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Problems and Solutions in EEG Neuropsychopharmacology

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The quality of biological and medicine science depends on the methods they utilize. The creation of new tools and methods of analysis demands the understanding of integrative, nonstationary and self-organized nature of biological processes. This is especially important for the brain related studies which are the base for new therapies and medical technologies in the field of neuropsychopharmacology.

Different psychotropic drugs appear to have their own "EEG portraits." At present, almost all methods of quantitative EEG analysis used in clinical practice are usually derived from averaged EEG techniques, based on extended periods of time and/or broad fixed frequency bands for a specific lead. However, the averaging of the EEG signal might not only mask the dynamics of potential effects of drugs on EEG, but also may lead to ambiguous data interpretation (Fingelkurts et al., 2004a). This is why no theoretical basis has yet been established linking EEG changes to changes in therapeutic effects or psychomotor side effects of psychotropic drugs. The relation between the effect of a drug and its therapeutic properties is often obscure, given that the nature of psychiatric disease is often poorly understood. Thus, psychotropic drug often produce particular EEG effects whose direct link to clinical efficacy and end-points or side effects are not established (for example increase in the EEG beta frequency band under benzodiazepines administration, Koelega, 1989).

Also, interactions between the pharmacological effect of a psychotropic drug and physiological effect (e.g. change from awake to sleeping state) may occur. In this case the interpretation of the conventionally measured EEG effect of the drug may be difficult. Moreover, the sensitivity to general changes in arousal may largely intermix with the relative sensitivity of drug effect parameters.

Hence, when examining the average brain EEG responses to drug administration, it is not clear whether the observed effect of the drug is real (not the "virtual" result of averaging procedure), stable and typical for the whole analyzed signal.

Measures of brain connectivity revealed specificity and sensitivity to different brain dysfunctions, psychiatric disorders and in patients undergoing anesthesia (see review; John, 2002). However, practically all existed measures of brain functional connectivity have several limitations in that they do not take into account the nonstationary nature of the data (Fingelkurts et al., 2004b), require long periods of analysis, and use linear mathematical models of the signal which for the brain is not typically the case (Landa et al., 2000).

In order to overcome the limitations of conventional EEG analysis based on averaging procedures and to reveal dynamic and temporal characteristics of brain activity the advanced micro-structural EEG (or MEG) analyses have been introduced (Kaplan, 1998; Fingelkurts et al., 2003, for the review see Kaplan & Shishkin, 2000; Fingelkurts & Fingelkurts, 2001; Fingelkurts et al., 2004b). Indeed, the intimate dynamic structure of the EEG is rich in information on the underlying cellular and intercellular processing, brain states, localization, forms of cooperativity and the stages of brain development. The ongoing neural activity as a summative electric potential reflects a functional brain state comprising its dynamical processes (Lehmann et al., 1998), and this summative potential may also act back on the functional architecture of the cortex (Freeman, 2003).

Thus, the temporal micro-structural EEG/MEG characteristics and new indexes of functional connectivity provide additional and new information on drug effects. They are capable

- to predict the brain response to a drug using a single dose and to adjust drug administration to the specific needs of the patient. This permits optimizing the therapeutic procedure and to minimize the drug's side effects;
- to establish the correlation between EEG micro-structural parameters and clinical end-points/metabolites;
- to clarify the drug effects for cases of unknown clinical significance;
- to distinguish between pharmacological and physiological effects of a psychotropic drug;

- to distinguish between general and more specific drug effects;
- to identify the real "EEG signature" of psychotropic drugs.

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