

5-HT_{2a} Receptor Agonist Psilocybin: Facilitation of Smoking Cessation

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We conducted an open-label pilot study testing psilocybin in combination with manualized cognitive behavioral therapy (CBT) in 15 treatment-resistant smokers. Data showed no serious adverse events attributable to psilocybin, and a very promising cotinine-verified point-prevalence abstinence rate of 80% at 6-month follow-up. A 2.5-year follow-up showed a cotinine-verified abstinence rate of 60%. We are currently conducting a comparative efficacy trial randomizing treatment-resistant smokers to a single psilocybin session (on their target quit date) or the transdermal nicotine patch (using FDA guidelines, beginning 24 hours after their target quit date), both in combination with a 13 week program of manualized CBT. Before their target quit date, and after 24 hours of nicotine abstinence, participants undergo fMRI, during which they complete the Multi-Source Interference Task (MSIT), a measure of cognitive control. Participants also complete the task 24 hours after the target quit date. Interim results show higher cotinine-verified 12-month abstinence rates with psilocybin vs. nicotine patch. MSIT results show significant pre vs. post target quit date reductions in the reaction time congruency effect in psilocybin participants, and no change in the nicotine patch group. MSIT congruency effect reaction time was significantly, positively correlated with superior parietal cortex activation during the task for the pre-psilocybin scan for psilocybin participants, but not for the post-psilocybin scan. In summary, interim smoking cessation efficacy analyses suggest promising results for psilocybin in comparison to transdermal nicotine patch when both are delivered in combination with CBT. Moreover, preliminary neurocognitive analyses suggest significantly improved cognitive control and a reduction of fMRI response in the superior parietal cortex the day after quitting for the psilocybin group, suggesting psilocybin may improve smoking cessation outcomes by enhancing cognitive control.