



Activation in the brain reward system reflects the relationship between motivation and pleasure in schizophrenia



Daniela Mier¹, Sabine Ronshausen², Peter Kirsch¹

¹Centre for Psychiatry and ²Department of Psychology, Justus-Liebig-University Giessen

Background

In schizophrenia, symptoms belonging to negative pathology, such as avolition (listlessness) and anhedonia (loss of positive emotional experience) are often conceptualized as a result of a pathologically reduced dopaminergic transmission to the frontal lobe (Weinberger and Lipska, 1995). On the other hand, excessive dopaminergic signaling in the ventral striatum leads to higher attribution of salience to internal and external events and thereby can elicit psychosis (Kapur, 2003). Antipsychotics that lower the dopamine level seem to reduce the heightened attribution of salience and thus causes an attenuation of psychosis (Mizrahi, 2005). A further reduction of the dopamine level in the nucleus accumbens leads to a decrease in seeking, but not in consumption of reward (Berridge und Robinson, 2003).

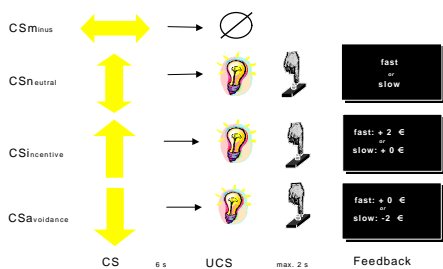
These findings point out, that, from a neurophysiological point of view, motivational disturbances are more likely in schizophrenia than disturbances of the consummatory system. Kring (1999) concludes that schizophrenics are constricted in their appetitive, but not in their consummatory pleasure. However, it still remains unclear, whether anhedonia in schizophrenia exists and if so, whether or not it can be better explained in terms of a motivational than an emotional impairment. This study was set up to investigate this relationship between motivational (anticipation of reward) and emotional processes (consummation of reward) in schizophrenia. Therefore, we looked on the correlation between dopaminergic reward system activation during a motivational paradigm and the activation of emotion processing structures during a picture perception paradigm.

Methods

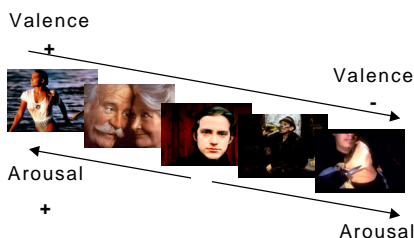
Participants: 20 medicated male schizophrenic patients (mean age=34,45 years, SD=6,2), mean duration of illness 11,6 years (SD=6,4) and 13 matched healthy controls (mean age=31,23, SD=5,2).

Study designs:

Experiment 1:
Anticipation of reward
(Kirsch et al. 2003)



Experiment 2:
Picture Perception



Scanning parameters:

1,5 T Siemens Symphony Scanner; echo planar imaging, TR 3000 ms, TE 50 ms, 30 slices à 3 mm, interleaved acquisition

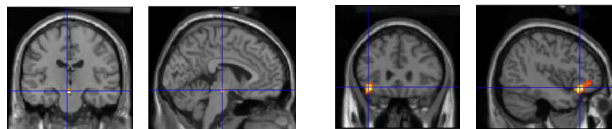
fMRI analysis:

Statistical analysis was done with SPM2 (www.fil.ion.ucl.ac.uk): realignment, normalizing (voxel size 3x3x3mm), smoothing (kernel=9mm); event related design with hrf as stick function, movement parameters as covariates, second level analysis: random effects, for the correlation analysis the highest T-Score in the nucleus accumbens in the contrast CSincentive>CSminus was used; ROI-analysis within the regions: VTA, Nac, OFC, amygdala and striatal areas

Results

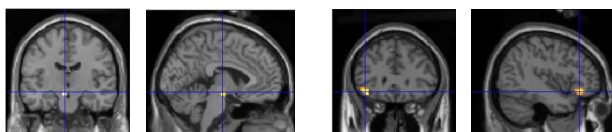
fMRI results:

Activation in the control group Cs_{incentive}>CS_{minus} x lowArousal



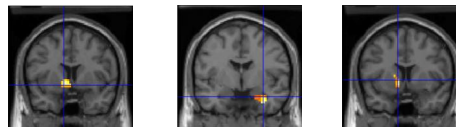
Area	k	p	T	x	y	z	r
VTA	5	0,008	4,81	-3	-18	-12	0.82
OFC	94	0,015	6,65	-42	27	-12	0.89

Activation in the schizophrenic group Cs_{incentive}>CS_{minus} x highArousal



Area	k	p	T	x	y	z	r
VTA	6	0,016	3,89	-6	-15	-12	0.68
OFC	79	0,025	5,13	-33	46	-5	0.77

Activation in the schizophrenic group Cs_{incentive}>CS_{minus} x highPositive>highNegative



Area	k	p	T	x	y	z	r
Amygdala	34	0,009	5,05	33	-4	-25	0.77
Pallidum	14	0,044	4,31	-15	-9	-2	0.71
Nac	41	0,049	3,87	-9	8	-5	0.67

Conclusions

The results demonstrate the relationship between motivation and emotional arousal in central emotion processing structures.

In healthy controls there is a positive correlation between the activation of the nucleus accumbens during the anticipation of reward and the activation in the ventral tegmental area and orbitofrontal cortex during the viewing of low arousing pictures, but not during the viewing of high arousing pictures. In contrast, in schizophrenia patients a positive correlation in the same areas occurred with the high arousing pictures, but not with the low arousing ones.

Concerning the valence there is a relationship between the anticipatory reward related activation and the activation in the amygdala, globus pallidus and the Nac during the processing of positive emotional content in the schizophrenic group. This effect is seen independent of arousal, but only in the schizophrenics. This might indicate that in schizophrenia, the relation between motivation and the experience of positive contents is stronger. This could explain that not only the symptom of avolition, but also the symptom of anhedonia is common in schizophrenia. Further research should investigate whether a motivational constraint affects the hedonic experience in schizophrenia or both systems are independently disturbed.

References:

- Berridge, K. C. & Robinson, T. E., 2003. Parsing reward. *Trends Neurosci* 26 (9), 507-513.
- Kapur, S., 2003. Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am J Psychiatry* 160, 13-23.
- Kirsch, P., Schienle, A., Stark, R., Sammer, G., Blecker, C., Walter, B., Ott, U., Burkhardt, J. & Vaitl, D., 2003. Anticipation of reward in a nonaversive differential conditioning paradigm and the brain reward system: an event-related fMRI study. *Neuroimage* 20, 1086-1095.
- Kring, A. M., 1999. Emotion in schizophrenia: Old mystery, new understanding. *Am Psychol Society* 8, 160-163.
- Mizrahi, R., Bagby, R. M., Zipursky, R. B. & Kapur, S. (2005). How antipsychotics work: The patients' perspective. *Progr Neuropsychopharmacol Biol Psychiatry* 29, 859-864.
- Weinberger, D. R. & Lipska, B. K., 1995. Cortical maldevelopment, anti-psychotic drugs, and schizophrenia: a search for common ground. *Schizophrenia Research* 16, 87-110.