Abstracts

1

Auditory steady-state response (40Hz) in rodents, a new tool for drug discovery in Schizophrenia?

Session P907 - Cognition: Animal Models of Schizophrenia

November 9, 2021, 9:15 AM - 10:15 AM CT

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Abstract: Schizophrenia is a severe psychiatric disorder associated with persistent alterations of diverse neurocognitive functions, leading to lifelong psychosocial disabilities. Although schizophrenia has long been considered as a condition that specifically impairs the higher-order functions, recent research has demonstrated that basic sensory processing is also impaired, especially in the auditory modality. Neurophysiological approaches have provided evidence that most schizophrenic patients exhibit a wide range of clinically measurable dysfunctions in the processing of auditory stimulations, including the Auditory Steady-State Responses (ASSRs) which is one of the most consistent functional biomarker across schizophrenic patients. ASSRs consist in cortical electrophysiological oscillations entrained by the frequency and phase of a periodic auditory stimulus presented at a rhythm in the gamma range (that is, 30-80Hz). ASSRs are believed to reflect the interplay between cortical pyramidal neurons and parvalbuminergic interneurons. Consistent with the theory of imbalance between cortical excitation and inhibition in schizophrenia, patients show reduced power and phase locking, to stimuli presented at 40Hz. In recent years, we have developed the characterization of ASSRs in mice and rats to propose a translational solution for drug candidates. In this work, we particularly studied the 40HzASSR modulations in a rat model of schizophrenia, induced by a glutamatergic antagonist MK-801. We will show in this poster how MK-801 (0.1, 0.15, 0.2mg/kg) induces a dose-dependent reduction of the 40Hz-ASSR phase locking in the cortex of rat and how antipsychotics (such as clozapine) modulate this pharmacological effect. We propose the 40Hz-ASSR phase locking as a specific translatable biomarker useful for the preclinical identification, selection and validation of new innovative therapeutics in psychiatric disorders.

Abstracts

2

The relevance of EEG biomarker in evaluating the anti-dyskinetic effect of drugs in Parkinson's disease

Session P260 - Mechanism of Neurodegeneration II

November 11, 2021, 9:30 AM - 10:30 AM

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Abstract: State-of-the-art clinical literature shows that motor symptoms of Parkinson's disease (PD) result from a dysfunction of the cortico-basal ganglia circuits. A hyper synchronization of beta rhythms in this circuit, positively correlated to motor symptoms, has been characterized in both parkinsonian patients and animal models. This aberrant excessive beta oscillation is suppressed by dopaminergic treatments, which simultaneously improve motor deficits. However, a chronic L-DOPA treatment induces abnormal involuntary movements (AIMs) and a prominent resonant gamma oscillation. This project aimed at investigating the effect of the antidyskinetic drug amantadine, which is routinely used in the clinic, on L-DOPA-induced gamma oscillations in the 6-OHDA rat model of PD. In this poster, we will show that chronic administration of L-DOPA low dose (6mg/kg) induces specific gamma oscillations and AIMs which gradually increase with repeated treatments. We will demonstrate that a pre-treatment with amantadine dose-dependently reduces L-DOPA-induced gamma oscillations and AIMs score. Our data will illustrate how the preclinical study of cortical beta and gamma oscillations offers relevant and translatable EEG biomarkers that add significant value to drug development as stable, quantitative, and objective endpoints for the development of new antiparkinsonian and antidyskinetic neurotherapeutics.