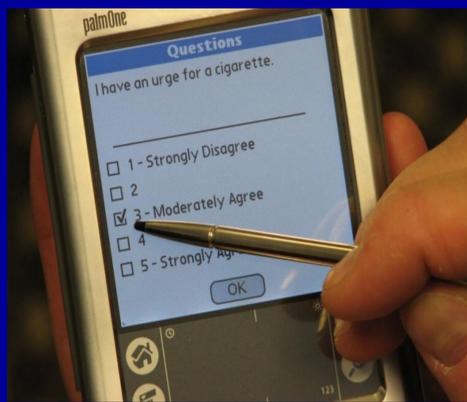


The Effect of Varenicline on Withdrawal, Craving, and Mood in Treatment-Seeking Smokers: An Ecological Momentary Assessment Study

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INTRODUCTION

- Varenicline is a highly selective $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist used as a smoking cessation aid.
- In a double-blind within-subject crossover experiment, varenicline was found to significantly reduce withdrawal symptoms, negative mood, and urge to smoke during abstinence compared to placebo (Patterson et al., 2009).
- The current research examines varenicline's effect on withdrawal, craving, and mood, and whether these effects are stronger in individuals receiving longer treatment.
- Eliminating the bias of retrospective recall, this study asked individuals to report symptoms through the use of ecological momentary assessment.
- Ecological momentary assessment (EMA) uses sampling methods to assess subjects' current behaviors and experiences as they occur in the natural environment, increasing ecological validity (Shiffman, Stone & Hufford, 2008).
- We expected that individuals who received longer treatment with varenicline would experience lower symptoms of withdrawal, craving, and negative mood relative to those who received placebo.

METHODS

- A total of sixty treatment-seeking smokers carried personal digital assistants (PDAs) with them for seven weeks of the study. During this time participants responded to several questionnaires on the PDAs.
- Refer to the graph below for participant demographics (Table 1).
- At the initial Clinic Visit, participants received PDA training. Data collected from this week serves as the Baseline Phase for this study.
- Refer to Table 2 for detailed descriptions of the four phases of the study.
- During the Varenicline v. Placebo Phase, participants were randomly selected into two groups. One group received active treatment with varenicline, while the other received placebo.
- At the start of the Final Pre-Quit Phase, those in the placebo condition began treatment with varenicline.
- All participants were asked to complete morning assessments during every day of the study. The total completion rate for assessments across phases was 90.085%.
- The number of daily smoking symptom sessions (EMA) participants received varied by phase, and these sessions were never received on Clinic Visit days. The total completion rate for sessions across phases was 86.867%.
- During the morning assessment, participants were asked to complete the 8-item Withdrawal Symptoms Questionnaire (Hughes & Hatsukami, 1986), the Craving Questionnaire, an item assessing general positive mood, and an item assessing general negative mood.
- Smoking symptom sessions (EMA) asked participants to respond to the 8-item Cigarette Withdrawal Symptoms Questionnaire followed by the 4-item Craving Questionnaire, as well as the Mood Form (Diener & Emmons, 1984), an 11-item questionnaire that assessed current positive and negative mood.

VARIABLE	VARENICLINE	PLACEBO
Female: Male (n)	18:14	17:11
Age (years)	47.7	48.8
Minority (%)	9%	18%
Years Smoking	26.9	27.0
Lifetime Quit Attempts	5.6	5.4

