

Evidence for the role of dopamine in brain activation associated with attentional bias in smokers: a pharmacological fMRI study

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Introduction

Attentional bias is the tendency of smokers to automatically direct their attention to smoking related cues in the environment. Attentional bias is known to influence smoking behaviours such as the ability to quit smoking.

Theoretical models¹ and behavioural studies² suggest that attentional bias emerges as a consequence of dopaminergic firing when smokers encounter smoking related cues. The current fMRI study employed a dopaminergic challenge using a dopamine antagonist (single dose of 2mg haloperidol) in order to test whether a reduction in dopamine indeed normalizes brain activation associated with attentional bias in smokers.

Methods

Participants: 25 smokers and 24 controls matched for age and gender (mean age = 22.56 and 21.80 years respectively). Smokers smoked at least 15 cigarettes a day (mean = 19.1 cigarettes). FTND³ scores indicated medium levels of nicotine dependence in smokers (mean score = 3.8).

Medication: Participants were administered a single oral dose of 2mg haloperidol or placebo four hours before each scanning session in a double-blind randomized cross-over design, which would result in about 30% D2 receptor occupancy during scanning⁴.

Scanner: 3T GE. TR: 2500, TE: 30, FOV: 240, 44 slices, voxel s: 2.5 mm³.

Figure 1. Attentional Bias Line Counting Task

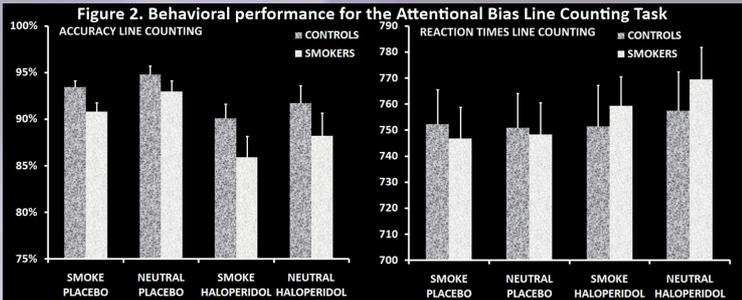


Attentional Bias Line Counting task: Participants counted the number of lines (2-5) presented in smoking pictures (LCSP) and neutral pictures (LCNP). By defining the LCSP minus LCNP contrast for fMRI analyses all brain activation related to line counting is cancelled out, what remains is brain activation reflecting the attentional bias for the smoking pictures.

Analyses: After preprocessing of fMRI images the contrast LCSP minus LCNP was calculated for both medication conditions. Between group two-sample t-tests per medication condition were performed ($p < 0.05$ FWE small volume) and masked by voxels showing a Group x Medication interaction ($p < 0.01$ whole brain uncorrected). Results for the between group two sample t-test for placebo are also reported without masking for the interaction to show overall brain activation associated with attentional bias in smokers. Accuracy scores and reaction times for line counting were analysed using a 2x2x2 RM-ANOVA (Group x Medication x Picture).

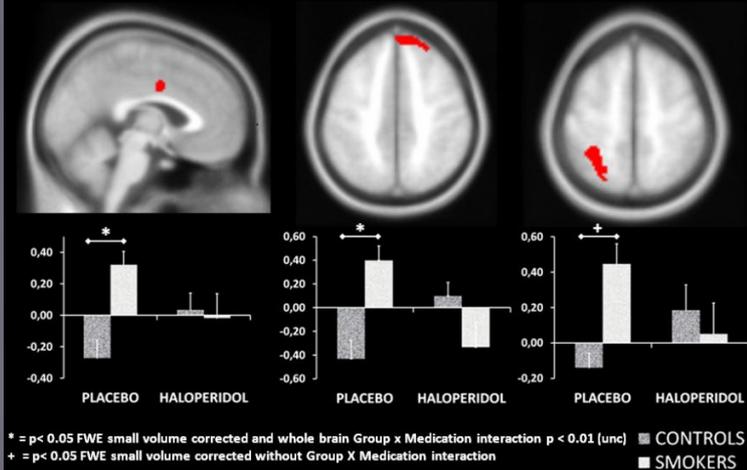
Results

Both groups were less accurate for line counting in smoking pictures, ($F(1,47) = 11.10, p < 0.01$). Haloperidol reduced line counting accuracy, $F(1,47)=10.36, p < .01$. Both groups showed faster reaction times for line counting in smoking pictures, $F(1,37) = 4.14, p < .05$. No main or interaction effects of Group were found for either accuracy or reaction times. In sum, behavioral results indicate that smoking pictures evoked an impulsive response style in both smokers and non-smoking controls (i.e., faster responses in combination with reduced accuracy).



After placebo, smokers showed attentional bias related brain activation (i.e., more activation than controls on the LCSP minus LCNP contrast) in the dorsal ACC (dACC), the left superior parietal gyrus (l-SPG) and the right dorsolateral prefrontal cortex (r-DLPFC) thereby replicating previous studies showing that these regions are involved in attentional bias⁵. The dACC and r-DLPFC showed a Group x Medication interaction and no differences between groups were found in these regions after haloperidol. The Group x Medication interactions and the lack of group differences after haloperidol suggest that attentional bias related brain activation in the dACC and r-DLPFC in smokers is normalized by a dopamine antagonist.

Figure 3. Brain activation associated with attentional bias in smokers



Conclusions

Activation in the I-ACC, r-DLPFC and l-SPG was found to be associated with attentional bias in smokers after placebo. As these regions are mainly involved in cognitive control it could be that dopaminergic firing evoked by smoking cues triggers cognitive control regions such that smokers can employ more cognitive control to continue ongoing behavior.

The current findings support theoretical accounts concerning the role of dopamine in attentional bias by demonstrating that brain activation in prefrontal regions associated with attentional bias in smokers is modulated by dopamine. That is, the dopamine antagonist haloperidol normalized brain activation in the dACC and DLPFC in smokers. These findings may have implications for the development of new pharmacotherapies for smoking. As haloperidol also reduced overall task performance it should be a future research agenda to investigate whether an optimal balance of dopamine in different brain regions in smokers can be achieved.