Effects of Intranasal Oxytocin on Cigarette Smoking
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Design Overview. The study will use a within-subjects design in which subjects will receive administrations of inOT (40 IU) and placebo. After an initial baseline session, participants will complete two experimental sessions at which an identical assessment battery of key outcomes will be administered. Session order will be counterbalanced and sessions will be separated by at least 5 days as a washout period. After completing all sessions participants will be debriefed.

Participants. We will complete approximately 60 current smokers, recruiting via online and community advertisements.

Inclusion Criteria: 1) Ages 18-40; 2) Smoke >= 10 cig/day for the past year; 3) English fluency.

Exclusion Criteria: 1) Current DSM-5 substance use disorder, excluding nicotine dependence (to minimize alcohol or drug withdrawal symptoms during the study sessions); 2) Any medical condition that would increase risk for study participation (such as sinus infection or other condition blocking access to the olfactory epithelium); 3) Women who are pregnant or nursing; 4) Current use of psychiatric medication; 5) Breath Carbon Monoxide (CO) levels < 10ppm measured during study intake (to exclude individuals who overreport smoking in order to participate in the study); 6) Planning to quit or reduce smoking in the next 30 days; and 7) Current regular use of other nicotine products.

Procedures

Experimental sessions: Sessions will be conducted sometime between 9:00 AM and 3:00 PM. Upon reporting to the lab, participants will provide breath samples to confirm abstinence from smoking as well as alcohol, urine samples to test for drugs and womens' urine samples will also be used to test for pregnancy. Sessions will be rescheduled if the participant provides a positive breath alcohol reading or a breath CO > 9 ppm.

At 9:15 AM, baseline cardiovascular measures (i.e., heart rate and blood pressure) will be obtained, and participants will complete self-report mood, withdrawal, and craving questionnaires. At 9:45 AM, participants will self-administer the intranasal spray. Cardiovascular and subjective measures will then be obtained repeatedly at 10:20, 10:50, and 11:20.

At 11:40 PM, they will begin the Smoking Lapse Analogue task, which begins with a 50-min delay period and ends with a 60-min self-administration period. After, participants will rest for an additional 60 min and then the final cardiovascular and self-report measures will be obtained (at 2:50 PM). Around 3:00PM, participants will be discharged.

inOT preparation and administration: inOT and placebo doses will be prepared by the USC Hospital's investigational pharmacy within 24 hours of use. All waste will be discarded, and no doses will be reused or stored longer than 24 hours. IN Placebo will consist of 4ml sterile saline (0.9% provided by USC pharmacy) and will be transferred into four, 1 ml intranasal atomizers (see figure: MAD100 by LMA Inc., San Diego, CA). Nasal sprays will be self-administered in four doses to each nare over the course of 15 minutes.

Experimental Session Measures

Cardiovascular and Subjective. The following measures will be given to all participants before the first intranasal spray administration and at repeated intervals thereafter. Heart rate and blood pressure will be assessed via a digital monitor as a physiological measure of withdrawal. Subjective measures will instruct participants to respond based on how they feel "right now." The Profile of Mood States (POMS) lists 72 affective adjectives that are rated on 4-point and includes subscales for subjective experiences (e.g., anxious). The Minnesota Nicotine Withdrawal Scale (MNWS) measures 11 DSM withdrawal symptoms on 6-point Likert-type scales. The MNWS total score will serve as the primary composite measure of subjective withdrawal. The 10-item Brief Questionnaire of Smoking Urges (QSU) measures desire, intention, urge, and need to smoke.

Smoking Lapse Analogue Task: This task measures ability to resist the temptation to initiate smoking under conditions in which it is advantageous to remain abstinent. Following the second intranasal spray, participants will be presented with a tray containing 8 cigarettes of their preferred brand, a lighter, and an ashtray. This task begins with the delay period, during which participants will be instructed that they can commence smoking at any point over the next 50 min, but that for each 5 min they delay smoking, they will earn between $0.20 to $0.50 (this $ value has shown sensitivity to abstinence in our prior work using smokers from the Los Angeles area). Thus, participants can earn between $2 to $5 during the delay period. When participants "give in" and indicate they want to initiate smoking (or at the end of 50 min for those who choose not to smoke), they begin the self-administration period. During this period, participants will be told they can

now smoke as little or as much as they wish over the next 60 min, that they start with a monetary credit ranging between $1.60 to $4.00, and that for each cigarette they light, it will cost them $0.20 to $0.50. At the end of self-administration, participants enter a rest period (with no smoking) that lasts until the final assessment. Including the rest period is necessary to prevent an impending opportunity to smoke once they leave the laboratory, which could reduce smoking during the delay and self-administration periods. The number of minutes before participants begin smoking is the primary outcome ("delay score"; range 0-50).

Data Analysis. We hypothesize that inOT will: 1) increase the "delay score" on the Smoking Lapse Analogue Task (Primary Aim 1); and 2) attenuate smoking urge and nicotine withdrawal (Primary Aim 2). For Primary Aim 1, we will analyze "delay score" data from the placebo and active inOT sessions using mixed linear models (MLMs). Drug (placebo, 40 IU inOT) will be an independent effect and we will control for session order, and sex. For Primary Aim 2, we will conduct similar analyses with the addition of time as an independent factor for all within-session repeated measures (e.g., subjective-effects).