Table 1: Demographics of Participants

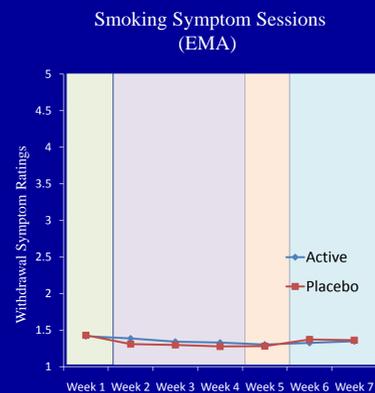


Figure 1: Withdrawal Symptoms Across Phases

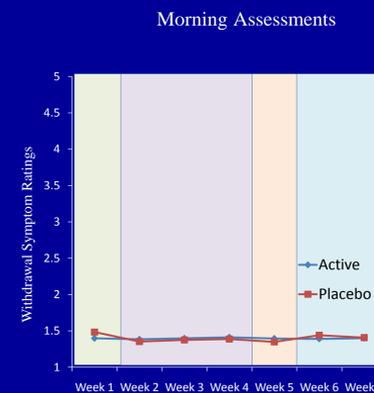


Figure 2: Withdrawal Symptoms Across Phases

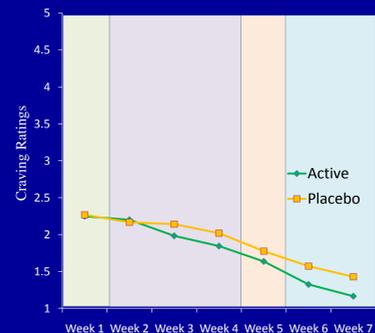


Figure 3: Craving Ratings Across Phases

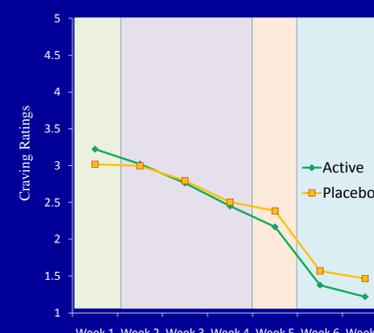
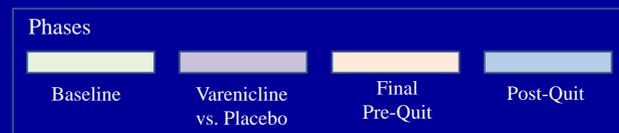


Figure 4: Craving Ratings Across Phases



RESULTS

- A mixed -design ANOVA was performed for Withdrawal, Craving, Positive Mood, and Negative Mood ratings for each of the four phases of the study. The factors in the ANOVA were Treatment Group, Sex, and Week (for the Varenicline vs. Placebo and Post Target Quit Date Phases).
- There was no significant group effect, sex effect, or group by sex interaction for Withdrawal symptom ratings from EMA or from morning assessments across phases, $ps > .05$ (See Figures 1 and 2).
- There was no significant group effect, sex effect, or group by sex interaction for Craving ratings from EMA or from morning assessments, $ps > .05$ (See Figures 3 and 4).
- There was no significant group effect, sex effect, or group by sex interaction for either Positive Mood or Negative Mood ratings from EMA or from morning assessments, $ps > .05$.
- Analyses of Week effects for EMA data across the two phases that had multiple weeks of data collection showed that there was a significant decline in craving across the three weeks of the Varenicline vs. Placebo Phase, $F(2, 108) = 7.74, p < .01$ and across the two weeks of the Post Target Quit Date phase, $F(1, 152) = 14.07, p < .001$. There were similar declines in craving during morning assessments: Varenicline vs. Placebo; $F(2, 108) = 18.45, p < .001$; Post Target Quit Date Phase, $F(1, 52) = 7.08, p < .05$.
- In an exploratory analysis, we examined changes in Craving ratings across all four phases of the study. This analysis showed that Craving declined significantly across phases during EMA, $F(3, 147) = 37.78, p < .0001$, and morning assessments, $F(3, 150) = 69.50, p < .0001$. Follow-up analyses showed that comparisons of adjacent phases were significantly different in each case across both EMA and morning assessments, indicating a progressive decline in Craving report across the study, $F_s \geq 6.27, ps < .05$.
- Analyses of changes in Withdrawal symptom ratings across phases with multiple weeks of data collection showed no significant changes in these ratings in either EMA or morning assessments, $ps > .05$. Across all phases, there were no significant differences in Withdrawal symptom ratings collected during morning assessments. Withdrawal symptom ratings from EMA did display significant differences across phases, $F(3, 147) = 5.10, p < .01$. Follow-up analyses of this effect indicated that these ratings declined significantly from the Baseline phase to the Varenicline vs. Placebo phase, $p < .05$. None of the other comparisons across successive phases were significant.

BASELINE PHASE (WEEK 1)	VARENICLINE V. PLACEBO PHASE (WEEKS 2-4)	FINAL PRE-QUIT PHASE (WEEK 5)	POST TARGET QUIT DATE PHASE (WEEKS 6-7)
Daily Morning Assessments	Daily Morning Assessments	Daily Morning Assessments	Daily Morning Assessments
2 Smoking Symptom Sessions per Day	2 Smoking Symptom Sessions per Day	2 Smoking Symptom Sessions per Day	4 Smoking Symptom Sessions per Day

Table 2: The Four Phases of the Study

DISCUSSION

- Longer treatment with varenicline (4 weeks prior to target quit date vs. 1 week) had no significant impact on Withdrawal, Craving, Positive Mood, or Negative Mood ratings.
- Craving declined across weeks, while no systematic changes were seen across weeks for Withdrawal ratings. A possible explanation for this is that the craving measure may have been more sensitive to change than the withdrawal measure. This could also explain why there were no significant differences between groups for Withdrawal. The same cannot be said for Craving, which did detect systematic reductions in craving report across weeks.
- Other analyses (data not shown) from this study showed that for the Varenicline v. Placebo Phase and the Final Pre-Quit Phase, people who received varenicline smoked significantly fewer cigarettes than those who received placebo. Based on the analyses presented here, these reductions in cigarettes smoked were not produced by group differences in Withdrawal, Craving, Positive, or Negative Mood.
- Additionally, this reduction in smoking was seen primarily in women. However, the analyses conducted in this study revealed no sex differences.
- These results are based on data collected in each participant's natural environment and in real time. The use of ecological momentary assessment increases the ecological validity of these results, while also reducing recall bias.

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