Structural brain deficits in smokers measured by MR volumetry at 3 T

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Introduction

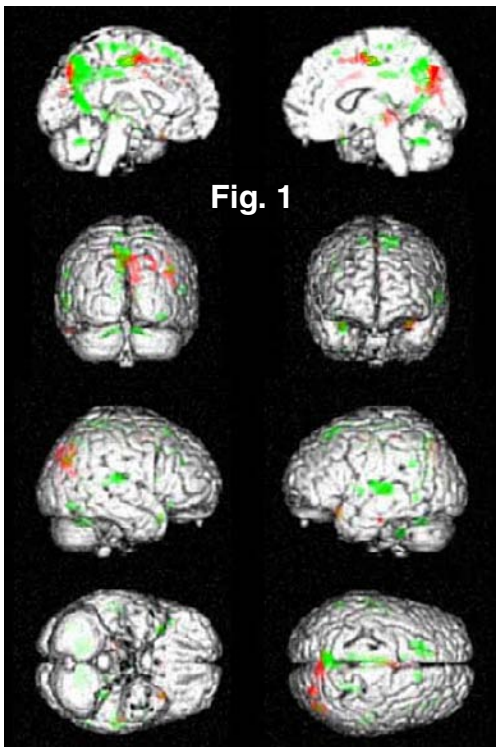
Tobacco smoking is the largest preventable cause of disease and premature death world wide [1]. Impairments in attention, accuracy of working memory, and verbal memory performance have been found in chronic smokers compared to nonsmokers [2, 3]. Cognitive deficits in smokers tend to be enduring [4] and are more severe with earlier age of onset of smoking [2]. These findings may imply structural brain deficits as a consequence of smoking. In humans, MR volumetric investigations in smokers with or without alcohol dependence reported reduced grey matter volumes and/or grey matter densities in the prefrontal, anterior cingulate and parietal cortex, in the temporal lobes and in the cerebellum compared to nonsmokers [5, 6]. Similarities of this deficit profile with the regional pattern of relative brain activation after acute nicotine application described in functional brain imaging studies are striking [6].
We hypothesized structural brain deficits in smokers relative to nonsmokers in cortical areas, the hippocampus, the thalamus and the cerebellum. Well-resolved MR imaging was performed in matched groups of smokers and never-smokers. Voxel-based morphometry (VBM) was carried out in order to detect differences in grey matter volume and grey matter density.

Methods

Twenty two smokers and 23 never-smokers matched for age, gender and education were recruited through newspaper advertisements. All subjects gave written informed consent. Subjects were excluded when fulfilling the criteria for an axis I or axis II disorder according to DSM-IV criteria. Alcohol consumption more than three times a week with more than two drinks per day was also an exclusion criterion. Occasional cannabis consumption (less than three joints per month in smokers) was accepted. Smoking behaviour was determined by a questionnaire specifically designed for this purpose and with the Fagerström Test for Nicotine Dependence. Nonsmokers were naïve with respect to tobacco consumption (never-smokers).
MR imaging was performed on a 3-tesla whole-body scanner (MEDSPEC 30/100, Bruker Biospin MRI, Ettlingen, Germany) using a quadrature head coil. A T1-weighted 3-D MRI was acquired using an MDEFT sequence (TR=19.3 ms, TE=4 ms, inversion time 550 ms, matrix size 192x256x128) yielding 128 transverse slices with a thickness of 1.5 mm and 1x1 mm^2 in-plane resolution. We used statistical parametric mapping software SPM2 (http://www.fil.ion.ucl.ac.uk/spm) to perform voxel-based morphometry. Group differences and correlations in regional grey and white matter volume and density were determined. Custom templates were created because the used scanner has a field strength of 3 T. The optimized VBM method as described previously [7] with SPM2 scripts by C. Gaser (http://dbm.neuro.uni-jena.de/vbm.html) was employed for data processing. The preprocessed data were analyzed with SPM2 employing the framework of the General Linear Model. The spatial coordinates obtained from the SPM2 results were transferred to the Talairach Daemon software (http://ric.uthscsa.edu/projects/talairachdaemon.html) for result localization.

Results and Discussion

We found no difference in whole-brain volume of smokers compared to never-smokers. Smokers showed reduced grey matter volume in frontal lobe subregions, the occipital cortex, cuneus and precuneus, as well as in the thalamus (Fig. 1; $p < 0.05$; FDR-corrected). Local decreases of grey matter density in smokers compared to never-smokers were found in several regions of the brain: the cerebellum, parts of the temporal and occipital lobe and areas in the middle cingulate cortex, superior frontal gyrus and supplementary motor area (Fig. 1). In the smokers group a significant negative correlation between magnitude of lifetime exposure to tobacco smoke (pack-years) and grey matter volume in the middle frontal gyrus, the superior, middle and inferior temporal gyrus, the lingual gyrus and the cerebellum was observed (Fig. 2; $p = 0.001$, FDR-uncorrected).



Our data indicate structural deficits of several cortical and subcortical regions in smokers relative to never-smokers, the topographic profile of the differences matching brain networks known to mediate drug reinforcement, attention and working memory processing. These findings may explain in part the reported cognitive dysfunctions in chronic cigarette consumers. Moreover, morphometric deficits in schizophrenia may partly be explained by the high smoking frequency in this disorder.

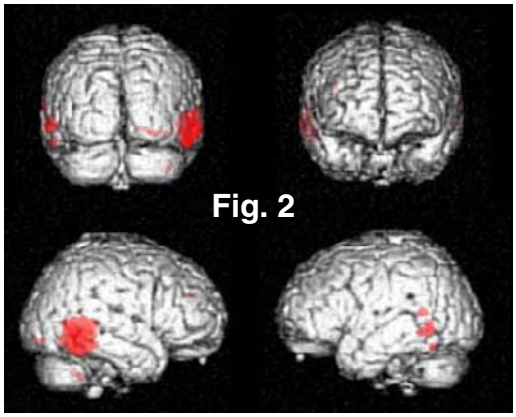


Fig. 2. Regions (red) in the brains of smokers for which negative correlation of gray matter volume with lifetime exposure to tobacco smoke was found.

References

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