Ability of Partial Inverse Agonist, Iomazenil, to Block Ethanol Effects in Humans

NCT01590277

June 10, 2022

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Principal Investigator: Deepak Cyril D'Souza, MD

Statistical Analysis Plan: All data will be transcribed onto respective teleforms, checked for completeness and clarity. Continuous variables will be checked for normality using normal probability plots and Kolmogorov- Smirnov statistics. Transformations will be applied if necessary. A criterion of $P < 0.05$ will be used throughout to determine statistical significance. In the mixed models described below, the correlation between repeated measures on an individual will be modeled using random effects and/or structured variance-covariance matrices. The best-fitting variance-covariance structure will be determined by information criterion. The mixed-effects approach is advantageous in that it is unaffected by randomly missing data and allows greater flexibility in modeling the correlation structure of repeated-measures data. We will test for order effects, although any such effects should be greatly minimized with the inclusion of the baseline session. All tests will be two-sided and considered statistically significant at alpha=.05. Significance levels for secondary comparisons will be adjusted for multiple tests using the Bonferroni correction, basing the adjustment on the number of conceptually related statistical tests within each hypothesis.

To determine whether iomazenil, attenuates the "buzzed" feeling state of ethanol intoxication in healthy human subjects. We expect that the behavioral data will not conform to normality as in our previous studies. Therefore, a nonparametric analysis for repeated measures data will be conducted with ethanol (active or placebo), iomazenil (active or placebo) and time as within-subject factors. The analysis will be performed by rank transforming the data, then fitting a mixed-effects model with an unstructured variance-covariance matrix using PROCMIXED in SAS (SAS Institute Inc, Cary, NC), and finally adjusting the *P* values for the analysis of variance–type statistics (ATS). One of the advantages of this approach is that it uses all available data on each subject including dropouts. If the 3-way interaction among ethanol, iomazenil, and time are significant, contrasts for testing interactions between iomazenil and ethanol will be performed at each time point. For the points where significant interactions are observed, the simple effects of ethanol, and iomazenil will be tested to determine the nature of the interaction. Bonferroni corrections will be applied for multiple analyses within, but not across, domains.