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Behavior-dependent pharmaco-electroencephalographic (pEEG) characterization of psychoactive drugs

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The use of electroencephalography (EEG) in drug discovery and drug development has mostly been limited to the analysis of pharmacological effects during a limited number of pre-defined vigilance levels (e.g., sleep-wake states) or during artificially induced constant behavior (e.g., in animals during enforced treadmill walking; in humans during 'eyes closed' condition). Although these approaches have been successful to some degree in the prediction and classification of the psychoactivity of pharmacological agents, more advanced applications of the high potential of the EEG in drug discovery have been hampered by the practical constraints in mastering the complexity of matching the EEG read-outs with their high time resolution to the dynamics of spontaneous behavior. As a consequence, the application of task-related and especially spontaneous behavior-related pharmacoEEG paradigms has not been paramount in (pre-)clinical drug research. Surprisingly so, because at the same time the value of using cutting-edge biomonitoring techniques to assess putative CNS active molecules in undisturbed, stress-free, freely moving animals over prolonged periods of time in order to simultaneously obtain a maximal number of neurochemical, electrophysiological and behavioral read-outs, is progressively acknowledged within the framework of biomarker research and translational medicine. The latter 'integrational' biomonitoring approach requires an advanced acquisition process and efficient analysis tools with a high level of automation in order to warrant practical feasibility in a drug company environment.

A number of studies will be presented, which reinforce the added, synergistic value of simultaneous analysis of EEG and behavior. Starting from investigations into the basic relationship between EEG and behavior, the opportunities for pharmacological differentiation based on high-resolution EEG will be exemplified by the study of drug effects on specific behaviors and behavioral transitions. The wealth of information that is presently still mostly 'hidden' and hence suboptimally used in the pharmacoEEG can be identified and interpreted more readily if we analyze our findings in strict time-locked synchrony with detailed behavioral and psychophysiological analysis.

Finally, the value of an integrative biomonitoring approach in the development and validation of a more naturalistic animal model for depression will be discussed to illustrate the necessity of a high-quality, automated acquisition and analysis tool for efficient use of such complex integrative models. The availability of such validated animal models for psychiatric diseases is especially important for discovering new drug targets with novel mechanisms of action, i.e., a new generation of drugs. Behavior-dependent pharmaco-electroencephalography is well positioned to be of instrumental value in this quest.