RESEARCH ARTICLE

Correlations between orbitofrontal dysfunction and tobacco smoking

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Abstract
Orbitofrontal cortex is involved in various reward and reinforcement processes in the human brain. There is both anatomical and functional evidence for a dysfunction of orbitofrontal cortex in substance abusers, and nicotine has been shown to activate reward-related structures in the brain similarly to other abused drugs. This study shows positive correlations between smoking parameters (smoking status and packs smoked per day) and impairment on putative measures of orbitofrontal dysfunction (go/no-go, antisaccades, delayed alternation and impulsivity ratings). While causality could not be determined, other research suggests that an orbitofrontal dysfunction predisposes one toward tobacco abuse.

Introduction

Abuse of psychoactive drugs has been associated with dysfunction of orbitofrontal cortex, due primarily to its role in programming behavior based on processes of reward and motivation.[1] Several studies implicate orbitofrontal cortex in processes of reward and punishment. For example, orbitofrontal activity relates to the specific motivational significance of rewards.[2,3] It represents the incentive value of both primary and conditioned associations in reinforcement.[4] This includes both anticipation and delivery of reward.[5] Humans with orbitofrontal damage have impairments in the learning and reversal of reward associations.[6] The orbitofrontal behavioral syndrome (altered personality and social conduct, verbal and behavioural disinhibition, jocularity, lack of concern) is explainable by an underlying change in responsiveness to reward contingencies.

There is both anatomical and functional evidence for orbitofrontal dysfunction in addiction. Human polysubstance abusers have a smaller volume of gray matter in prefrontal cortex relative to controls.[7] Functional neuroimaging studies show that the orbitofrontal cortex is involved in the expectancy, cravings and decision-making aspects of drug abuse.[8] Neuropsychological measures sensitive to orbitofrontal dysfunction, such as Bechara's Gambling Task, reveal impairment in substance abuse populations.[9] Orbitofrontal cortex is differently activated in substance abusers relative to controls performing the Stroop task, which requires self-inhibition.[10]

Nicotine is a psychostimulant drug that has dose-dependent mood-altering effects.[11] Similar to other addictive drugs, it has been shown to activate reward-related structures in the brain, including prefrontal cortex. Thus, this study was undertaken to test the possibility that tobacco smoking is related to dysfunction on measures of orbitofrontal cortex function.

Materials and methods
Subjects
Subjects ($n = 30$) were a convenience sample recruited voluntarily, and did not receive any financial compensation for their participation. A large proportion were college students ($n = 25$) who received a miniscule amount of course credit for participating. The study was approved by an institutional review board and all subjects read and signed an appropriate informed consent, in accordance with Declaration of Helsinki. The subjects (19 females, 11 males) ranged in age from 19 to 70 years of age (mean 31.17 ± 16.76 years). There was a mean of 14.10 ± 1.63 years of education. Both smoking status (smoker vs. non-smoker) and the number of cigarette packs consumed per day were recorded. Subjects had no previous diagnosis of psychiatric or neurological disorder, and denied any history of head trauma with loss of consciousness.

Behavioral measures
Go/no-go tapping. Go/no-go (GNG) tapping involves regulation and inhibition of automatic motor responses.[12] An imitation tapping set (20 trials) is performed where the subject imitates a standardized sequence of taps (either one or two taps) performed by the examiner. A conflict tapping set (GNG-conflict) requires the subject to respond *opposite* the examiner (one tap for two, and vice versa) and an inhibition set (GNG-inhibition) requires suppressing a response (subject imitates when the examiner taps once, but refrains from tapping when the examiner taps twice). Conflict and inhibition sets involved standardized sets of 30 trials each. All taps by the examiner are performed at 1-second intervals. An incorrect response or a response delayed by more than 1 second is counted as an error.

