months. Data on several atypical medications including clozapine, olanzapine and amisulpride will be reviewed.

## S14.3

Executive functions in schizophrenia

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Studies of patients with schizophrenia have repeatedly shown a wide range of neurocognitive disturbances, including deficits in executive functions, memory and attention. Executive impairments are among the earliest described and clinically most prominent cognitive deficits that are present in schizophrenia and appear to be related to long term outcomes, disability and quality of life. Many domains of executive functions are impaired in patients with schizophrenia including forward planning, concept formation, set shifting, initiation, self-monitoring, ABSTRACT ion and the ability to direct attention and memory. A variety of neuropsychological tasks have been used in examining these functions, such as the Wisconsin Card Sorting Test, the Stroop Test, object-sorting tests, proverb tests and mazes. Specific executive deficits appear to be related to specific symptom clusters in schizophrenia and are linked to structural and functional brain abnormalities.

Anatomic and functional neuroimaging studies have begun to identify specific cortical deficits. Although no single brain region has been found to identify schizophrenic pathology, specific hypotheses about fronto-temporo-limbic system dysfunctions have been consistently implicated in the pathogenesis of schizophrenia.

## S14.4

FMRI and cognitive dysfunctions in schizophrenia

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Cognitive dysfunctions in the domains of attention, working memory, and executive functions are a core feature of schizophrenia and a major challenge for treatment interventions. We directed our research efforts to the question, whether schizophrenic patients demonstrate changes in fMRI-activation patterns in the entire cortical-subcortical information processing network while performing different cognitive tasks.

In a series of studies, the Wisconsin Card Sorting Test (WCST) has been employed to challenge executive functions. Blunted prefrontal activation could be detected even after patients where matched for task performance. Another paradigm adapted, the Continuous Performance Test (CPT) is the classical procedure to detect attention deficits in schizophrenic patients compared to normal controls. Since this task consists of different subcomponents such as feature detection, selective attention and working memory, tests for each of these subcomponents have been constructed. Already in the feature detection task exploring basal visual analysing performance, schizophrenic patients exhibited activation deficits particularly in temporal lobe areas belonging to the ventral visual stream. These findings suggest a disturbed early visual processing pathways in schizophrenic patients. The "2-back" working memory task was implemented, since it is particularly related to working memory and executive functions. Effective connectivity analysis using structural equation modeling revealed that atypical antipsychotic drugs as compared to the conventional neuroleptic haloperidol enhanced prefrontal-thalamic and prefrontal-cingulate connectivity during task performance. This finding may be interpreted as restored integrity of fronto-striato-thalamo-cortical circuitry.

Taken together, the findings are consistent with the notion of an imbalance of different processing components in terms of a "cognitive dysmetria". The results provide evidence that both early and later steps of sensory and cognitive information processing might be affected in schizophrenic patients. And finally, the findings suggest that a disruption of widespread neural networks in schizophrenia can be favorably influenced by atypical antipsychotic treatment – an observation which could at least partially be attributed to the atypical receptor binding profiles of atypical antipsychotic drugs.

## S14.5

The influence of antipsychotic treatment on cortical activations in patients with schizophrenia using functional magnetic resonance imaging

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Cognitive dysfunction is an enduring deficit in schizophrenia. It may underpin some of the psychopathology of schizophrenia as well as contribute to the patient's impaired social and vocational functioning. Treatment with atypical antipsycotics have shown that there is a significantly greater improvement in several domains of cognitive function, especially attention and verbal fluency, compared to classical antipsychotics, a result which may be due to the effects of 5HT and other neurotransmitter systems and normalisation of dopamine function by these compounds. Social cognition perhaps the domains most likely to have relevance to functional outcome. It is thus possible to map the functional anatomy of neurocognitive improvement with atypical antipsychotics in schizophrenia using functional magnetic resonance imaging and investigate the effects of atypical antipsychotics on social cognition.

Our group has previously shown the effects of atypical antipsychotics on brain activation in schizophrenia using a working memory task (Honey et al, 1999). In that study there was a possible ceiling effect in patients with schizophrenia and normal controls thus preventing any conclusions about the neural correlates of cognitive improvement with atypical antipsychotic medication. We have now completed a study of a new cohort of patients where we have parametrically increased cognitive load to examine cortical activation in patients switched to newer atypical antipsychotics. This presentation will outline new methods of brain imaging and how these methods may allow us to understand the effects of antipsychotic drugs in schizophrenia. The new data set will be presented and discussed.

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