Dose-Related Effects of Cigarette Smoking on Olfactory Function

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Little is known about the influence of cigarette smoking on the ability to smell; previous studies on this topic have led to contradictory findings and have failed to take into account smoking dose and duration. In the present study, the 40-odorant University of Pennsylvania Smell Identification Test was administered to 638 subjects for whom detailed smoking histories were available. Smoking was found to be adversely associated with odor identification ability in a dose-related manner in both current and previous cigarette smokers. Among previous smokers, improvement in olfactory function was related to the time elapsed since the cessation of smoking. Logistic regression analysis found current smokers to be nearly twice as likely to evidence an olfactory deficit than persons who have never smoked. Overall, the data suggest that (1) smoking causes long-term but reversible adverse effects on the ability to smell and (2) the failure of some studies to demonstrate smoking effects may be caused by the inclusion of persons with a history of smoking in the nonsmoking groups.

Methods

Subjects.—The volunteer study group was composed of 553 male and 85 female employees of a large chemical manufacturing facility (mean age, 42.97 years; SD = 11.22 years; age range, 17 to 69 years; for a detailed description of the study population, see reference 11). Two hundred sixty-two of the subjects had never smoked cigarettes, 197 had smoked cigarettes previously, and 179 currently smoked cigarettes. Fourteen subjects also reported smoking cigars or pipes. Ethnically, 524 were white, 81 were black, and 33 were of other backgrounds (eg, Oriental, Hispanic).

Data Collection.—Olfactory function was assessed using the University of Pennsylvania Smell Identification Test (UPSIT—commercially marketed as the Smell Identification Test, Sensonic Inc, Haddonfield, NJ), a standardized, self-administered quantitative test that incorporates 40 microencapsulated odorants. This test has been shown to be highly reliable, to correlate well with detection threshold tests, and to detect the influences of age, sex, and various disease states on smell function.

THE SENSE of smell is of considerable importance to man. This primary sense (1) signals such environmental dangers as leaking natural gas, spoiled food, and smoke, (2) largely determines the flavor of foods and beverages, and (3) may be of diagnostic value for the early detection of a number of neurological disorders, including Alzheimer's disease and parkinsonism. In addition, this sense purveys aesthetic pleasure, as evidenced by the predilection of our species for the smell of such objects as flowers, condiments, and scented consumer products.

Although several studies suggest that cigarette smoking has an adverse effect on the ability to smell, other studies have failed to find such an influence, and some authors suggest, without the benefit of data, that tobacco smoking only temporarily alters smell function. Unfortunately, few odorants have been tested, which could preclude the detection of a smoking-related effect, and the potential influences of past smoking or smoking dose have not been determined. Animal studies demonstrate that relatively brief exposures to cigarette smoke (once or twice per day for 6 to 9 days) can cause anatomic changes within the olfactory epithelium, including a reduction in the size and number of olfactory vesicles and cilia. It is not known whether such effects are short- or long-term.

In the present study we determined, using a 40-odorant test, the odor identification ability of a large number of persons for whom complete smoking histories were available. As indicated herein, the results of this study reveal a clear adverse effect of cigarette smoking on olfactory function that is dose related and present in past smokers. This effect is reversible, at least to some degree, and the time course of this reversibility is dependent on the duration of cessation from smoking and the amount of prior smoking activity.
Data Analysis.—Study variables included subject age, sex, and education level, as well as smoking history, smoking dose, and in previous smokers, years since the last cigarette was smoked. Cigarette dose was calculated in pack-years by multiplying the number of packs smoked per day by the number of years that smoking occurred. Information regarding current and past jobs, which allowed us to control for the potential confounding by exposure to chemicals used in the workplace that might interfere with smell function (ie, acrylates and methacrylates), was provided by the company's personnel office. Exposure to these chemicals was represented in our analyses as “ever” or “never” employed for at least 6 weeks in a job category where such exposure occurred.5

Statistical analyses included linear regression and logistic regression.7 All statistical tests were two tailed with α = .05. Linear regression analysis allowed us to assess the relative influence of the aforementioned variables on the olfactory measure. The UPSIT scores were subjected to a log(41 – UPSIT) transformation to reduce distribution skewness.8 Factors were entered into the linear regression to control for confounding by subject age, ethnic group, chemical exposure, and cigar or pipe smoking. To increase power and reduce intersubject variability, a four-level ordinal smoking dose variable was incorporated into the model. Cutoff points for each level of this variable were chosen to provide approximately equivalent numbers of subjects in each dose group and similar smoking dose means across the current and previous smoking dose levels; the smoking dose of each subject was represented by the mean of the subject’s respective dose group. For this analysis, the time since cessation of smoking data were similarly transformed to a four-level ordinal variable.

The logistic regression analysis allowed for the calculation of an olfactory dysfunction odds ratio for current and previous smokers while adjusting for potential confounders (eg, age, sex), thereby providing estimates of the relative risk of olfactory dysfunction associated with smoking. In this analysis, subjects were classified as either current, previous, or never smokers, and the UPSIT score was used to define case and control subjects as a dichotomous outcome. Case subjects were defined as those individuals whose UPSIT scores fell at or below the 10th percentile for their decade of age within the study population. This criterion is used as a measure for assessing olfactory dysfunction in our clinic9 and is a form of stratified sampling that ensures that the same proportion of case and control subjects will be compared within each decade of age. Control subjects were defined as those individuals whose UPSIT scores fell at or above the 50th percentile for their age decade in this population.

Results

A relatively large inverse relation between pack-years and UPSIT score was present for both current and previous smokers when cumulative cigarette smoking dose was evaluated. However, when such dose was not considered (as is the case in previous studies), only current smokers evidenced a significant decrease in smell function relative to persons who have never smoked (respective t values for never vs current smokers and never vs previous smokers, 3.67 [df = 629, P = .001] and 0.90 [df = 629, P = .368]).