Both electrophysiological and lesion studies support the role of orbitofrontal cortex in GNG tasks.[13–16]

Antisaccades. Antisaccades involve suppression of an automatic saccade toward a target.[17] The examiner and subject face each other and the examiner extends both arms directly out to the side, perpendicular to the subject. The subject fixates gaze on the tip of the examiner's nose. All saccade trials were administered according to a standardized random set, with equal numbers of left- and right-sided stimuli. In the prosaccade set (10 trials), the subject makes a saccade toward the fingers moving on either side. In the anti-saccade set (25 trials), the subject must look in the direction opposite of the moving fingers. Any movement of the eyes toward the stimulus was scored as an antisaccade error. Activity in the supplementary eye fields and medial orbitofrontal cortex (gyrus rectus) has been shown to correspond to antisaccade activity.[18]

Delayed alternation. The subject is shown two opaque cups and told a penny will be placed underneath one of them.[19] A screen is employed to prevent the subject from seeing the placement of the penny. A felt board was used under the cups and both cups were manipulated on every trial to prevent extraneous auditory cues. Both cups were baited with pennies for the first trial and on every successive trial, the cup opposite the subject's last choice was baited. The task involves 25 trials, with 24 possible alternations, and approximately 10 seconds between trials. Thus, the subject must correctly remember the placement of the penny on the last trial and alternate his response on each successive trial. Trials-to-criterion is the number of trials needed before five consecutive alternations are made. Several lines of evidence indicate that orbitofrontal cortex is essential for performance on alternation tasks, including human lesion studies and functional neuroimaging.[20,21]

Barratt Impulsiveness Scale (BIS-11). The Barratt Impulsiveness Scale is a 30-item self-rating scale which measures various aspects of impulsivity.[22] Subscales of the BIS-11 assess non-planning (orientation toward the present rather than the future, BIS-A), motor impulsivity (acting without thinking, BIS-B) and cognitive impulsivity (hasty decision making, BIS-C). Impulsivity is a frequent sequela of orbitofrontal dysfunction.[23,24]

Results

Pearson product-moment correlations were performed between smoking characteristics and the behavioural measures (Table 1). Smoking status correlated with GNG inhibition errors ($r = 0.35$, $p < 0.02$), antisaccade errors ($r = 0.36$, $p < 0.02$), delayed alternation-trials to criterion ($r = 0.33$, $p < 0.05$) and BIS non-planning ($r = 0.30$, $p = 0.05$). Packs of cigarettes smoked per day correlated with GNG inhibition errors ($p < 0.001$), GNG total errors ($r = 0.31$, $p < 0.05$), antisaccade errors ($r = 0.45$, $p < 0.001$) and BIS motor impulsivity ($r = 0.31$, $p < 0.05$).

Discussion

Several of the putative orbitofrontal tasks showed correlations between smoking parameters and errors of response inhibition and impulsivity. The correlations are all positive and in the direction predicted for smokers, i.e. greater smoking correlates with greater impairment.

These results are suggestive of subtle orbitofrontal dysfunction in smokers that are proportionate to the amount of smoking. While the causality of these findings cannot be determined due to the correlational nature of the study, it seems less likely that tobacco smoking caused the orbitofrontal dysfunction. Nicotine typically has cognitive-enhancing effects, particularly in tasks involving prefrontal cortex and associated subcortical structures.[25–27] On the other hand,

normal variations occur in cerebral development, which have functional consequences.[28] It is suggested that such normal variations in orbitofrontal development serve as one of many possible predisposing factors toward the development of substance abuse.

Table 1. *Pearson correlations*

	Smoking status	Packs/day
GNG-Con	0.17	0.28
GNG-Inh	0.35**	0.50‡
GNG-T	0.21	0.31*
AS-Err	0.36**	0.45‡
DA-Alt	−0.21	−0.22
DA-TTC	0.33*	0.18
BIS-Tot	0.06	−0.09
BIS-A	0.30*	−0.25
BIS-B	0.27	0.31*
BIS-C	0.21	−0.03

* Significant at the 0.05 level; **significant at the 0.02 level; †significant at the 0.01 level; ‡ significant at the 0.001 level. BIS: Barratt Impulsiveness Scale, GNG-C: go/no-go conflict errors; GNG-I: go/no-go inhibition errors; GNG-T: go/no-go total errors; AS: antisaccade errors; DA-Alt: delayed alternation-total alternations; DA-TC: delayed alternation-trials to criterion.

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