"The Sniffer"

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A. Statement of Study and Purpose Rationale

Cigarette smoking is a leading cause of premature death in the United States (McGinnis) and it is unanimous among the medical community that abstinence from cigarette smoking would lead to the betterment of the health of an -individual as well as the general health of the nation. Breaking any habit is difficult, but confounding the already challenging task of smoking cessation is the fact that smokers typically gain weight quitting (Klesges). The threat of post-cessation weight gain after they quit has been put forth as a potent obstacle to stopping smoking for some (Perkins) and especially for those-OArho may consciously or unconsciously smoke as a means of weightcontrol (Pomerleau). just as the threat of weight gain may deter initial smoking cessation attempts, so too has actual weight gain been postulated to contribute to smoking relapse. Given that weight gain seems to be a consistent sequela of smoking cessation, a successful intervention for weight gain prevention might attract smokers who fear weight gain and might potentially reduce relapse.

The exact cause of post-cessation weight gain is yet unknown, but changes in both metabolism and food intake are implicated. Most studies concur that smoking and nicotine do not have chronic effects on metabolism, in that "smokers and nonsmokers have similar resting metabolic rates (RMR) and that RMR declines very little after smoking cessation" (Perkins, 401). An acute rise in RMR post-smoking seems to be less than 10% and transient - on the order of a 30 minute duration (Perkins). It is possible then that postcessation weight gain in ex-smokers could in part be related to short-term decreases in metabolic rate, but it would seem unlikely that these small changes could explain the weight gain entirely.

Current consensus relates post-cessation weight gain perhaps more importantly to longer-term increases in caloric intake (Hall). Studies suggest that this increased caloric intake and subsequent weight change occur most dramatically within three weeks from the quit date and continue for six months thereafter (Hallet al.). There is no concessus on the mechanism for the increased calorie intake, but many researchers have tried to relate changes in perception of food taste and olfactory cues to the eating change (Epstein).

"Researchers have found differences in perception of gustatory sensations between smokers and nonsmokers (Krut), decreases in perception of gustatory sensations after nicotine presentation (Perkins), and increases in perception after smoking cessation(Hall)" (Epstein, 641). In addition to demonstrating gustatory changes, other studies have shown decreases in olfactory function secondary to smoking (Frye).

On the basis of these findings, It can be inferred that smoking reduces perception of food flavors or "food cues"- namely, food taste and olfactory cues, and if this assumption holds true, then it is reasonable to postulate that the "hedonic value of food is reduced for smokers" (Epstein, 641). It follows that food, which appeals to both gustatory and olfactory senses may be less enjoyable and therefore less sought after by the smoker thereby potentially explaining the increased calorie intake of the ex-smoker who now has revitalized senses. Thus it is not surprising that after cessation, smokers often report that their food tastes different and that their sense of taste becomes more sensitive and discriminating (Peterson). It would ' seem then that a safe intervention at the time of smoking cessation that would dull the gustatory and olfactory senses would perhaps reduce the hedonic value of food, decrease caloric intake, and thereby limit post-cessation weight gain.

a. Study Purpose

This study proposes that a group of smoking cessation subjects who smell a non-nicotine containing , tar-smelling substance before meals and snacks will have no post-cessation weight gain as compared to the control group of smoking cessation subjects who smell a neutral smell before eating.

B. Description of Study Design and Statistical Analysis

We will study 160 smokers, all of whom desire an attempt at quitting. Subjects will be recruited by self-referral in response to posted fliers, mass mailings and advertisements. Subjects will also be recruited from local primary care practices and referring physicians. Each subject will be evaluated by his/her primary care provider with a brief physical exam before entering the study.

Primary care providers as well as subjects will be told that this is a study on smoking cessation and the sense of smell. Those subjects passing the physical exam requirements and meeting inclusion and exclusion criteria will all be administered a nicotine patch for the six week duration of the study with the patch dose being decreased as per standard 6 week stepwise patch instructions every two weeks. Each subject will watch an instructive video tape with a lecture by a dietician and an exercise therapist. No special attention to weight gain during or after smoking cessation will be discussed, but rather these will be 20 minute talks on healthy lifestyle and the benefits of smoking cessation. At this time, subjects will fill out a brief questionnaire about demographics, smoking history, lifestyle, . - . etc. Also at this time, subjects will meet with a health care provider who will conduct a brief physical exam including height and weight measurements- on a calibrated study scale that will remain constant throughout the length of the study. The study subjects will be weighed in underwear only at each visit for precision's sake and given the brevity of the study, attention must be paid to even small changes in weight. Also at this time, BNU- body mass index will be calculated. This will mark the first physical exam and the initial data points of the study.

Subjects will be randomly assigned to be in either Group A, the study group, or Group B, the control group. On the initial questionnaire, subjects will be asked to answer questions in addition to those about demographics and lifestyle, ones about their self-perceptions as "weight-control smokers." This subgroup of women as defined by Pomerleau. in a 1993 edi ' tion of The journal Of Substance Abuse, "were significantly more likely to report weight gain and increased hunger during abstinence from smoking" (Pomerleau, 391). Because of the suspected existence of a high risk group of "female weight-control smokers," those subjects implicating themselves as this prototypic personality type will be initially stratified and then randomized to either Groups A or B. Also, past studies have shown that, for women only, the amount of weight gained at six weeks post-cessation is linearly predictive of wei'-' gained and kept on 6 months after the quit date (Hall, Weight Gain Prevention). the same predictive value or extrapolation was not seen for male ex-smokers and for this reason, subjects will be stratified by gender as well as "femal weight-control smoker" profiles.

