Sex differences revealed in the dopaminergic signature of tobacco smoking

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Background: Women have more difficulty quitting smoking than men. The neurobiological basis for this difference is unknown. Dopamine (DA) is a critical neurochemical that is implicated in nicotine reinforcement and smoking cessation treatment success, with evidence supporting stronger associations for men compared to women. A recent methodological innovation allows us to probe the DA response to smoking in highly localized striatal regions. This is the first investigation to examine sex differences in anatomical and temporal signatures of smoking-induced DA release.

Methods: Sixteen healthy smokers (8 male, 8 female) abstinent overnight, participated in one [11C]raclopride positron emission tomography (PET) scan. Subjects smoked their preferred brand of cigarette while being imaged. Brief DA responses (lasting only minutes) were extracted from the dynamic PET data. Voxel-wise analyses produced spatio-temporal patterns of DA release, visualized as “DA movies”. Parametric images of magnitude and timing of DA release were compared between groups.

Results: Men were significantly more likely than women to release DA in some fraction of the right ventral striatum in response to smoking. The male activation pattern in right ventral striatum in response to cigarettes was characterized by a faster and greater peak response to cigarettes than the female pattern. Additionally, women responded faster than men in a discrete sub-region of the dorsal putamen.

Conclusions: This is the first demonstration of sex differences in the DA response to tobacco smoking in the living human brain. We demonstrate that the magnitude and the timing of the DA response differs between men and women. Our finding, that men activate more ventrally than women, is consistent with the established notion that men smoke for the reinforcing drug effect of cigarettes. Women smoke for other reasons, such as mood regulation and cue reactivity, which may be more habit-driven, and dorsally localized. The DAergic signature of smoking may represent an important multi-dimensional biomarker of smoking dependence and a tool for the development of new gender-sensitive medications for smoking cessation.

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