Neural correlates of reward processing in schizophrenia – relationship to apathy and depression

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Background
A dysfunction of the reward system has been proposed as a core deficit in schizophrenia (Juckel et al., 2006). A reduced activation of the ventral striatum during reward anticipation has been observed in unremitting patients and those treated with typical neuroleptics (Juckel et al., 2006; Kirsch et al., 2007; Schlagenauf et al., 2008). Group differences in brain activation during outcome evaluation have received less attention. One study showed no difference between patients treated with typical and atypical antipsychotics (Kirsch et al., 2007).

One previous study has shown a negative correlation between negative symptoms and reward anticipation (Juckel 2006). A further differentiation of the relationship between symptoms of schizophrenia and dysfunctions of the reward system can be based on the differentiation of neural activation related to wanting and liking (Berridge & Robinson, 1998).

Therefore, the study had two aims: (1) to investigate group differences between healthy controls and schizophrenic patients treated with atypical neuroleptics during both reward anticipation and outcome. (2) to differentially relate apathy to brain activation during reward anticipation and anhedonia/depression to reward outcome.

Methods
Subjects: 15 healthy control subjects and 15 patients with schizophrenia or schizoaffective disorder were included in the study. All patients were treated with atypical antipsychotic drugs.

| Age | 25.2 ± 3.2 (20-32) | 26.3 ± 5.4 (18-38) |
| Gender | 5 females, 10 males | 5 females, 10 males |
| Reaction Time | 486 ± 54.5 | 498 ± 70.1 |
| Win total (Euro) | 34.3 ± 2.97 | 34.7 ± 3.71 |

Paradigm: We employed a monetary incentive delay task (Knottson et al., 2001, 2005). Subjects were presented a cue indicating the possibility of winning either 1 Euro, 20 Cent, or 0 Euro. After a delay period they had to perform a left or right button press within 1 s. After correct performance they would win the cued amount of money with 60% probability.

Results
Behavioral data: Groups did not differ significantly in reaction time or total win (see table).

During feedback both groups showed significant activation in the ventral striatum and the medial orbitofrontal cortex in the contrast win outcome vs no-win outcome. There was no significant difference between groups.

Correlations psychopathological ratings – signal change ventral striatum: There was no significant correlation between ventral striatal activation during win anticipation and PANSS negative subscale. However, the Apathy Evaluation Scale was negatively correlated with ventral striatal signal change. There was a significant negative correlation between the Calgary Depression Scale and ventral striatal signal change during outcome evaluation. There was no significant correlation between the Chapman anhedonia scales and brain activation during outcome evaluation.

Discussion
Our findings provide additional evidence that on a group level schizophrenic patients treated with atypical antipsychotic drugs do not show dysfunctional activation of brain regions involved in reward processing. In addition to the existing literature our data also show intact processing of rewarding outcomes in the ventral striatum and the medial orbitofrontal cortex.

Regarding the relationship between brain activation patterns and psychopathological ratings we did not find a relationship between PANSS negative symptoms and ventral striatal activation during reward anticipation. Since our patients were treated with atypical antipsychotics, this is consistent with one other study that failed to find this relationship in patients treated with clozapine (Schlagenauf et al., 2008). However, patients with higher apathy scores showed lower activation of the ventral striatum during reward anticipation, which suggests that the positive link between negative symptoms and reward anticipation might more specifically relate to a lack of motivation and drive.

The most important finding regarding processing of reward outcomes is a negative relationship of depressive symptomatology with ventral striatal activation. This is consistent with a decreased striatal response to positive feedback in patients with major depression (Steele et al., 2007). We have not found a relationship of outcome processing with anhedonia as assessed by the Chapman scale, which might be related to the self-rating procedure.

Overall, although the present study is limited by sample size and medicated status of the patients it shows that a differentiation of common negative and depressive symptoms of the schizophrenic illness might be important to understand the role of the reward system in the pathogenesis of these symptoms.

References