
 S9 *Integrative research approaches to schizophrenia*

INTEGRATIVE RESEARCH APPROACHES TO SCHIZOPHRENIA

M. Koukkou University of Berne, Department of Psychiatry, Bolligenstrasse 111, 3072 Berne, Switzerland

The aim of the symposium is to present findings of empirical methods used to study the working brain as it is engaged in psychologically meaningful activities in normals and in schizophrenics, and to discuss the functional significance of deviations of the workings of the brain in schizophrenics in order to understand the pathogenesis of the symptoms which have been found to be influenced specifically by pharmacological treatments or by psychological treatments.

The methods used included Evoked Potentials, Autonomic Components of the Orienting Response, EEG measures of Working Memory and Brain Electric Microstates in combination with psychological measurements. Some results suggest fluctuating, but also generalized deviations and other results suggest specific deviations of brain functioning during productive schizophrenic symptomatology.

The results of the different approaches will be discussed within the framework of a broad heuristic model of the functions of the human brain and specifically on the basis of the concept of the working memory.

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MICROSTATES OF THE BRAIN ELECTRIC FIELD IN SCHIZOPHRENIA

D. Lehmann, M. Koukkou, K. Kochi, T. Konig. The KEY Institute for Brain Mind Research, University Hospital Department of Psychiatry, Lenggstrasse 31, Zurich 8082, Switzerland

Brain electric activity can be imaged as sequences of momentary electric field configurations (maps of landscapes). The changes of landscape are discontinuous: the landscape remains stable in the sub-second range ("microstate") and then quickly changes to a new landscape. Different landscapes (maps) must have been generated by different active neural populations. Therefore, it is reasonable to assume that different microstates represent different mental operations. Brain field data (after "close your eyes") from 9 first-break schizophrenics with productive symptomatology and 9 matched controls were analysed. In confirmatory testing, the patients' microstates had shortened durations. A clustering strategy assigned all maps to a minimal number of classes. The controls' brain field maps and the patients' maps were optimally accounted for by three prototypes (classes) of microstates. Using the controls' and patients' prototypes, all maps of patients and controls were assigned to the best-fitting prototype. Normals' maps were classified significantly more often as normal prototypes than patients' maps. Also, the normals' maps were significantly more often classified as normal than patient prototypes, but the patients' maps had no such preference. This is physiological evidence for a partially altered repertoire of mental operations in schizophrenia. The specific functional meaning of the different map classes can be explored experimentally. The microstate analysis offers a unique possibility to study the spatio-temporal organization of mental operations and their deviations during psychiatric disorder.

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EEG STUDIES OF UPDATE OF WORKING MEMORY IN SCHIZOPHRENIA

M. Koukkou University of Berne, Department of Psychiatry, Bolligenstrasse 111, 3072 Berne, Switzerland

In a series of studies, we test the hypothesis that the brain's functional organization as reflected in the electric field (EEG) defines the memory contents (the dimensions of working memory) which are activated and thus accessible to the brain's information processing operations for the organization of the behaviour. The working memory contents are continuously readjusted via the memory-driven pre-attentive operations underlying the initiation of an adaptive orienting response and the allocation of attention. This readjustment corresponds to the updating of the working memory and can be measured as EEG-reactivity. Deviations of EEG-reactivity suggest accessibility of state and/or age inadequate memory contents for the organization of the current behaviour. We report on the spatial distribution of EEG-reactivity of 9 new admissions with first manifestation of productive schizophrenic symptoms before any treatment, and 18 normal controls (two age and sex-matched controls for each schizophrenic patient). Furthermore, in order to test the possibility of an age-inadequate update of working memory in schizophrenics (the neurodevelopmental hypothesis) we compare the EEG-reactivity of schizophrenics with the EEG reactivity of 15 eleven year old children. We found statistical differences in the topography, direction and intensity of EEG-reactivity between schizophrenics and age matched controls. As compared to the EEG-reactivity of the children, we found some indications of an age inadequate update of working memory, which however, refers mainly to the frequency domain of the brain's electric field.

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EEG IN EARLY AND LATE RESPONDERS OF FIRST-EPISODE PSYCHOSIS

M. C. G. Merlo, H. Kleinlogel, M. Koukkou. University of Berne, Department of Psychiatry, Bolligenstrasse 111, 3072 Berne, Switzerland

The aim of this study was to detect whether or not there are EEG differences in a population of 17 first episode, mostly drug-free psychotic patients who presented different time courses of response, i.e., early or late time course of response. Resting EEGs and psychopathological ratings were assessed before antipsychotic treatment, and after 7 and 28 days of treatment. EEG data were spectrally analysed to compute mean amplitude values for six frequency bands and nineteen leads. A psychopathological score for schizophrenic syndrome was calculated with AMDP system. Patients were divided between those who displayed a clinically meaningful improvement of this syndrome after 7 days (early responder ER) and those who improved after 28 days (late responder, LR). The ER group had most differences in beta2 band compared to its control group matched for age and gender. On the contrary, the mean amplitude of alpha2 frequency band of the LR group was statistically significantly increased as compared to its control group and to the ER group. These findings point to differences in brain physiology between ER and LR. The implications for diagnosis and treatment are discussed.