## 210 – NEURONAL INTEGRITY, EMOTION RECOGNITION AND THEORY OF MIND IN SCHIZOPHRENIA AND ASPERGER DISORDER: A MAGNETIC RESONANCE SPECTROSCOPY STUDY

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**Background:** Theory of Mind (ToM), ability to infer one's own or other's mental states is impaired in Asperger Disorder (AD) and schizophrenic patients. The objective of this study was to compare the ToM performance of AD and schizophrenia patients with healthy controls and to evaluate the relationship between ToM abilities and frontal lobe activity as assessed by magnetic resonance spectroscopy (MRS).
**Methods:** Fifteen AD, 20 schizophrenia patients and 30 healthy controls were included. Dorsolateral prefrontal cortex(DLPC), anterior cingulate( ACC), amygdala(A) and orbitofrontal cortex(OFC) neurometabolites were investigated with multi-voxel MRS. Correlations among MRS variables, ToM tests(ToM-1/ToM-2), Weschler Adult Intelligence Scale(WAIS-R), emotion naming and recognition test scores were evaluated.
**Results:** AD patients had lower arithmetic, comprehension and picture completion and schizophrenic patients had lower comprehension and block design scores compared to the control group. Both AD and schizophrenic patients had lower emotion recognition and ToM-2 scores than controls. AD patients had lower ToM-1 score from both schizophrenia patients and controls. In AD, Tom-1 performance was negatively correlated with DLPC NAA/Cho($r=-.738$, $p=.004$) and positively correlated with DLPC Cho/Cre($r=.656$, $p=.015$). OFC Cho/Cre was negatively correlated with severity of disorder ($r=.656$, $p=.015$). In schizophrenia group, DLPC NAA/Cre was negatively correlated with ToM-1 performance ($r=-.441$, $p=.050$).
**Conclusions:** Verbal comprehension and ToM performance were significantly impaired in both AD and schizophrenia patients. DLPC metabolite levels seemed to be negatively correlated with ToM performance in both groups. Although AD and schizophrenia are separate disease entities, they might be sharing common pathophysiologic mechanisms relevant to frontal cortex activity.
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## 211 – EXPLORING THE NEURAL SUBSTRATE OF THE VULNERABILITY TO FIRST EPISODE PSYCHOSIS USING FMRI

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**Background:** The neural substrate of the vulnerability to the first break of psychosis is unknown. At a behavioral level object working memory task performance is abnormal in and may discriminate between the early stages of schizophrenia. Such tasks also reliably recruit frontal and temporal cortices, possible sites of progressive volume change over the early course of the disorder. We wanted to clarify if functional changes can be detected in the early stages of schizophrenia and to identify both their anatomical location and relationship to the stage of illness using a functional object working memory task in which the length of memory delay was manipulated.
**Methods:** A sample of 40 subjects contributed to the study: 10 first episode psychosis (FEp) patients, 16 at risk mental state (ARMS) and 14 healthy controls. We collected functional MRI data while the subjects performed a modified version of the delayed matching to sample (DMTS) task from the Cambridge Automated Neuropsychological Test Battery (CANTAB).
**Results:** At a behavioral level there was a trend to a group by delay interaction, the two patient groups making a greater number of errors at longer memory delays. At successful recognition a main effects of group was detected in the medial temporal lobe bilaterally, while a main effect of delay was detected in the left medial temporal lobe. At each length of memory delay the patient groups showed consistently greater activation of medial temporal regions when performing the task accurately.
**Conclusions:** Both ARMS and FEp groups showed greater activation than controls in the medial temporal cortex across all lengths of memory delay. These differences were not related to poorer task performance, but suggest an inefficiency or compensatory mechanism that may correlate with the vulnerability to psychosis rather than psychosis per se.

