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Cognitive and Negative Symptoms in Schizophrenia - Studies of Patients and Healthy Controls Using Magnetic Resonance Imaging

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ABSTRACT

Schizophrenia is a severe psychiatric illness. It affects young people and often results in lifelong complications such as a distorted perception of reality, decreased cognitive ability and impairment in the realms of motivation and emotions. There is no effective treatment available for two of the symptom domains: cognitive symptoms and the so-called negative symptoms. In recent years, attention has been drawn to the fact that these are the symptom domains resulting in the greatest functional impairment and which best predict a negative prognosis. The need for increased knowledge of the underlying neurobiological correlate is therefore great. Another aspect of the disease - diagnosis in the new onset phase - is an area also requiring more attention, as it is of the utmost importance that a reliable diagnosis be made quickly in order that the correct treatment may be initiated. This thesis describes four studies carried out by myself and my colleagues. Each study addresses different aspects of these schizophrenia-related problems.

Diagnostic stability (DS) in the new onset phase of schizophrenia and other psychotic disorders was investigated in the first study. The diagnostic development was analyzed in material documenting 146 first episode psychosis patients that were followed prospectively and longitudinally over 3 years. A large variation in DS was found between the various diagnoses and diagnostic groups. Generally, schizophrenia and the schizophrenia spectrum had high DS, while the DS of diagnoses such as delusional disorder and schizoaffective disorder was low. On the basis of this it is suggested to be restrictive in the use of specific diagnoses in the early phase of a psychotic disorder.

The second study examined whether the network of brain regions which processes cognitive control activates different circuits depending on whether the distraction to be processed in parallel with solving a task is of a cognitive or affective nature. A group of 11 healthy subjects were asked to perform counting Stroop (cStroop) and affective counting Stroop (aStroop) during one session while being scanned by a magnetic resonance imaging (MRI) camera. The blood oxygen level dependent (BOLD) functional MRI (fMRI) data shows that this division is present not only in the anterior cingulum cortex (ACC) as expected from previous studies, but also in the dorsolateral prefrontal cortex (DLPFC). This implies separate circuits within the cognitive control network for affective and cognitive distractions.

The third study was devoted to the neurochemical regulation of the cognitive control network. Pharmaco fMRI technique was used to investigate whether brain regions, as activated by aStroop and cStroop respectively, react differently to the selective serotonin reuptake inhibitor (SSRI) agent escitalopram when it is used as a pharmacological probe. A group of 11 healthy subjects performed aStroop and cStroop while being scanned by an MRI camera. Escitalopram was administered after the first session, and the subjects repeated the same examination after a period of four hours. It was found that activation in the rostral ACC by aStroop was significantly decreased following intake of escitalopram. The implication is that the ability to pursue goal-oriented behavior while being disturbed by affective stimuli - an ability which is often impaired in states such as schizophrenia - may be improved on administration of an SSRI.

The amygdala’s involvement in the negative symptoms of schizophrenia was examined in the fourth study. The amygdala is a region in the medial temporal lobe of the brain which is critical to faculties such as assigning value to affective stimuli. It was found that the volume of the amygdala as measured by MRI and the activity of the amygdala during an affect inducing paradigm called the Face Matching Task paradigm as measured by BOLD fMRI had a negative correlation to the level of negative symptoms in a group of 28 schizophrenia patients. No significant difference was however found in the volume or activity of the amygdala between this group of patients and a group of 28 matched healthy control subjects. We believe this indicates that the amygdala is involved in the neurobiology of negative symptoms.

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