The dose-related detrimental effect is shown for current smokers in Fig 1 (where the adjusted UPSIT scores are shown as a function of cumulative smoking dose) and for previous smokers in Fig 2 (where the adjusted UPSIT scores are depicted as a function of both cumulative smoking dose and years since cessation of smoking). The cumulative dose, for both current and previous smokers, was significantly related to olfactory test scores (t = 2.948 [df = 627, P = .003]). The number of years since cessation of cigarette smoking was significantly related to an improvement in olfactory function in previous smokers (Fig 2, t = −2.091 [df = 627, P = .04]). The regression coefficient for the years since cessation of smoking variable was more than twice as large as that for the cumulative smoking dose variable (but related to the UPSIT score in the opposite direction), indicating, for example, that the improvement per year in olfactory function following cession of smoking would counteract the yearly deficit acquired for a two-pack-per-day smoker.

No influence of cigar or pipe smoking was observed, probably because of the small number of subjects who reported this behavior. There were no significant interactions between smoking dose and any of the aforementioned model variables (including potential confounders). Age of the subject did not interact with smoking dose, indicating that age did
not potentiate or attenuate the smoking dose effect. Following centering of the age variables, the condition indices of the linear regression analyses indicated that collinearity was not a problem. Specifically, age, smoking dose, and the smoking cessation variable were not colinear to a degree that would prevent control of confounding by linear regression.

The results of the logistic regression analysis revealed that persons who currently smoke are nearly twice as likely to have an olfactory deficit than persons who have never smoked (adjusted smoking odds ratio [95% confidence interval] = 1.9 [1.0 to 3.8]). No elevated risk of olfactory dysfunction was found for previous smokers when compared with never smokers (adjusted odds ratio [95% confidence interval] = 0.7 [0.3 to 1.5]).

An examination of each of the 40 odorants suggested that the effects were general and not confined to any given subset of stimuli. A Spearman correlation computed across the 40 UPSIT items (ranked on the basis of percent correct) between the current and never smokers was r = .78. Given the limited range of the percent of the subjects who missed each item, such a correlation is relatively strong. Examination of odds ratios in current vs not current smoking groups, calculated from individual logistic regression analyses for each UPSIT item, did not provide evidence that the smoking effect was limited to a subset of items.

Comment

The primary finding of this study—that cigarette smoking adversely influences odor identification ability in a dose-related manner in both present and past smokers—suggests that smoking causes long-term changes in the olfactory system. While improvement in smell function appears to occur following cessation of smoking, such improvement is not rapid (eg, for a two-pack-per-day smoker, restoration of smell function to the level observed in non-smokers requires approximately the same number of years as the number of years smoked). Despite the fact that olfactory function was depressed in previous smokers when dose was considered (Fig 2), logistic regression analysis failed to find a significantly elevated smoking odds ratio in this group when subjects were dichotomized into cases and controls and dose was not considered. This likely reflects the improvement in UPSIT test scores as a result of time since cessation of smoking.

Our observation that previous smokers evidence dose-related decrements in their odor-identification ability analogous to those observed in current smokers has significant implications for studies of chemosensory function. This finding may explain, for example, why previous studies have often observed marginal or nonexistent effects of smoking on the ability to smell. Such studies categorized previous smokers as non-smokers—some of which may have had high previous smoking doses or only recently stopped smoking. In addition, such studies did not control for the effects of cumulative smoking dose. Our results imply that complete smoking histories are needed in studies of human olfactory function if the influences of smoking are to be identified or controlled.

It should be noted that the magnitude of the adverse effects of smoking on olfactory function is not large compared with the effects of such variables as age and sex. Nevertheless, as can be seen in Figs 1 and 2, an average difference of nearly 4 points on the UPSIT scale is evident between individuals at the lowest and highest cumulative smoking doses within both the previous and current smoking groups. Although most of the test scores are within the general normal range (as determined from UPSIT norms), a number of heavy current and previous smokers evidenced test scores considered to be abnormal for subjects in the age range of 21 to 60 years.

The biological basis for the decreased ability to smell associated with smoking is not known. Long-term effects could be caused by the adverse influence of chemicals in cigarette smoke on the olfactory receptor cells within the olfactory mucosa. It is well known that animals exposed to a number of chemicals present in cigarette smoke (eg, acrolein, acetaldehyde, ammonia, and formaldehyde, among others) exhibit damage to the olfactory mucosa and receptor cells, often in a dose-related manner. Short-term effects could be caused by the influence of such chemicals on (1) the consistency or nature of the mucus overlying the receptors (thereby altering odorant transport), (2) adaptation or habituation of the receptor system, or (3) nasal airway constriction. However, if the latter influence is of significance, considerable airway obstruction must be present.
Although the present findings, which imply long-term general effects of cigarette smoking on smell function, could be explained by the adverse effects of airborne chemicals on the olfactory receptors, the basis of the relatively slow return of smell function following cessation of smoking is less certain, since it is generally believed that renewal of the olfactory epithelium via regenerative processes, at least in nonhuman mammals, occurs within a matter of weeks. Our findings suggest the possibility that longer-term restorative processes are present in the human olfactory epithelium, although the nature of such processes have yet to be elucidated.

This research was supported by the Rohm and Haas Company, Philadelphia, Pa, by grant DC00161 from the National Institute on Deafness and Other Communication Disorders, Bethesda, Md (Dr Doty and Mr Frye), and by the Andrew W. Mellon Foundation, New York, NY (Dr Schwartz).

References