

## **Pursuit eye movement dysfunction in schizophrenia: Characteristics of oculomotor disturbance and diagnostic specificity**

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Abnormalities of visual pursuit are among the most robust psychobiological abnormalities observed in schizophrenia. These abnormalities are present and associated with schizotypal characteristics in relatives of affected probands, suggesting that the abnormality is a familial marker for the illness. Yet, the diagnostic specificity of the abnormality has not been well studied, and the neurophysiologic significance of the abnormality is not understood. Therefore, we studied pursuit performance in 101 schizophrenic inpatients (19 never medicated), 18 unmedicated manic inpatients (DSM-III-R diagnoses), and 46 age and sex-matched normal controls. Patients visually tracked a cursor oscillating at 0.4 Hz for 30 second trials in a block room. Performance was quantified by assessing the relative velocity of pursuit eye movements (gain), and the frequency of two forms of intrusive saccades that interrupt pursuit: square wave jerks (SWJ) and anticipatory saccades.

Pursuit gain of both manic and schizophrenic patients was significantly lower than in normals, but the impairments were of a similar order of magnitude. It was expected that schizophrenics would show more SWJ, as is the case in several neurological disorders involving disease of the frontal lobe or basal ganglia where there is a failure to suppress irrelevant saccades. Contrary to this expectation, schizophrenic patients demonstrated fewer SWJ than the other groups. The sub-sample of 19 never-medicated acutely-disturbed schizophrenics had higher leftward than rightward pursuit velocity and more rightward SWJ, suggesting greater relative left hemisphere activation in these patients. Manic patients demonstrated a significant increase above normal levels in anticipatory saccades, while schizophrenic patients did not.

Schizophrenic patients with fewer SWJ had poorer adult social adjustment and earlier onset of illness, and more perseverative errors on the Wisconsin Card Sort, poorer verbal list learning, and poorer perception of line orientation. Thus, reduced SWJ may identify a group of more severely affected cases. In schizophrenics, low gain was unrelated to symptom indices, but was related to impairments on cognitive tests – Trails B, Judgement of Line Orientation (JLOT) and Digit Span.

The results indicate that different forms of pursuit disturbance occur in manic and schizophrenic patients, and that in schizophrenics pursuit impairments were associated with neuropsychological dysfunctions. Lateralized disturbances of pursuit suggesting greater relative left hemisphere activation occur in the acute phase of illness, consistent with findings from studies that have used other cognitive and neuroimaging assessment strategies.

## **Sleep encephalographic studies in schizophrenic patients: Comparison of neuroleptic-naive and previously-medicated patients with healthy controls**

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Investigations of schizophrenic patients by polysomnography have yielded variable findings, including impaired sleep continuity, decreased slow-wave sleep (SWS), and shortened REM latency. In order to better characterize polysomnographic abnormalities in schizophrenia and investigate their clinical correlates and relationships with ventricle-brain ratios (VBR), we undertook sleep EEG studies of 19 drug-naive and 20 previously-treated, but drug free for at least 2 weeks, schizophrenic patients diagnosed by SADS/RDC and DSM-III-R and studies in their own hospital beds. The patients were rated with BPRS, HRSD and SANS in the drug-free state. We compared the patient group to 15 healthy controls. Both the neuroleptic-naive and previously-treated schizophrenics showed impaired sleep continuity, shortened REM latency and increased REM density in the first REM period when compared to the normal controls. Compared to both the neuroleptic-naive patients and the healthy controls, the previously-treated group had a greater percentage of stage-two sleep and shorter REM latency. The duration drug-free had a significant effect, with the group

drug-free from 2 to 4 weeks ( $n = 9$ ) having a greater percentage of REM sleep and greater first period REM density than the group drug-free for more than 4 weeks ( $n = 11$ ). In the previously-medicated group, but not in the neuroleptic-naïve group, REM latency had a strong inverse correlation with global severity by BPRS ( $r = 0.59$ ,  $p < 0.005$ ) and with negative symptoms by SANS ( $r = 0.70$ ,  $p < 0.001$ ) but not depressive symptoms (by HRSD). SWS did not differ among any of the groups and did not correlate with any clinical parameter. VBR did not correlate with any sleep parameter. Although our results suggest that careful attention be paid to the drug-status of patients in sleep EEG studies, additional longitudinal studies need to be carried out to assess more precisely the effects of medications and their withdrawal. Our results are consistent with hypothesized cholinergic/dopaminergic interactions in the pathophysiology of positive and negative symptoms in schizophrenia.