseline, 6, 12 and 24 months: clinical (syndromes and motor disorder), neuropsychological (general cognition, memory, executive function) and social (social/self care abilities, behaviour problems, global rating). Neuropsychological and social function assessments are made independently of clinical ratings. Baseline assessments have not differed significantly between CLOZ and TAU groups. 6 month data (8 CLOZ, 12 TAU) and 12 month data (5 CLOZ, 8 TAU) showed significant improvements in global cognition, memory and executive function, negative symptoms and behaviour problems on clozapine: there were no improvements on any assessment with TAU. However, there was no simple correspondence between improvements in syndromes and improvements in aspects of cognition, the former appearing to precede the latter contrary to theoretical expectations. The most marked improvements were in global social function and behaviour problems. Clozapine appears to have a general 'humanising effect' rather than specific actions on a neuropsychological substrate. I will report further 6 month (14 CLOZ, 12 TAU) and 12 month findings (9 CLOZ, 10 TAU) plus preliminary 24 month data (4 CLOZ, 6 TAU).

CPT-LINKED SCHIZOPHRENIA VULNERABILITY, PSYCHOSIS PRONENESS AND FRONTAL DYSFUNCTION IN NORMAL ADOLESCENTS

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Introduction: Schizotypy, as a construct referring to liability to schizophrenia, is becoming nowadays a hot spot in schizophrenia research. Following the new strategies in the investigation of the high risk for schizophrenia condition (strategies that involve detection of schizotypic individual in the general population through a *psychometric high risk strategy*), we have studied a sample of 1498 (774 males and 724 females) normal adolescent junior highschool students randomly selected from the educational center census of Barcelona.

Methods: The main goal of this study was to examine the performance on frontal lobe tests of a group of normal adolescent subjects (Control group) and a group of subjects psychometrically defined as schizotypics (Index group) using a double criterium: 1) Continuous Performance Test identical pairs version (CPT-IP, Cornblatt et al., 1988) -linked attentional deficit vulnerability and 2) a psychosis proneness measured with the Chapman's Perceptual Aberration Scale (PAS, Chapman et al., 1978) and the Social Anhedonia Scales (SAS, Chapman et al., 1976). The original sample (1498) was examined with the CPT-IP. The worst CPT-IP performers (lowest 10%, i.e. bottom decile) were selected and constituted our 'Index group' (n = 162). A group of matched (sex, age, schoolroom) subjects with

normal CPT-IP performance were selected and formed the 'Control group' (n = 140). These subjects (n = 302) were then assessed with two measures of 'psychosis-proneness', the SAS and the PAS, and a frontal-lobe tests battery which included the Wisconsin Card Sorting Test (WCST), the Trail Making Test (TMT forms A and B) and a word generation test. The 10% highest and lowest PAS and SAS scorers (i.e. top and bottom deciles) of the working sample (n = 302) marked the cut-off points to classify 'low/high-PAS' and 'low/high-SAS' subjects. We hypothesized that 'schizotypic' adolescents, defined by their CPT-linked schizotypy vulnerability and by their proneness to perceptual distortions and social anhedonia, would show subtle defects in frontal lobe function compared with control subjects.

Results: Results show that Index subjects obtained higher scores on the psychosis-proneness measures (PAS and SAS), even though the difference was only statistically significant for the SAS scores. We also found that Index subjects performed worse in all the frontal-lobe tests when compared to control subjects. Most of the measures reached statistical significance. A one-way analysis of variance showed that subjects with both CPT-linked vulnerability and psychosis proneness were the worst performers when compared with subjects with only one or none of these conditions. These results suggest the existence of a subtle frontal lobe dysfunction in 'normal' adolescents that are at increased risk for schizophrenia. Our results agree with current theories that hypothesize a possible frontal-limbic dysfunction latent in the schizophrenia spectrum disorders.

COGNITIVE NEUROPSYCHOLOGY OF DELUSIONAL MISIDENTIFICATION SYNDROMES

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Introduction: Recent cognitive neuropsychological studies of the delusional misidentification syndromes (DMI) have demonstrated face recognition impairments associated with right hemisphere (RH) dysfunction. Cases of DMI have also been reported in which recognition impairments have been associated with items other than faces. We decided to determine whether these impairments in RH function extended beyond faces to another category (animals) in which high levels of within-category visual similarity exists.

Method: DMI cases, each diagnosed with paranoid schizophrenia and identified as having Fregoli syndrome were selected on the basis of earlier clinical interviews. Fregoli syndrome is characterised by the delusional belief that a familiar person has adopted a disguise, thus, whilst appearing as a different person in physical terms, the identity of the person remains unchanged. A group of age- and education-matched paranoid schizophrenic controls were selected from the same patient pool. None had experienced any reported episode of delusional misidentification. The performance of a group of age-matched nonpsychotic subjects is also reported. Pairs of computer-stored stimuli were presented to either the left (LVF) or right visual field (RVF) in a forced-choice format. The subject's task was to indicate whether they were the same (i.e. identical) or different. Exposure duration for the test stimuli was 160 ms (to control for eye-movements). Reaction time and error rates were recorded.

Results: No group showed a visual field preference for the inanimate stimuli. However, we found a LVF/RH processing advantage for the animate stimuli amongst both our set of normals and psychotic controls. The DMI-group on the other hand showed an abnormal RVF/LH preference for this class of stimuli.

Conclusions: We have shown that the DMI group are impaired with the processing of animal stimuli. This deficit was observed during the non-psychotic phase of the disorder, suggesting a sustained rather than a transitory impairment. Explanations of DMIs should