# 9. Summary of PhD thesis

A series of four studies was conducted to find the limits and potentials of the application of positron emission tomography (PET) in the assessment of brain function in schizophrenia.

We detected higher resting $^{18}$FDG uptake (PET) in cortico-cerebellar regions and lower deoxyglucose uptake in the frontal cortex among 67 patients with schizophrenia in comparison to a control group (n = 18) in our first study. The data do not allow to assign the changes either to the underlying disorder or the effect of medication.

In the following study we focused on medication naive patients with the first episode of schizophrenia. The deoxyglucose uptake of eight untreated patients with schizophrenia and the control group (n=22) were compared. The differences in glucose brain metabolism between psychotic and control group included a significantly increased metabolism in the cerebellum, the left middle temporal gyrus and left inf. frontal gyrus in the drug naive patients. Using individualised PET analysis, cerebellar hypermetabolism was detected in 5 and frontal hypermetabolimus in 6 patients.

In order to clarify further the effect of medication, we assessed 7 antipsychotic naive patients with first episode of schizophrenia before and after risperidone therapy (4-6 weeks). Within-subjects comparisons before and after risperidone treatment revealed a decrease of $^{18}$FDG uptake in the inferior semi-lunar lobule in the posterior lobe of right cerebellum, in the left superior temporal gyrus (BA 22) and in the left insula (Brodman area - BA13). Risperidone increased $^{18}$FDG uptake in the right lingual gyrus (BA18), in the right superior frontal gyrus (BA 6) and in the right postcentral gyrus (BA 3)

Our results suggest that the increased metabolism in the cerebellum and the temporal cortex are present before an antipsychotic therapy is initiated. Risperidone therapy decreased metabolism in these areas. We detected similar changes after the application of repetitive transcranial magnetic stimulation over temporo-parietal cortex in patients with pharmacoresistant auditory hallucinations. We found increased metabolism in the cerebellum and frontal cortex by both methodological approaches: group difference analysis and also individualised analyses. These findings open search for hypotheses of specific metabolic patterns associated to psychopatology and/or the course of the disease. It also leaves open the question whether individualised metabolic patterns can be used as markers of various subtypes of schizophrenia. Our first study put a cornerstone for building a large database with data about brain metabolism, psychopatology and cognition of patients with schizophrenia. We have complemented this database with information on course of a disorder and genetic polymorphism variants. In the future it may help to clarify the role of factors that modify brain metabolic pattern and help to explain inconsistencies in literature.

SPM analysis revealed an increased uptake of $^{18}$FDG in the right middle frontal gyrus (Brodmann area 46) in subjects with high auditory verbal hallucinations (AVH) score (n=15) compared to non-hallucinating patients (n=15). Activation in BA 46 positively correlated with the intensity of hallucinations (Spearman $R=0.57$; $p<0.001$). The observed functional recruitment of the right prefrontal cortex in subjects with high score of hallucinations may reflect impairment in the integration of intended actions and sensory feedback, which results in misattribution of internal events to an external source. This mechanism may form the cognitive basis for AVH.

Our finding of an increased metabolism in the cerebellum led to designing of studies focused on the possibility to apply cerebellar rTMS (Kopeček et al., 2006). The assumption that cerebellum, temporal and frontal cortex can be a candidate target of rTMS in the therapy of schizophrenia is based on literature reports and also on our findings. However, our pilot results did not show any effect of high-frequecy rTMS over dorsolateral prefrontal cortex in treatment of negative symptoms (Novák et al., 2006) or cognitive deficit (Mohr et al., 2006) of patients with schizophrenia.

This thesis is aimed to support the effort to add neuroimaging methods to phenomenological approach in psychiatry (psychopatology, course of disease) and eventually to genetic information, in order to help understand patophysiology of schizophrenia and be instrumental in assisting diagnosis and treatment decisions.