Abstract

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ECNP Symposium hosted by the EPA: The neuroimaging of pharmacological effects**ECNP0001****Pet imaging of receptor occupancy**

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The discovery and development of drugs for treatment of brain disorders is an extremely challenging process requiring large resources, timelines, and associated costs. Positron Emission Tomography (PET) enables in vivo neuroimaging of various components of receptors, transporters, enzymatic activity and other types of proteins. PET also allows for studying the response to physiological or drug interventions in experimental medicine studies. Moreover, PET neuroimaging can assist to establish diagnoses in certain brain disorders and thereby improve patient selection and stratification for clinical trials. Over the past couple of decades, PET neuroimaging has thus become a central component of the evaluation of novel drugs for brain disorders, enabling decision-making in phase I studies, where early discharge of risk provides increased confidence to progress a candidate to a later phase testing at the right dose level or alternatively to kill a compound through failure to meet key criteria. The so called "3 pillars" of drug survival, namely; tissue exposure, target engagement, and pharmacologic activity, are particularly well suited for evaluation by PET imaging. Molecular neuroimaging has thus increasingly established itself as a unique tool that not only can demonstrate drug penetration and kinetics in the brain, but also identify pharmacodynamic effects, e.g., changes in glucose metabolism. It can also quantitate therapeutic action in vivo by determining, e.g., drug occupancy whereby the relevant dose ranges to be used in clinical efficacy trials can be determined.

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ECNP0003**EEG and ECG based response predictors in depression: Time for personalised medicine or treatment stratification?**

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In depression (MDD) treatment there is a clear need for novel treatments, biomarkers and individualized treatment approaches. One of the most promising and most widely investigated biomarkers for antidepressant treatments is the EEG. Most EEG biomarkers however, still lack robustness and reproducibility and suffer significant publication bias as highlighted in a recent meta-analysis (Widge et al., 2018). Therefore, large controlled validation studies are needed with a focus on robustness, replication and clinical relevance. In this presentation results will be presented from the largest EEG Biomarker study to date, the international Study to Predict Optimized Treatment in Depression (iSPOT-D), where 1008 MDD patients were randomized to Escitalopram, Sertraline and Venlafaxine. Drug-class specific (Arns et al., 2016) and drug-specific (Arns, Gordon & Boutros, 2015) biomarkers will be highlighted as well as preliminary data from a prospective feasibility trial. Furthermore, data will be presented on repetitive Transcranial Magnetic Stimulation (rTMS) treatment in MDD on EEG and clinical predictors (Krepel et al., 2018; 2019) and a new method called Neuro-Cardiac-Guided TMS (NCG TMS), that exploits network connectivity in the frontal vagal pathway, as a target engagement approach (Iseger et al., 2019).

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