blink rate) of DSMIIIR schizophrenics are sampled during laboratory tests, in which Ss are exposed to a set of experimental stressors (two situations with a cognitive load, two with a predominantly emotional impact). Patients are followed up for 18 months, with lab measures and clinical course (via PSE ratings) being reassessed at 6-month intervals.

A total of 50 schizophrenic patients have completed the protocol in the still ongoing project. At this point two major results seem to emerge:

(1) Quite a few psychophysiological measures taken exhibit retest stabilities of $r > 0.60$ (i.e. electrodermal spontaneous fluctuations, breath rate, blink rate), supporting a trait marker notion for at least some psychophysiological parameters in schizophrenia.

(2) For virtually all measures examined patients, who subsequently developed psychotic relapses during a 1-year-follow-up, tended to show less psychophysiological responsivity to the distressing tasks (particularly those with a cognitive load) in the initial lab test, in which a non symptomatic state was prerogative for participation. Contrary to the traditional view of heightened stress reactions in schizophrenics these data appear to indicate that a failure to generate adequate ANS arousal levels in demanding situations may be a crucial factor for an increased risk for psychotic episodes.

## VII.7

# SMOOTH PURSUIT EYE MOVEMENT DEFICITS IN SCHIZOPHRENIC PATIENTS: SYMPTOMATIC, NEUROLOGICAL, AND NEUROPSYCHOLOGICAL CORRELATES

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Smooth pursuit eye tracking performance was examined in 96 schizophrenic patients and 51 normal controls. All patients were under 35 years of age and not hospitalized more than 12 months during the previous two years. At the time of testing, all patients were on neuroleptic medication and considered close to discharge from hospital. Tracking performance was assessed on the basis of horizontal EOG measurements. Subjects followed the visual target as it moved sinusoidally at 0.4 Hz across a computer screen. In Conditions I and III subjects were instructed to press a button whenever the target changed its colour, in Condition II whenever the background bar on which the target was moving changed its colour. In contrast to Conditions I and II, the sinusoidal movements of the target were irregular in Condition III. Median root mean square scores were determined across the 20 cycles of each condition.

Schizophrenic patients performed worse than control subjects ($F(1,128) = 21.93$, $p < 0.001$). Comparing conditions ($F(2,128) = 152.12$, $p < 0.001$), tracking performance was found to be best in Condition III with irregular but on the average slower movements of the target, and to be worst in Condition II when attention was directed toward changes in background colour. The interaction Group × Condition ($F(2,128) = 7.10$, $p < 0.01$) indicates larger differences between conditions among patients than among normals.

In schizophrenic patients tracking performance in all three conditions was correlated with the anticholinergic potency of medication and in Conditions I and III also with the chlorpromazine equivalents of neuroleptic medication ($0.23 \leq r \leq 0.30$). Tracking performance correlated ($0.24 \leq r \leq 0.43$) with the total score of the Neurological Evaluation Scale (Buchanan and Heinrichs), and with perseverative errors in the Wisconsin Card Sorting Test ($0.20 \leq r \leq 0.27$). There were no significant correlations with negative symptoms scores, although all the subscores from 'classical' rating scales tended toward a positive association.

## VII.8

# THE USE OF ELECTROPHYSIOLOGICAL MARKERS IN LINKAGE ANALYSIS IN SCHIZOPHRENIC AND BIPOLAR PEDIGREES

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Genetic linkage studies in schizophrenia and bipolar affective disorder have been seriously hampered by uncertainties regarding their modes of inheritance, and have provided considerable impetus in the search for biological traits which might assist in diagnosis and reduce dependence on the clinical interview. It is known that a proportion of schizophrenics and their relatives show disordered smooth-pursuit eye movements, but several studies have failed to demonstrate a comparable abnormality in drug-free bipolar patients.

Endogenous event-related potentials show consistent changes of both amplitude and latency not only in schizophrenic subjects and their relatives but also in bipolar illness. In particular, the P300 response to an auditory 'odd ball' stimulus has been carefully studied in a variety of psychiatric conditions. P300 latency is increased and amplitude is reduced in both schizophrenics and bipolar affectives compared with controls; the effect is independent of medication and clinical state at the time of testing.