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## 212 – FUNCTIONAL IMAGING FINDINGS IN HEALTHY SUBJECTS WITH AUDITORY VERBAL HALLUCINATIONS

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**Background:** Auditory verbal hallucinations (AVH) are highly prevalent in schizophrenia. AVH are also present in 5–10% of healthy subjects. These subjects are free of other symptoms and medication, which provides an opportunity to assess the substrate of AVH in its isolated form. The aim of the present study is twofold: to assess brain deviations that may predispose a subject to AVH and to observe the underlying neurological basis of AVH in healthy subjects.
**Methods:** Healthy subjects with AVH were recruited from a website that provides information on "hearing voices". Absence of axis I and II pathology was using Comprehensive Assessment of Symptoms and History (CASH) and Structured Clinical Interview for DSM-IV (SCID-II) interviews. We selected 20 healthy subjects with frequent AVH. They were matched to 20 healthy subjects without AVH and to 20 schizophrenia patients with chronic AVH. AVH, inner speech and auditory imagination were assessed using fMRI, EEG and MEG.
**Results:** During AVH the right insula was more involved than during inner speech or auditory imagery, which was present in both the healthy hallucinators and in the patients. The hallucinating subjects showed less coherence during inner speech than non-hallucinating subjects. Hallucinating subjects had more activation of the right sided language areas during inner speech than controls.
**Conclusions:** The right insular appears to play a prominent role in AVH. Two brain deviations may predispose for AVH: decreased language lateralization and decreased coherence between Broca's and Wernicke's area.

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## 213 – TOWARDS MODEL-BASED INDICES OF PATHOPHYSIOLOGICAL MECHANISMS IN SCHIZOPHRENIA

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**Background:** Despite all efforts, psychiatry still lacks qualitative, objective tests for diagnosis and classification of schizophrenic patients. Ideally, such tests should probe putative pathophysiological mechanisms, e.g. abnormal synaptic plasticity resulting from aberrant regulation of NMDA receptors by modulatory neurotransmitters.
**Methods:** Here, we present a framework which combines neuroimaging, computational modeling and pharmacological manipulations to establish model-based indices of synaptic plasticity as diagnostic markers for schizophrenia. This framework rests on Dynamic Causal Modeling (DCM), a novel approach to analyzing effective connectivity in the human brain. It characterizes the mechanisms of non-linear neural systems whose dynamics depend on experimentally designed inputs and their intrinsic connectional structure. The modeled neural dynamics are linked to measured data through a modality-specific biophysical forward model. Currently, implementations exist for fMRI, EEG/MEG and local field potential measurements. Using a Bayesian estimation scheme, DCM enables the user to investigate and make inferences about complex neural architectures and context-dependent changes in their connection strengths.
**Results:** Several practical applications are presented that demonstrate how mechanistic principles underlying neurophysiological processes can be inferred using DCM. For example, in a sample of 16 healthy volunteers, we show how mechanisms underlying visuo-auditory associative learning can be scrutinized by DCM and fMRI. Furthermore, we describe preliminary results from ongoing invasive recording studies in rats ($N=90$) designed to validate the ability of DCM to infer the functional status of muscarinic receptors from electrophysiological data. If successful, this will enable us to apply the same model to human EEG data from patients.
**Conclusions:** Our approach may not only be useful for diagnostic classification and to provide potential endophenotypes for genetic studies, but, because the model parameters have a direct physiological interpretation, may also inform the development of novel therapeutic strategies.
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## 214 – TEMPOROSPATIAL CHARACTERIZATION OF BRAIN OSCILLATIONS ASSOCIATED WITH SUBPROCESSES OF VERBAL WORKING MEMORY IN SCHIZOPHRENIA

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**Background:** The studies of the neural correlates of verbal working memory in schizophrenia are somewhat inconsistent. This could be related to experimental paradigms that engage differentially working memory components or methodological limitations in terms of characterization of brain activity. The objective of this study isto characterize brain activity in the spatial, temporal and frequency domains associated with information encoding and maintaining online components of working memory.
**Methods:** Magnetoencephalographic recordings were obtained on 10 schizophrenia patients and 11 healthy while performing a modified Sternberg paradigm to investigate subprocesses of verbal working memory. Time frequency analysis was applied for the whole head and 4–48 Hz time–frequency surface.
**Results:** Patients were similar to controls with respect to the 8–32 Hz desynchronization in the occipital lobes during encoding, but differed from controls with respect to the synchrony in the same band and area