

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

functions, but from recurring, deviant brain states interspersed between normal brain states.

S54-5

FUNCTIONAL ASYMMETRIES OF THE BRAIN IN SCHIZOPHRENIA

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Some of the most characteristic schizophrenic symptoms such as acoustic hallucinations and thought disorders are related to speech. Speech is a strongly lateralized brain function and is, like schizophrenia, exclusive for humans. Therefore, it is reasonable to hypothesize disturbances of language related brain areas to be at the basis of at least part of schizophrenic disorders. Accordingly, neuropathological and brain imaging studies have shown alterations of left temporal areas in schizophrenia. In event-related potential (ERP) studies, functional asymmetries of the brain electrical fields have been shown in schizophrenic patients. Based on a standard oddball paradigm, the P300 component of ERPs was investigated with 20-channel recordings in different schizophrenic subgroups. Pathological asymmetries in the form of right-lateralized P300 peaks were found only in a subgroup of residual schizophrenics (Strik et al, *Psychiat Res: Neuroimaging*, 55: 153–166; 1993), while acute and remitting forms had normal P300 field configurations (Strik et al, *Acta Psychiat Scand*, 94: 471–476; 1996). The pathological asymmetry was correlated with impairments in verbal memory functions (verbal pairs test), but not with performance in the abstract control task (Heidrich and Strik, *Biol Psychiat*, 41: 327–335; 1997). Source localization of the P300 component with LORETA (Pascual-Marqui et al, *Int J Psychophysiol*, 18: 49–65; 1994) indicated relative hyperactivity of the right temporal lobe as an explanation for the pathological asymmetries in the surface potential. The results are interpreted as a support for the hypothesis that language-related brain functions are deficient in subgroups of schizophrenia and might be associated with compensatory contralateral activation.

S54-6

EEG FFT APPROXIMATION SOURCE LOCATIONS IN SCHIZOPHRENIA

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Imaging procedures are steadily gaining importance in psychiatric research. The morphology of the brain can be visualized by means of CT and MRI while cerebral blood flow and the cerebral metabolic state can be evaluated by PET. Neurophysiological methods not only have the advantage of being readily available in a clinical setting, but by now have reached a stage of allowing the estimation of intracerebral generators of electrical activity of the brain. In psychiatric diseases where alteration of background activity is of interest, the method of FFT-approximation allows the estimation of intracerebral EEG-generators in the frequency domain. In the present study we investigated 22 schizophrenic in comparison to 22 control subjects. Schizophrenic patients exhibited more anterior and superficial equivalent-dipoles in the beta-bands and a tendency of increased beta-activity was found. With increasing severity of schizophrenic symptoms, the equivalent-dipole in the beta1-band was localized more anteriorly and the dipole in the theta-band was localized more inferiorly. These new

developments may allow a physiological interpretation of neuro-physiological investigations similar to other functional imaging methods and consequently enhance the clinical relevance of the EEG in psychiatry in the future.

SEC55. Diagnostic tools for primary care in psychiatry

Chairs: P Bech (DK), C Pull (LUX)

SEC55-1

THE MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW

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The Mini International Neuropsychiatric Interview (MINI) is a short diagnostic structured interview designed to generate 17 DSM-IV or ICD10 axis I diagnosis. It systematically explores the presence of diagnostic criteria for current diagnosis within a 10–25 minutes period depending on the number of diagnoses presented by the patient. The reliability, sensitivity and specificity were explored in a clinical population versus the CIDI (Lecrubier et al, 1997) and versus the SCID (Sheehan et al, 1997). In both cases the performance of the MINI was equivalent to that of the longer interview. A multicenter trial organised in 4 different European countries compared the diagnoses generated by GPs using the MINI (after a very short training of 2–3 hours) and a specialised interviewer (psychiatrist expert with DSM diagnoses. For the 3 most frequent diagnoses, the concordance was: .68 for Major Affective Disorder, .62 for GAD and .66 for social phobia. Positive predictive values >.70 while negative predictive values >.90. therefore, very few false positive are likely to be generated by the GPs using the MINI. The screening questions of the different sections (passation: 5') did predict the existence of the full diagnosis in about 2/3 of cases. The GPs found the instrument to be easy to use. In parallel, a MINI plus version has been developed which comprises:

- different additional diagnoses to allow their optional introduction in a diagnostic assessment such as PTSD, PMS...
- a full exploration of psychotic disorders according to DSM-IV (7 diagnoses) while the very short core version only identifies the presence of a psychotic syndrome.

Overall, more than 100 studies and 20 departments currently use the MINI. The interview is translated (and back translated) in more than 30 different languages with a specific attention to semantic rather than to literal translation.

SEC55-2

A SPANISH VALIDATION STUDY OF THE MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW

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Aim: To determine the psychometric properties in terms of sensitivity, specificity, positive predictive value and negative predictive value of the Spanish version of the M.I.N.I. when diagnosis by the psychiatrist is used as the gold standard.

Patients and Methods: A total of 126 primary health care patients from two Spanish provinces (Asturias and Alava) were included. First evaluations were made by the general practitioner