

resting and after three auditory stimuli (presentations of short sentences). 20 sec EEG epochs were spectral analyzed for each condition, and mean power and mean frequency was computed for the different frequency bands. The spatial characteristics of EEG reactivity were computed as arithmetic difference between maps or frequency values at initial resting and after the three stimuli. The severity of psychopathology was assessed with the AMDP system immediately after the EEG recording. Significant differences in the spatial distribution of reactivity power as well as in the direction (increase or decrease) of the reactivities were observed between patients and controls. Particularly interesting among the correlations with psychopathology was the observation that with higher ratings on the hallucinatory syndrome there were lower alpha and beta-1 reactivities, as well as more frequent reversed reactivities. - The study confirmed our earlier findings of a dissociated and partially inverted EEG reactivity (EEG reactivity reflects the update of working memory) in acute schizophrenia, and demonstrated reliable correlations of specific features of EEG reactivity with psychopathology features.

S54-2

EEG MAPPING BEFORE AND AFTER ANTIPSYCHOTIC TREATMENT IN CHRONIC AND FIRST-EPISODE SCHIZOPHRENICS

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The present study was aimed at evaluating the possibility of predicting response to treatment with antipsychotic drugs in schizophrenic patients by means of quantitative EEG (QEEG) indices. The study was carried out in 37 DSM-III-R schizophrenic patients, 24 chronic and 13 first-episode. For each subject, at the end of a two-week wash-out period, 10 min of resting QEEG were obtained in the morning; then a single dose of the drug chosen for the patient's treatment was administered and further QEEG recordings were obtained 6 hours after drug administration. All patients completed a 4-week monotherapy, at the end of which they were considered as responders when a reduction of at least 50% of the total score on SANS + SAPS was observed. For first-episode patients, the follow-up period was extended up to six months.

Baseline QEEG characteristics did not discriminate responders from nonresponders. The only drug-induced QEEG change that showed a significant correlation with clinical improvement was the increase of the slow alpha band. A discriminant analysis on the slow alpha changes, carried out in chronic patients, correctly identified 22 out of 24 subjects as responders or nonresponders. Using the same discriminant function, 11 out of 13 first-episode patients were correctly classified. Since first-episode patients were not included in the calculation of the discriminant function, their classification can be considered a validation of the procedure. For patients who completed the six-month follow-up, the response prediction was still correct at the end point, suggesting the possibility that the slow alpha changes observed six hours after the first dose of an antipsychotic predict response to long-term treatment.

S54-3

EEG MAPPING IN POSITIVE AND NEGATIVE SCHIZOPHRENIA AND UNDER DIFFERENT NEUROLEPTICS

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Schizophrenics with predominantly negative and positive symptoms exhibit significant differences in their EEG maps, as compared with normal controls: while the former exhibited an increase of

delta/theta activity mostly over temporal and frontal regions, the latter showed just the opposite; both groups, however, exhibited an alpha attenuation and beta augmentation. While the latter findings indicate a state of sustained CNS hyperarousal in schizophrenics, the increase of slow activity suggests an organic factor in the pathogenesis of the negative syndrome. Thus, neuroleptic drugs for the treatment of the two subtypes should differ as well, which was demonstrated by us recently: while neuroleptics of benefit for negative schizophrenia (e.g. amisulpride, low-dosis fluphenazine) decreased delta/theta, neuroleptics for positive schizophrenia (e.g. chlorpromazine, haloperidol) increased delta/theta activity.

Indeed, already earlier pharmaco-EEG studies in phase-I trials in normals demonstrated different profiles, but mainly 2 subtypes: One after sedative, low-potency neuroleptics, characterized by a decrease of total power, an increase of absolute and relative delta and theta power, a decrease of alpha and beta power and a slowing of the centroid, and another after non-sedative, high-potency neuroleptics, characterized by a lack of attenuation of total power and of delta power increase, but showing a theta and beta power increase and only minimal attenuation or no change in the alpha power and the centroid.

In addition to its classification purposes, EEG mapping may also be utilized for determination of the neuroleptics' bioavailability at the target organ - the human brain. Thus, one may determine at an early stage of drug development: (1) whether a drug is CNS-effective in man at all as compared with placebo; (2) what its clinical efficacy will be; (3) at which dosage it acts (minimum CNS effective dose, dose-efficacy relations); (4) at what time it acts (onset, peak, end of central effect); (5) the equipotency of different galenic formulations.

S54-4

DEVIANT MICROSTATES ('ATOMS OF THOUGHT') IN BRAIN ELECTRIC FIELD SEQUENCES OF ACUTE SCHIZOPHRENICS

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Different topographies of the brain's electric field reflect activity of different neural networks, and thus indicate different functions. Parsing spontaneous series of momentary multichannel EEG fields into microstates isolates the building blocks of cognition and emotion, the putative "atoms of thought". Microstates in acute, neuroleptic-naive schizophrenics and matched controls were clustered, and resulted in 4 classes of microstates in either group. Arranged into best-fitting pairs, 3 classes had similar topographies in patients and controls, but one class differed significantly. (While the controls' microstate topography resembled an attention state, the patients' deviant one resembled an "ignore information" state of earlier experiments). The deviants covered about 20% of total time, occurred about three times per second, and lasted on the average about 65 msec (shortest of all 8 classes). The duration of the deviant microstates were systematically shorter with more severe pathology of the AMP syndrome "paranoid". Further, the corresponding microstate in the controls was significantly longer and covered more total time. Since access to memory and processing strategies in the brain depends on momentary functional state, the occurrence of deviant microstates explains how patients recurrently access memory contents and processing strategies which differ from those normally available. The deviant brain microstates may thus give rise to the irregularities of thought, emotion and behavior which lead to the diagnosis of schizophrenia. Our results imply that schizophrenic symptomatology does not result from continuously biased brain