Group A, the study group, will be given a "sniffer," a non-nicotine containing, tar-smelling substance which they will be instructed to sniff before meals and snacks. Group B, the control group, will be given a barely scented mineral water sniffer, a neutral smell, to be sniffed before all meals and snacks. Each subject in both groups will return two weeks later for a "mock sensory perception quiz" and a physical exam. The sensory perception quiz will consist of 15 minutes with one of the study representatives, three odors, and a brief questionnaire. The questionnaire will consist of mock questions on the quality, intensity , bouquet, . . . of the three smells- a fruit, a flower, and a nonexistent smell, and will include questions regarding compliance with the sniffer and with cigarette smoking relapse. The physical exam will include measurements of height, weight, vital signs, calculations of BMI, carbon monoxide monitoring and blood cotinine measure. The subjects will be instructed to return again at 4 and 6 weeks where they will undergo the same mock sensory perception quiz and physical exam. This last physical exam will mark the end of the study.

a. Statistical Analysis

We will implement an intent to treat analysis. Primary analysis will be a T-test comparison that our treatment was effective between Groups A and B ie; zero weight gain in the treatment group. Assuming no gain over six weeks, with 80 subjects in each group, we will assess the data with a power of 80% and a p value of .05. We will screen subjects initially for "female weightcontrol" personality type

and gender and have a stratified treatment allocation scheme ensuring that they are allocated to groups A and B equally. Analysis will be on the pooled sample across the strata.

Secondary analysis will be an analysis of covariance adjusting for baseline BMI. And a tertiary analysis of covariance will be conducted to control for demographic differences between subjects; differences learned on the initial trial questionnaire: ie. single status, sedentary job, gender. . . A second set of analysis will be an efficacy analysis-(the rules of which will be developed later) designed to exclude cases where lack of compliance with the sniffing protocol, or ciagarette smoking relapse would confound the results.

C. Description of Study Procedures

The study will be a randomized double-blind entrol trial. Subjects and referring physicians will be told that the study is investigating the changes in the sense of smell post-smoking cessation. The study subjects are not told outright that we are investigating post-cessation weight gain because eating and food cravings are highly suggestible behaviors. Although it is likely common knowledge to most smokers and would-be ex-smokers that many people gain weight after quitting, it is our feeling that advertising weight gain as the study parameter could falsely alter subjects' behaviors and levels of consciousness about their own eating, thereby distorting study results.

The study is scheduled to last for six weeks with an initial evaluation and three follow-up evaluations at 2, 4, and 6 weeks. Each follow-up visit is expected to last 30 minutes with 15 minutes being devoted to the sensory perception quiz and the other 15 minutes being devoted to the physical exam. Six weeks was felt to be an appropriate study length given that multiple trials have demonstrated that the most significant weight gain occurs within three weeks from the quit date (Hall) (Hughes).

Carbon monoxide has been shown to be an objective and successful way of monitoring smoking cessation status in studies for the last twenty years (Lando, 1975). Expired air carbon monoxide readings of 10.9 ppm or less will be used in this study as meeting criteria for smoking abstinence (Hall) (Lando). Also, blood cotinine levels drawn at 6 weeks post-quitting of 10 ng/ml or less will be another objective criteria for smoking abstinence Benowitz).

D. Description of Study Subjects

All study subjects will be current cigarette smokers with desires to quit. All subjects will undergo an initial physical exam and general screening by a primary care physician. Exclusion criteria would consist of medical conditions that would either place a subject at increased risk given the study design or would confound the results if their medical condition artificially affected BMI or weight. For example, asthmatics or those with acute bronchospastic conditions exacerbated by smells or inhalants will be excluded. Subjects with migraine headache conditions that are worsened by smells will be excluded. All subjects with contraindications to the nicotine patch will be excluded. Subjects with type 1 diabetes, thyroid disease, those on chronic steroids or drugs altering appetite or RMR will be excluded.

Subjects will be permitted to stop the study at any time and especially if any subject feels that his/her participation is contributing to smoking relapse, premature termination will be expected.

E. Confidentiality of Study

All study subjects, their physical exam data, and their questionnaire information will be coded by their study number, randomly assigned to them at the study outset. Data will be stored and secured with access only by study investigators.

F. Location of the Study

The study will be based at CPMC and all outpatient physical exams and follow-up visits will be conducted in the PH 10 outpatient study research facility.

G. Risks and Benefits

The largest risk of this study would be smoking relapse, but perhaps that is a risk of any trial on smoking cessation. Another potential risk would be aesthetic displeasure with the tar-smelling sniffer. It is unclear whether an ex-smoker would find that smell pleasing, repulsive, or tempting. Another risk would be unwanted weight gain after quitting.

A potential benefit to all members of the study would be abstinence from smoking or at least reduction in cigarette use. Another potential benefit would be abstinence from smoking with reduced or potentially no weight gain. The benefit to society as a whole would be the discovery of a safe intervention to limit or eliminate post-cessation weight gain, perhaps making quitting more appealing to current smokers and reducing relapse rates for once successful ex-smokers who have suffered undesireable weight gain at prior attempts.

H. Alternative Therapies

Although post-cessation weight gain has been recognized for years, few interventions for its prevention have been successful. Other studies have investigated the success of fluoxetine therapy and oral anti-depressant therapy with equivocal results. "The sniffer" is an experimental therapy with a different mode of entry from other therapies tried in that it is a nasal inhalant. To date, there is no entirely safe or effective intervention known.

I. Compensations and Costs to Subjects

All travel expenses and costs to the subjects will be paid for. Subjects will not be charged for carbon monoxide monitoring or blood cotinine level evaluations.

"To Sniff or Not to Sniff- That is the Question."