investigators have found evidence of progressive deterioration in SBA’s in patients who are treatment refractory. We will be examining the association of duration of illness, treatment response and positive and negative symptoms with structural brain abnormalities in 57 schizophrenic patients compared to healthy controls matched for age, SES, gender and handedness. The first patient group has less than 5 years duration of illness (n = 32) and the second patient group will be chronic patients who have more than 10 years duration of illness (n = 25). MR images will be processed using MRX software. This software can employ the contrasts from both images of a dual echo set (proton density and T2 weighted images) to segment tissue types. Volumetric assessments will be made for the whole brain volume, total brain white and gray matter, gray and white matter in the left and right hemispheres, total ventricles, left and right lateral ventricles, 3rd ventricle, hippocampal complex (hippocampus-amygdala), caudate nucleus, and putamen. We hypothesize that: (1) treatment refractory patients will have more SBA’s than treatment responsive patients and (2) within the treatment refractory group, longer duration of illness will be associated with more structural brain abnormalities, and this will provide evidence supporting the hypothesis of progressive deterioration in treatment refractory patients.

85. DISTURBANCES OF AUDITORY INFORMATION PROCESSING IN SCHIZOPHRENIA REFLECTED BY MMN

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Cognitive dysfunction in schizophrenia is associated with disturbances of working memory systems. The mismatch negativity (MMN), a short latency event-related potential, can be used as an objective measure of echoic memory. Reduction of MMN in schizophrenia patients has been shown in several studies. Effects of the antipsychotic medication are discussed controversially. The mismatch negativity (MMN), elicited by an auditory odd-ball paradigm with rare (20%) deviant 1200 Hz stimuli and 1000 Hz standards, was recorded in frontal and central electrode sites. Fifty-seven schizophrenia patients and forty-four healthy controls were included. Never medicated: n = 11 and 36 medicated patients (typical neuroleptics: n = 12, risperidone: n = 24). The MMN amplitude was measured as the first negative peak of the difference wave obtained by subtracting ERP’s for standards from those for deviants.

The MMN amplitude was significantly reduced in patients compared to controls. Furthermore, patients medicated with typical neuroleptics exhibited a significantly lower MMN amplitudes than did unmedicated patients. Never medicated patients exhibited lower MMN amplitudes in central electrode sites, whereas MMN amplitudes in frontal electrode sites were higher compared to controls.

The present findings support the hypothesis of an impairment in automatic processing of auditory stimuli in schizophrenia reflected by the MMN and indicate differential influences of antipsychotic medication on auditory echoic memory functions. Further research is necessary to elucidate, why never medicated patients exhibit higher MMN amplitudes in frontal sites. This might reflect an overexcitatory processing of auditory stimuli.

86. EFFECTS OF MEDICATION ON N100 TOPOGRAPHY IN SCHIZOPHRENIA

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N100 is an event related potential (ERP) component appearing about 100 ms after an auditory stimulus. In schizophrenia patients a deficit in auditory information processing is assumed, which has been shown for an earlier ERP component, the P50, as well as for later components, e.g., the mismatch negativity (MMN) or the P300.

Forty-nine schizophrenia patients (24 unmedicated, 25 treated with antipsychotic medication) and thirty-nine healthy controls were investigated. ERPs elicited by an auditory odd-ball paradigm were recorded according to the 10/20 system. Frequent stimuli (80%) consisted of 1000 Hz sounds (75 dB SPL), rare stimuli (20%) of 1200 Hz sounds (75 dB SPL). Mean amplitudes were normalized by a scaling procedure. Peak amplitudes as well as mean amplitudes were analysed with multifactorial ANOVAs.

The total group of schizophrenic patients showed significantly lower N100 amplitudes in central sites in comparison to the control group. This was also true for both, the medicated and the unmedicated subgroup. An effect of location was only observed in the medicated subgroup, having significantly lower mean amplitudes in frontal sites than controls.

In central, but not in frontal sites, the decrease of the N100 amplitude in schizophrenia patients was independent from medication. The topographic findings indicate differential effects of illness and medication on neural subsystems involved in auditory stimulus processing. Thus, it can be assumed that the N100 amplitude reduction in central sites has a very close association with the illness itself and is a robust parameter to discriminate between schizophrenia patients and healthy controls.

87. ATTENTION AND MEDICATION IN SCHIZOPHRENIA—AN ERP STUDY

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Attentional deficits are one of the main symptoms in schizophrenia. The “negative difference” (Nd) has been described as an electrophysiological correlate of attentional effects. The Nd is obtained by subtracting the event related potential (ERP) wave to unattended stimuli from the ERP wave to the same kind of stimuli when being attended. Therefore, the Nd has been interpreted as a correlate of an “attentional trace.” It is well known that attention may be impaired by antipsychotic medication. Controversial results have been published concerning the influence of antipsychotic medication on auditory ERPs.

