Alcohol craving correlates with striatal dopamine receptor density and dopamine synthesis capacity

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Aim:
It is known from animal experiments that stimulus-associated dopamine release in the striatum directs attention towards drug associated cues and elicits drug craving. In alcoholics it is expected that alcohol associated cues trigger striatal dopamine release in the reward system and induce or enhance craving for alcohol. It has been shown that alcohol, like other drugs of abuse, stimulates dopamine release and induces down regulation of striatal dopamine receptors. In this study we investigated therefore presynaptic dopamine synthesis capacity and postsynaptic dopamine D2 receptor density in abstinent alcoholics and healthy volunteers to further examine the association between striatal dopaminergic dysfunction and alcohol craving.

Methods:
N=11 male abstinent alcoholics (according to DSM-IV and ICD 10 criteria) (age 35-57) and n=13 age matched healthy volunteers (age 32-60) were scanned with ^{18}F-Fluorodopa (DOPA) and ^{18}F-Desmethoxyfallypride (DMFP). After application of 194±27MBq DMFP or 198±37MBq DOPA respectively a dynamic emission scan in 3D mode over 124min was started using a Siemens ECAT EXACT PET-camera. Attenuation correction was done applying measured attenuation correction. Binding potential (BP) was calculated on a voxelwise basis using a simplified reference tissue model with the cerebellum as reference region resulting in parametric BP-images (1). For stereotactical normalization of these images a ligand specific template was used created from mean images of healthy volunteers. DOPA-Influx (Ki) was calculated for each pixel using the Gjedde-Patlak analysis with a cerebellar input function (2). Stereotactical normalization was done normalising early summed frames to a flow weighted PET-template and applying the derived normalisation parameters to the Ki-images. Using statistic parametric imaging software (SPM) we calculated categorical group comparison between patients and volunteers as well as pixelwise correlation analyses between the individual scans and craving for alcohol measured with the Alcohol Craving Questionnaire (ACQ).

Results:
In the categorical group comparison we found no significant differences between the patients and volunteer at a give significance threshold of $p<0,001$ neither for DOPA nor for DMFP. The correlation analyses showed in the patient group a close negative correlation between the craving scale (ACQ) and the dopamine receptor density (DMFP) exclusively in the bilateral ventral striatum (r= -0,9; x/y/z 16/14/-6 respectively –15/14/-6). For DOPA as well a negative correlation was found between craving and the patient group in the bilateral putamen (r= -0,7; x/y/z 20/6/-6 –22/8/-10 respectively). For the healthy volunteers no significantly correlating voxels could be detected for DMFP and DOPA.

Conclusions:
These results suggest a dysfunction in the striatal dopaminergic neurotransmission in abstinent alcoholics and support the hypothesis that the reward system plays a key role in the origin or conservation of alcohol craving.

References:
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