

# Alcoholics exhibit spatially distinct changes in D2-receptor-binding dependent on drinking habits and craving: a PET correlation analysis

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## Aims:

Dopamine release and turnover probably plays a key role in development and maintenance of alcoholism. Aim of this study was to correlate dopamine D2 receptor binding with a D2 receptor ligand with affinity similar to dopamine and psychological parameters reflecting drug induced craving (ACQ) and amount of alcohol intake (LDH) in abstinent alcoholics .

## Methods:

9 male (age 35-57) alcoholics fulfilling DSM-IV and ICD-10 criteria who were abstinent for 2 to 4 weeks were examined with PET and evaluated extensively with neuropsychological questionnaires. Special emphasis was put on craving scales (ACQ) and on alcohol intake during the drinking period (LDH). Their data were compared with 8 age matched volunteers. PET data were acquired dynamically with an ECAT EXACT PET scanner after administration of 194 +/-27 MBq 18F-Desmethoxyfallypride to image dopamine-D2-receptor binding. Following extensive model evaluation the pixelwise simplified reference tissue model using the cerebellum as D2 receptor free region (Gunn et al. 1997) was found to be suitable to quantify D2-receptor binding with this radiopharmaceutical.. This model was applied to the dynamic PET-data yielding parametric images of the binding potential (BP). After stereotactic normalisation to the Talairach space a categorical comparison between the two groups and statistic parametric correlations (Spearman) were performed using SPM99.

## Results:

Categorical comparisons did not yield statistically significant differences in D2-receptor binding between the patients and volunteers. The severity of alcohol craving in was significantly associated with reductions in D2 receptor availability exclusively in the bilateral ventral striatum and the caudate nucleus. The strongest correlation was observed in the right nucleus accumbens (xyz 6/14/-6;  $p < 0.005$ , z-score 3.42) and the ventral left caudate nucleus (xyz -14/16/-2;  $p < 0.005$ , z-score 4.5) (Fig 1). An exclusive positive correlation between D2-receptor binding of the amygdalo-hippocampal complex and alcohol intake was observed as well (xyz -6/22/14;  $p < 0.005$ , z-score 3.12) (Fig. 2).

## Conclusion:

The data suggest that the dopaminergic system is involved in development and maintenance of alcoholism. The association between decreased D2-receptor availability in nucleus accumbens /ventral striatum (Fig. 1) and alcohol craving in abstinent alcoholics supports the hypothesis that stimulus induced dopamine release may trigger the attention towards alcohol associated stimuli and may be associated with compensatory changes in postsynaptic D2 receptors. These findings support the hypothesis that dopaminergic transmission in nucleus accumbens and ventral caudate plays a key role in drug craving.

Gunn RN, Lammertsma AA, Hume SP, Cunningham VJ. Parametric imaging of ligand-receptor binding in PET using a simplified reference region model. *Neuroimage* 1997 Nov;6(4):279-87

Publication: in preparation