Over 90 members of a single five-generation pedigree were interviewed using the SADS-L, resulting in the diagnosis of 17 cases of bipolar and unipolar affective disorder, and no cases of schizophrenia. Auditory event-related potentials and eye tracking were recorded from 72 of those interviewed, revealing an increase of abnormalities in both clinically affected and unaffected members.

The results suggest that these electrophysiological measures may be promising as phenotypic markers in both schizophrenia and bipolar illnesses, aiding genetic linkage studies and supporting the argument that there is no clear boundary between the two major psychoses.

## VII.9

## P300 AMPLITUDE DECREMENTS AND GLOBAL PERSONALITY FUNCTIONAL DEFICITS

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P300 amplitude is thought to reflect expectancy and attention deployment. P300 amplitude decrements are seen in schizophrenic patients on and off medication, in patients in remitted and acute stages of the disorder and in a subset of first-degree relatives of schizophrenic index cases. Duncan et al., have proposed that, in the visual modality, reduced P300 amplitude represents a schizophrenic state related deficit, whereas in the auditory modality it represents a trait indicator. To examine this proposal, we used data on a subset of subjects from the New York High-Risk Project to relate (1) results of P300 evaluations in adolescence (mean age 15 years), prior to expression of schizophrenic or related disorders, and (2) results of clinical assessments 10 years later (mean age 25 years). Subjects were: 25 offspring of parents with schizophrenic disorders, 25 offspring of parents with affective disorders, and 65 offspring of normal control parents. Assessments were blind to previous electrophysiological and clinical measures on the offspring and parental clinical status. The expected link between reduced amplitude and subsequent schizophrenic and schizophrenic-related disorder (i.e., schizotypal, schizoid or paranoid personality traits and disorder) was not observed. However, a robust association between a global assessment of personality (SCID II, GAP) and reduced amplitude in the visual modality ($F=9.8$; $p=0.0001$) and in the auditory modality ($F=6.3$; $p=0.003$) was seen. This association remains significant after adjusting for offspring I.Q., and for parental social class.

## VII.10

## RELATIONSHIP BETWEEN EVENT-RELATED POTENTIAL MEASURES OF INFORMATION PROCESSING AND POSITIVE AND NEGATIVE SYMPTOMS

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Two ERP amplitude measures, processing negativity (PN) and P300, have been found to be reduced in schizophrenics compared to healthy controls and were correlated with ratings of positive and negative symptoms (Michie et al. 1990; Ward et al. 1990, 1991). The present study was designed to examine these relationships in patients on and off neuroleptic medication.

Subjects met DSMIII criteria for schizophrenia and included 20 patients who had been neuroleptic-free for at least three months (UNMED) and 20 patients who were receiving neuroleptic medication (MED: mean CPZ Equiv = 507 mg/day). ERPs were recorded during a complex multi-dimensional listening task, in which subjects were presented with tones differing in ear of delivery and pitch and were required to attend to a particular ear/pitch combination and respond to infrequent longer duration (100 ms vs 50 ms) targets. PN (mean attended − unattended difference 100–200 ms poststimulus at Fz for nontargets) and P300 (mean amplitude in the 300–800 ms epoch at Pz for correctly identified targets) amplitudes were correlated with symptom ratings obtained with the SAPS and SANS.

The two groups did not differ in total SAPS and SANS scores or PN and P300 amplitudes. The UNMED group had significantly higher alogia and anhedonia scores on the SANS. There was a negative correlation between P300 amplitude and alogia in both UNMED and MED groups ($p<0.01$). The correlation between reduced PN and higher total SAPS and SANS scores was significant in the UNMED ($p<0.05$) group but not the MED group. The pattern of results remained the same after partialling out age and medication dosage. These findings indicate that the cognitive disorder indexed by reduced P300 amplitude is associated with negative thought disorder. Further analysis will examine whether the presence of more negative symptoms in the UNMED group may account for the association between reduced PN and total schizophrenic symptoms in unmedicated, but not medicated patients.

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## VII.11

## POSITIVE AND NEGATIVE SYNDROMES IN SCHIZOPHRENIA: A CLINICAL-NEUROPSYCHOPHYSIOLOGICAL APPROACH

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