Complex Mismatch Negativity to Extra Tone Gestalt Pattern Deviance may be a Putative Biomarker for Schizophrenia

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Presently there is no biological marker that can detect incipient psychosis. We measured complex mismatch negativity to deviant tones that violate the Gestalt perceptual principle of grouping by proximity in the first-episode schizophrenia spectrum, individuals early in the course of psychosis, to validate potential biomarkers of disease presence. Participants attended a silent video and repeated series of 3 identical tones were presented with short gaps in between. Occasional tone series that included a deviant extra 4th tone identical to the others were pseudo-randomly interspersed. Participants also were presented a simple physical parameter mismatch negativity task, where rare pitch- and duration-deviants were presented among standard repetitive tones). Twenty-two individuals at their first psychotic episode were compared to 22 volunteer healthy controls. First episode individuals did not show reductions of pitch-deviant MMN (d =0.08) or duration-deviant MMN (d =-0.02). Importantly, first psychotic episode individuals showed reductions of the complex mismatch negativity (d =0.83). Reduction in complex mismatch negativity but not in simple mismatch negativity in the first-episode schizophrenia-spectrum suggests impairments in late perceptual pattern processing that are sensitive to subtle pathology early in disease course whereas simple detection of stimulus change is unaffected. Thus, the extra tone Gestalt complex mismatch negativity displays the properties of a biomarker of disease presence at the first psychotic episode. Future studies in clinical high risk individuals are needed to determine whether this putative biomarker of disease presence is sensitive to the true prodromal state prior to the emergence of psychosis.

Resting state and ERPs in Deficit and non-deficit schizophrenia patients

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Heterogeneity of schizophrenia is a major obstacle towards understanding the disorder. One likely subtype is the deficit syndrome (DS) where patients suffer from predominantly primary negative symptoms. This study investigated the EEG/MEG during resting state and evoked EEG/MEG responses. Ten subjects were recruited for each group (Control, DS and Non-Deficit Schizophrenia [NDS]). Resting state was recorded for 10 minutes, then an odd-ball paradigm (P300) and mid-latency evoked responses in a sensory gating paradigm were administered. MEG Coherence Source imaging (CSI) in source space and spectral analysis of the EEG and MEG waveforms in sensor space were performed. For resting state: (1) Significantly higher relative power at low frequencies (delta band) at sensor space in DS compared to NDS patients (MEG); (2) Source analysis revealed larger delta and theta power in the DS compared to NDS group in the frontal region; and (3) NDS patients showed significantly higher resting-state MEG signal relative power in beta bands in sensor space compared to DS patients. For evoked responses; 1) CSI during P300 task revealed a significantly higher average coherence value in DS than NDS subjects in the gamma band (30-80 Hz), when listening to standard stimuli; 2) only NDS subjects had a higher average coherence level in the gamma band than controls when listening to the novel sounds; and 3) P50, N100 and P3a amplitudes were significantly decreased in NDS

compared to DS subjects. The data suggest that the two syndromes may not be representing different levels of severity but may be qualitatively different.

Neurophysiology tools as diagnostic and therapeutic applications in substance use disorders

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Neurophysiology techniques, i.e. the assessment of brain activity at rest (EEG) or upon stimulation (ERP) allow brain functional characterizations of psychiatric disorders with diagnostic, predictive and therapeutic implications. Neuropsychiatric disorders are often associated with deficits of executive functions, including response inhibition, voluntary decisions or reward related responses. The processing of these functions is modulated by brain regions, which can be assessed by EEG and or ERP studies. In substance use disorder (SUD) studies have shown that the craving is associated with increased responses predominantly in frontal and striatal brain regions. Based on EEG/ERP data in patients with SUD, a neurophysiology-based therapeutic strategy using a real-time neurofeedback paradigm has been developed. Patients were trained to voluntarily modulate craving-associated neuronal responses. Both biological and clinical effects of neurophysiology-based treatments will be presented and the feasibility of their implementation in a psychiatric context will be discussed.

What is the impact of anti-craving medication on cue reactivity in alcoholic patients?

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Alcohol-cue reactivity has been tagged as a principal mechanism of addictive behaviour, as repeated alcohol consumption leads to dopaminergic neurological changes and meso-cortico-limbic sensitization resulting in heightened incentive salience of stimuli associated with drinking. However, to our knowledge, no study has up to now tested the impact of anti-craving medications on this cognitive process. We performed an ERP study with recordings both at the beginning (T0) and at the end (T1) of a three-week detoxification cure. Fifty-eight patients were confronted at both moments with a visual oddball task, in which patients have to detect among a series of neutral stimuli target deviant stimuli, related or unrelated to alcohol. Our objective was to verify whether anti-craving medication (placebo, acamprosate, naltrexone or baclofen) would have an impact on the evolution of the oddball P300 (between T0 and T1), recorded in response to (non)alcohol-related targets. These results will also be correlated with the number of days of complete abstinence (post-detoxification cure). Preliminary data will be presented and clinical implications will be discussed.