Title of Study: Oxytocin Suppresses Substance Use Disorders Associated With Chronic Stress

NCT02742532

Date 2019.06.05

Study Procedures

Subjects:

Active Duty Service Members between the ages of 18-65 with a current Alcohol or Substance Use Disorder and current PTSD or trauma anxiety were recruited to be in the study.

Screening:

Screening of recruited participants occurred after the subjects have been given a full description of the study procedures and have signed an IRB approved consent. Subjects were assessed for an alcohol or substance use disorder using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al.,1998) or AUDIT, and PTSD using the Clinician Administered PTSD Scale (CAPS; Weathers et al., 2001) or MINI or clinician assessment for anxiety disorder NOS or DASS for anxiety/stress. The MINI will also assess for other exclusionary diagnoses where applicable (e.g., bipolar disorder, drug use disorders). The screening will include: basic vitals (heart rate, blood pressure, etc), background information including substance use history, family history of problem drinking or drug use, inclusion /exclusion criteria evaluation, as well as behavioral interviews and questionnaires listed below in data collection.

Female subjects screening:

All female subjects were required to be non-pregnant, non-lactating, not trying to become pregnant, and not having unprotected intercourse during the course of the study. Females were tested for pregnancy at both study visits—at screening and on testing day. All females were

required to not have unprotected intercourse while enrolled in the study and will be tested for pregnancy at both study visits—at screening and on testing day.

Testing Procedures:

Participants were breathalyzed and given a urine drug screen test prior to beginning the laboratory test. Participants were acclimated for approximately 60 minutes to the testing environment. Following the acclimation, baseline assessments of subjective craving and physiologic (HR, BP) measures were collected. Forty-five min prior to stress task, participants self-administered one dose of intra-nasal oxytocin (40 IUs; 5 puffs in each nostril) or saline placebo. Post-administration assessments of subjective craving and physiologic (HR, BP) measures were collected.

Trier Social Stress Test Procedure (TSST is a standardized psychological stress challenge asking subjects to give a speech and do math in front of a panel. This produces a reliable stress response across a number of subject populations. This test was adapted to be used in a group setting (TSST-G) (von Dawans, 2011). The total time for the TSST-G is 20 min.

Participants were told that they would be asked to perform a speech and mathematical calculations in front of a committee. The topic of the speech was personalized to the population. Participants were given 10 min to prepare the speech and a countdown clock placed in view of the individual. Following the speech preparation, assessments of subjective craving and physiologic (HR, BP) measures were collected.

All participants were guided to the testing room and asked to stand in a row in front of the "committee" and two conspicuous video- cameras. Participants were separated by mobile

dividing walls from other participants. Participants were instructed to deliver their speeches successively, for ~2 min each. To standardize the group experience for each subject, the first participant in each group was a confederate with a predetermined speech. After all participants had given their 2-min speech (a total of 12 min), the committee asked the subjects to serially subtract in increments of 17. Each participant received an individual starting number to avoid learning effects. If participants made a mistake, they had to restart at their starting number. Participants generally have a total of 80 s of subtraction for each participant (a total of ~8 min). Following the TSST-G, all participants were escorted back to the preparation room to obtain 4 post-task measurements over 60 minutes measuring subjective craving and physiologic (HR, BP) measures.

Debriefing:

After the post-task assessments, participants were debriefed about the nature of the experiment. Study staff disclosed to participants that the purpose of the task to create stress and the results are not a reflection of the participant's abilities. They were informed that there was no voice, video, or behavioral recording or analysis performed based on the task, and their performance would not affect their treatment program or standing. Participants will be asked to not disclose this information to other potential participants who may not have yet participated in the study. In our experience, most cravings return to baseline (i.e., < 5) within 15 min following the stressor. Clinical staff will be notified if in the event that the craving post-test rating is significantly elevated (i.e., > 5 on the 0-10 scale. Participants will also be provided a snack or lunch at the end of the data collection.

Statistical/Data Analysis Plan

Sample Size Estimation:

It is expected that subjects treated with OT, as compared to placebo, will exhibit significantly lower levels of craving in response to the TSST. The expected effect size for these analyses (craving, d = 1.2) is based on pilot data (N=16) from a sample of marijuana-dependent individuals exposed to the TSST (McRae-Clark, Baker, Moran-Santa Maria, & Brady, 2013). To detect an effect size of 1.02 with a Type 1 error protection level of .05 and power (1-ß) of .85 (Cohen, 1988), a sample size of 20 per group would be required. Similarly, recently published data involving marijuana-dependent individuals (N=16), suggest an effect size of .69, which would require a sample size of 33 per group (N=66 total).

Data Collection:

Subjective craving was measured with a modified Within Session Rating Scale (Childress et al., 1986) currently used in ongoing human laboratory studies which will be used to assess subjective craving at each assessment time point during the procedure. This 100 mm visual analogue scale is anchored from 0 = none to 10 = extreme and will be measured in mm from the left side to the participant marking to score

Data Analysis:

Standard descriptive statistics will be used to summarize the demographic and clinical data. Analyses will be guided by the specific hypotheses of the study. All hypotheses will be tested at level of significance $\alpha=0.05$. We will also estimate the effect sizes of interest and provide 95% confidence intervals. Primary outcome measure is change in craving (visual analogue scale).

Overall statistical significance for the effects of group and time, their interaction, and the baseline measure will be assessed.