FUNCTIONAL CORTICAL ABNORMALITIES DURING SMOOTH PURSUIT EYE MOVEMENT IN SCHIZOPHRENICS — A NEUROACTIVATION STUDY WITH ^{99m}Tc-ECD SPECT

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Background: A characteristical eye tracking abnormality with an increased number of saccadic intrusions during smooth pursuit eye movements (SPEM) has been described in 60–80% of schizophrenic subjects. In this context saccade related neural activity was observed in centers of the frontal cortex. Further evidence suggests that the frontal eye field (FEF) is critical for the performance of saccades. To evaluate the role of the FEF for cortical saccadic control we performed activation studies using high resolution single photon emission tomography (SPECT) and compared the results with resting patterns.

Methods: 18 schizophrenic patients were diagnosed according to DSM-IV criteria. Psychopathological symptoms were assessed on the BPRS, SANS and SAPS Scale. Neuroophthalmological and electrooculographic examinations were carried out in all patients. Under resting conditions and following an activation with a horizontally oscillating visual target (Nicolet Nystar Plus Task Design), 750 Mbq ^{99m}Tc-ECD were intravenously given and SPECT images were accomplished 1 h after injection. Neuroactivation images were calculated by subtracting resting from activation patterns and rCBF values compared by statistical parametric mapping (SPM 95). Tailarach atlas coordinates were used for SPM projections. For identifying anatomical structures SPECT images were fused with MRI data.

Results and conclusion: The calculated images showed hot spot areas in the primary visual cortex (SC), temporal, unilateral frontoparietal (FEF), in the left dorsomedial frontal region (SEF) and to a smaller degree in the basal ganglia and cerebellum. This activation pattern is in coincidence with the known functional anatomy active during the generation of saccades, visual attentional processing for saccades and visual motion processing. In addition, reduced enhancement rCBF values ($p < 0.05$) in several subjects presenting an increased number of saccadic intrusions was observed within the frontal eye field (FEF) and might indicate a functional impairment of the FEF to suppress inappropriate saccades towards a visual stimulus. Our data seem also to confirm the possibility to visualize functional well defined areas of the ocular motor system with SPECT by using specific task designs.

DISTURBED TEMPERATURE SENSITIVITY IN SCHIZOPHRENIC PATIENTS WITH A NEGATIVE SYNDROME

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The clinical observation that the sensitivity to temperature and pain is disturbed in various psychic disorders is well known. There are corresponding studies on patients with eating disorders. Every doctor has noticed that there are psychotic patients who do not dress according to the outside temperatures, they wear warm clothes when the temperatures are high and light clothing when temperatures are low.

In our study we attempted to objectify these clinical observations. The study was carried out using the Path-Tester MPI 100. Thereby the thresholds of warm and cold stimuli were measured as well as sensitivity to pain. 30 healthy subjects and 27 patients diagnosed as schizophrenic according to DSM-III-R were tested. All patients had not had any medication for at least two months prior to the study, there was no history of medication, drug or alcohol abuse, neuropathy or thyropathy. Based on the positive and negative syndrome rating scale (PANSS), the patients were divided into two groups: those with a positive syndrome (Crow Type I) and those with a negative syndrome (Crow Type II):

When comparing the results of the healthy subjects and the schizophrenic patients, there are significant differences in the warm and cold threshold but not the pain threshold ($p = 0.019$; 0.037; 0.760). When comparing the results of the healthy subjects with the two schizophrenic sub-groups, there are only significant differences between the healthy subjects and schizophrenics with the negative syndrome and between the two sub-groups of schizophrenic patients. This shows that the temperature sensitivity is disturbed in schizophrenic patients with a negative syndrome (Crow Type II) but not in those with a positive syndrome.

PHARMACOLOGY OF 'SEROQUEL' (ICI 204,636): AN ATYPICAL CLOZAPINELIKE ANTIPSYCHOTIC

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'Seroquel' (ICI 204,636) is a new antipsychotic drug that resembles clozapine in a broad range of pharmacologic tests predictive of antipsychotic activity and extrapyramidal side effects (EPS) or tardive dyskinesia (TD). In receptor binding, ICI 204,636 interacts with multiple neurotransmitter receptors including dopamine (DA) D_1 and D_2 (IC_{50} = 1243 and 329 nM, respectively), serotonin 5-HT_{1A} and 5-HT_{2A} (IC_{50} = 720 and 148 nM, respectively), adrenergic $\alpha 1$ and $\alpha 2$ (IC_{50} = 90 and 270 nM, respectively), and histamine H_1 receptors (IC_{50} = 30 nM). ICI 204,636 has no appreciable affinity for muscarinic and benzodiazepine receptors (each $IC_{50} > 5000$ nM). In behavioral tests, ICI 204,636 blocks conditioned avoidance in primates with potency greater than clozapine, and reverses the behavioral effects induced by DA agonists in mice, rats, cats, and monkeys. Like clozapine, it produces only weak catalepsy at doses that antagonize other DA agonist-induced behaviors. In electrophysiologic tests, ICI 204,636 reverses the inhibitory effects of amphetamine on midbrain DA cell firing with limbic selectivity. Neurochemical indices of D_2 receptor blockade, eg, increase in DA metabolites in brain, could also be demonstrated. ICI 204,636 also meets other pharmacologic criteria that indicate clozapinelike properties. These include low affinity for the D_2 site and greater 5-HT_2/5-HT_6 relative to D_2 ratios, limbic selectivity as evidenced by depolarization blockade of A10 but not A9 DA-containing cells after 28 days' administration, a tendency to produce nonsustained elevations in plasma prolactin levels, minimal dystonic liability in haloperidol-sensitized and drug-naive monkeys, full substitution for clozapine in drug discrimination tests in squirrel monkeys, selective limbic expression of the early gene products c-Fos and FosB, reversal of apomorphine and PCP-induced disruption of prepulse inhibition, reversal of social isolation induced by amphetamine in monkeys, and clozapinelike actions in the Paw Test. The pharmacologic profile of ICI 204,636 predicts that this agent should have atypical antipsychotic actions including enhanced efficacy, compared with standard agents, and minimal EPS and TD liability.

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