171. Impaired Hippocampal Oscillations in the Chronic Ketamine Model of Schizophrenia

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Background: Brain oscillations are critical for cognitive processes, and their alterations in schizophrenia are proposed to contribute to cognitive impairments. Network oscillations primarily rely upon GABAergic interneurons, which also show characteristic changes in schizophrenia. The aim of this study is to examine the capability of hippocampal networks to generate theta and gamma oscillations after repeated ketamine administration in a rat model exhibiting schizophrenia-relevant cognitive deficits (Becker et al., 2003) and a loss of hippocampal GABAergic interneurons (Keilhoff et al., 2004).

Methods: Hippocampal EEG recordings were performed in freely behaving rats, two weeks before and two weeks after a 5 day treatment by subanesthetic doses (30 mg/kg i.p.) of ketamine (n=11) or saline (n=5). The recordings were made over a period of 5 hours to include periods of activity as well as REM sleep, when coupled theta and gamma oscillations normally occur in the hippocampus. Changes in GABAergic interneuron networks of the hippocampus were examined using parvalbumin immunocytochemistry.

Results: By the end of the second week postinjection rats treated with ketamine showed significant decreases in theta (44.7%, p=0.013) and gamma (58.9%, p=0.0014) oscillations, which were assessed as spectral power within the 5-10 and 50-50 Hz frequency bands, respectively. No significant changes were found after vehicle injection.

Conclusions: The decreases in theta and gamma oscillations concur with the known impairments of oscillations reported in schizophrenic patients, indicating that understanding the mechanism of impaired oscillations in animal models may help find the link between structural damage of cortical interneuron networks and cognitive deficits in schizophrenia. Supported by NIMH, Sepracor Inc.

172. Evoked Coherence in Alzheimer Patients Upon Application of Basic Visual Paradigm

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Background: In this study the evoked coherence of patients with Alzheimer type of dementia (AD) was analyzed by using simple light stimuli.

Methods: A total of 22 mild probable AD subjects (11 untreated, 11 treated with cholinesterase inhibitors) were compared with a group of 19 healthy controls. The evoked coherence was analyzed for delta (1-3.5 Hz), theta (4-7 Hz) and alpha (8-13 Hz) frequency ranges for (F 3-F4, C3-C4, T3-T4, T5-T6, P3-P4, O1-O2) (F, P, C, T, O) electrode pairs.

Results: The only significant results were found in left fronto-occipital pair (F3-O2). Control group showed higher values of evoked coherence in “delta” and “theta” bands in comparison with the untreated AD group (p<0.01). However there was no difference in fronto-parietal electrode pairs between groups.

Conclusions: In the present results there is no difference in simple sensory evoked coherences between healthy subjects and AD patients in fronto-parietal recordings. However, in responses to a cognitive paradigm delta, theta and alpha coherences were highly reduced in AD patients versus healthy subjects especially at left fronto-parietal pair (Güntek et al. 2008 Brain Res. Oct 15;1325:109-16). The highly decreased delta, theta, alpha responses in AD during a cognitive task indicate the existence of additionally activated neural networks in the fronto-parietal systems only during a cognitive paradigm. The cholinesterase inhibitors have more influenced these neural assemblies related to cognitive performance. These findings can also serve a model in all type of cognitive deficits including psychiatric disorders.

173. Time-Frequency Analysis of Response Inhibition Using Magnetoencephalography

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Background: While event-related evoked potentials and fields for response inhibition have been studied in both adults and children as well as in special populations such as Attention Deficit-Hyperactivity Disorder (ADHD), little is known about the cortical oscillatory activities related to stop signal tasks.

Methods: Twelve healthy adult volunteers performed a visual stop signal task while being measured with a magnetoencephalography (MEG) machine. The participants were presented with either the letter A or B (Go stimuli) and asked to respond by pressing one button for A and another button for B but to withhold response whenever a stop signal followed the A or B. We extracted epochs containing failed inhibitions (FI) and successful inhibitions (SI) from -1500 to 1000 ms relative to the stop signal. Time frequency plots were then generated between 0.5 to 50 Hz for each condition separately using BESA in both sensor and source space.

Results: Both evoked and induced activities were observed in the time frequency plots. A right frontal low frequency (below 10 Hz) power increase was observed in both FI and SI conditions near the timing for N200. However the power was spread over a wider time range than with increased amplitude for the FI condition.

Conclusions: Previous evoked analysis of this data and other studies have shown a larger amplitude N200 peak for the SI condition compared to the FI condition. The time-frequency results suggest that the cortical oscillatory activity related to the N200 may contain a non-phase-locked component. Supported by Canada Foundation for Innovation, President Research Grant (to M.L.)

174. The Effect of Aripiprazole Alone and in Combination with Escitalopram on the Firing Rate of Serotonin, Dopamine and Norepinephrine Neurons

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Background: Aripiprazole is an atypical antipsychotic approved by the FDA for use in Major Depressive Disorder as an adjunct to antidepressants. However, precise mechanisms responsible for the effectiveness of Aripiprazole augmentation are not fully understood. Therefore, the current study was aimed at examining the effects of Aripiprazole administration as well as its concomitant use with the SRI Escitalopram on the firing of serotonin, norepinephrine and dopamine neurons.

Methods: Electrophysiological experiments were carried out in anesthetized Sprague-Dawley rats. Escitalopram was delivered via subcutaneously implanted osmotic minipumps at a dose 10 mg/kg/d. Aripiprazole was injected i.c. daily at a dose 2 mg/kg/d. Both drugs were administered for 2 and 14 days alone and in combination. Control rats received physiological saline in analogous regimens.