Smoking: A TBSS and VBM-style Investigation of White Matter Integrity and Grey Matter Volume

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Introduction

Tobacco smoking is the most widespread substance addiction with a prevalence that varies between gender and developing vs developed countries (47% for males, 12% for females on average). Functional MRI and PET have demonstrated increased activity in the anterior cingulate cortex and in the ventral striatum as well as increased dopamine release in the ventral caudate nucleus (Brody et al., J Psychiatr Res 2006; Brody et al., Am J Psychiatry 2004). Two previous studies have explored grey matter changes related to smoking, showing inconsistent results (Brody et al., Biol Psychiatry 2004 ; Gallinat et al., Eur J Neurosci 2006). The aim of this study was to investigate differences in the topographic distribution of grey matter and the integrity of white matter between smokers and non-smokers, and to examine if there is any apparent link between these changes.

Data

84 subjects (48f vs 36m, 41smokers (>10cigarettes per day) vs 43non-smokers) were selected to match for age, gender and ethnic classification across smoking status, from the imaging database built up by the IXI (Information eXtraction from Images, www.ixi.org.uk) imaging collaboration. T1-weighted images were acquired on a 3T Philips Intera with MP-RAGE (0.94×0.94×1.2mm^3, TE/TR=4.6/9.6ms). Diffusion images were acquired on the same scanner with: 15 directions, b=1000s/mm^2, 1.75×1.75×2mm^3, TE/TR=51/12000ms, 2 NEX).

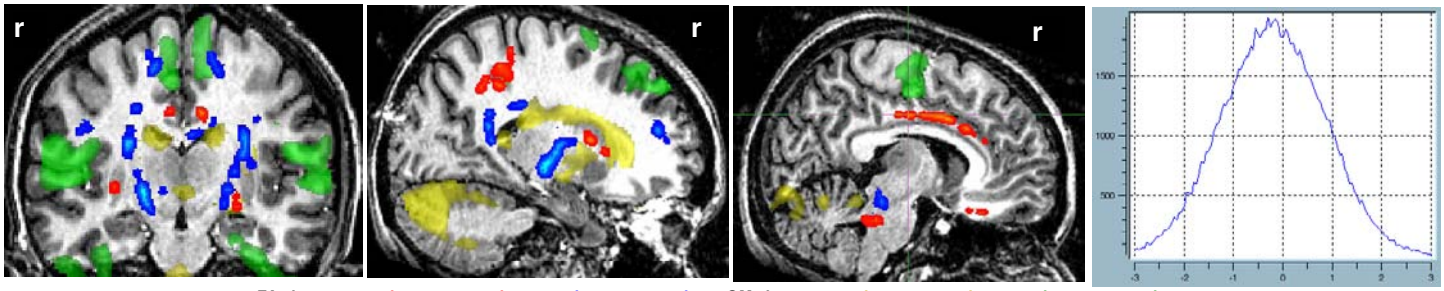
Methods

White matter integrity was investigated through the use of fractional anisotropy (FA) maps, derived from the diffusion data. Differences in FA maps were assessed using TBSS (Smith et al., Neuroimage 2006). TBSS projects all subjects' FA data onto a mean FA tract skeleton, before applying voxelwise cross-subject statistics. To assess differences in the distribution of GM between smokers and non-smokers, an optimised VBM-style analysis (Good et al., Neuroimage 2001) using FSL tools for brain extraction and segmentation (www.fmrib.ox.ac.uk/fsl) and non-rigid registration using free-form deformations (Rueckert et al., IEEE Trans Med Imaging 1999) was carried out. Changes in FA and in the distribution of GM between smokers and non-smokers (age and gender were both matched between the groups, and also pre-correlated out of the data as confounds) were analysed using permutation-based inference.

Results

"Negative" pattern in smokers: GM analysis revealed bilateral loss of grey matter volume in smokers (green) in the inferior-frontal and parietal opercular cortex, in both Heschl's gyri, in the DLPFC and the right VLPFC and in the dorsal primary sensorimotor cortex, the right FEF and the SMA. Decrease of FA in smokers (blue) was mainly found in the posterior limb of the internal capsule (presumably the pyramidal tract). A general global decrease of FA in smokers can be seen in the group-difference *t*-map histogram below.

"Positive" pattern in smokers: More strikingly, smokers showed bilaterally increased GM volume (yellow) in the caudate nucleus – particularly in the ventral area - and in the middle cingulate gyrus. Several areas show an increase in FA in smokers (red); in particular, ROI analysis across the middle cingulum bundle shows a significant increase in FA (P<0.05) bilaterally.



FA changes: smokers>non-smokers, smokers<non-smokers. GM changes: smokers>nonsmokers, smokers<non-smokers.
Images show differences at P<0.05 uncorrected. Histogram: smokers-non-smokers FA t-map.

Discussion

Grey matter loss of volume in the sensorimotor and premotor regions appears to be consistent with the decrease of FA found in the pyramidal tract. Atrophy in the DLPFC and the VLPFC confirms previous voxelwise findings (Brody et al., Biol Psychiatry 2004). Interestingly, increase in the caudate nucleus was found in the smokers, which could be linked with a higher dopamine release in the caudate observed with PET (Brody et al., Am J Psychiatry 2004). This limbic "positive" pattern is also supported by the increase in the volume of the middle cingulate gyrus together with a higher apparent WM integrity in the middle cingulum bundle, which is known to connect the cingulate cortex to the limbic system. Interestingly, the cingulate cortex, the caudate nucleus and the cingulum bundle, which are all part of the reward circuitry and involved in behavioural control, are reported to exhibit abnormalities in obsessive-compulsive disorders (OCD), and the volume of the caudate nucleus during childhood seems to inversely correlate with obsessive-compulsive symptoms developed in early adulthood (Rauch et al., CNS Spectr 2001; Bloch et al., Neurology 2005). Moreover, a DTI study has shown FA increase in the left cingulum of OCD patients (Cannistraro et al., Depress Anxiety 2006). Altogether, these results might suggest a common compulsive behaviour underlied by the common structural abnormalities found in the cingulate, the caudate and the cingulum bundle. In line with this, there is accumulating evidence that OCD may have close links with drug addiction (Fontenelle et al., Psychiatry Clin Neurosci 2005; Serrano et al., G J Psy 2002). It remains unknown if the "positive" pattern that we found in smokers is indeed due to smoking or due to a confounding effect, as we are possibly looking at a population that has structural and genetic predisposition for addiction (Brody et al., Arch Gen Psychiatry 2006).

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