In fifty-five schizophrenia patients (19 unmedicated, 36 medicated) and thirty-one healthy controls the negative difference (Nd), elicited by nonattended and attended sounds, was compared. For stimulation, an auditory odd-ball paradigm with rare (20%) deviant 1200 Hz stimuli and 1000 Hz standard stimuli was used. ERPs were recorded in frontal and central electrode sites. Data were acquired with an A/D rate of 500 Hz, 0.1 Hz high-pass, and 70 Hz low pass filter. Off line, a 30 Hz low pass filter, an ocular artifact correction, and a ± 50 μV artifact rejection criterion were applied.

Nd was significantly reduced in the total group of patients compared to controls (Cz, Fz). ANOVA with controls and schizophrenia subgroups
showed again significant differences in Cz and Fz. In post hoc tests, these results were due to a significant difference between medicated patients and controls. The present findings indicate a significant effect of medication on attention/task related auditory information processing in schizophrenic patients.

88. PERCEPTUAL DEFICITS IN SCHIZOPHRENIA MAY BE EXPLAINED BY ABER RANT GAMMA RANGE OSCILLATIONS

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Problems in cognition in schizophrenia may be explained by a problem in the timing of neural processes across different cortical regions. We explored a possible connection between backward masking deficits in schizophrenia and aberrant gamma range cortical oscillations. Backward masking is a procedure that assesses the earliest components of visual processing. On this procedure, the visibility of a briefly-presented target is reduced by a visual mask. Schizophrenic patients consistently show deficits on this procedure. As the interval between target and mask increases, backward masking performance sometimes shows an oscillating pattern, which is thought to reflect gamma oscillations of visual pathways. Previously, we found that normal controls showed an oscillating pattern, whereas schizophrenic patients did not show such a pattern.

We recently developed a computerized version of backward masking that is well suited for modeling the performance pattern in masking. Intervals between target and mask were set regularly at 13 ms increments, and a threshold procedure was used to equate subjects for initial performance. On this procedure we found the predicted qualitative differences between patients and normal comparison subjects. There was a significant oscillating component for the comparison subjects, (i.e., a sine wave fit the data), but there was no such component for patients. The pattern of results suggest that a fundamental abnormality in establishing cortical oscillations may partially account for backward masking deficits in schizophrenia. It is likely that sensory and perceptual neurocognitive deficits in schizophrenia may have common roots in a failure to establish cortical oscillations.

89. ALTERED PLATELET MITOCHONDRIAL COMPLEX I ACTIVITY IN SCHIZOPHRENIA

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Mitochondrial abnormality has been observed in several neurological disorders. Changes in energy metabolism and thereby disturbed neuronal function, is an attractive explanation for some of the pathological aspects observed in schizophrenia. Indeed, PET studies have suggested that a change in energy metabolism in cortical and subcortical structures is involved in the pathophysiology of schizophrenia. An electron microscopy study in autopsied anterior limbic cortex of schizophrenic patients revealed deformation and reduction in the number of mitochondria. Our results show that in platelets of medicated and unmedicated schizophrenic patients at acute relapse complex I activity, but not complex IV, is increased significantly (240%, p < 0.001). No such change was observed in patients with affective disorder. To find out whether the increase in complex I activity is state dependent we have measured its activity in patients with acute relapse, chronic patients with positive symptoms and patients with residual schizophrenia and compared them to normal subjects. Complex I activity was significantly increased in both the acute and chronic patients with positive symptoms while reduced in chronic patients with residual schizophrenia as compared to normal subjects. A positive correlation was observed between complex I enzymatic activity and mRNA of 24kDa iron-sulfur flavoprotein subunit of complex I, which has catalytic proprieties. mRNA levels of subunit 75kDa, the largest transmembranous iron-sulfur flavoprotein which demonstrate no catalytic activity, was similar in all groups. If complex I abnormality in platelet reflects brain alterations, it may further support the relevance of abnormal energy metabolism to the pathophysiology of schizophrenia and might become a useful peripheral marker for this disorder.

90. A LONGITUDINAL STUDY OF HIPPOCAMPAL VOLUMES IN SCHIZOPHRENIA

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Cross-sectional MRI brain studies have shown a similar degree of hippocampal volume reduction in patients with chronic schizophrenia and first-episode psychosis. It remains unclear whether these abnormalities predate the onset of symptoms, occur during the initial development of psychosis or whether they progress over the course of the illness.

We examined hippocampal volumes longitudinally (time 1/time 2) in patients with chronic schizophrenia (n = 22), an ‘at-risk’ group (n = 27) and control subjects (n = 23). At time 2, 11 of the ‘at-risk’ group had developed a psychotic illness. Hippocampal, whole-brain and intracranial volumes were estimated from high-resolution 1.5-mm cortical images. There was no group by time interaction for either left (F(4,77) = 0.2, p = 0.93) or right (F(4,77) = 0.4, p = 0.77) hippocampus (covaried for intracranial volume. In addition, there was no group by time interaction for whole brain volume, covaried for intracranial volume (F(4,77) = 1.5, p = 0.20).

These data did not show longitudinal changes in hippocampal volume in patients with chronic schizophrenia, first-episode psychosis or the at-risk group who developed psychosis, consistent with the neurodevelopmental model. It is possible that the manual tracing technique used is not sensitive enough to identify small hippocampal changes in small samples.