Correspondence

N-Acetylcysteine in Treatment of Substance Use Disorders

To the Editor:

Spencer *et al.* (1) present an innovative and comprehensive rodent model of cannabinoid self-administration that increases our understanding of the neurobiology of cannabis use disorder and promises new leads for its treatment. One major finding was the prevention of cue-induced reinstatement of self-administration by pretreatment with *N*-acetylcysteine (NAC). The authors relate this finding to a similar effect of NAC in inhibiting "cue-induced reinstatement to many addictive drugs." They then imply a clinical extrapolation by mentioning "a clinical trial found that NAC reduced adolescent cannabis use" (2). However, they do not mention that a later clinical trial using similar NAC doses and study design found no significant effect of NAC in reducing adult cannabis use (3). More convincing supportive evidence for the authors' suggestion of a broad effect of NAC comes from a recent systematic review and meta-analysis that found a significant effect of NAC in reducing human craving for cocaine, methamphetamine, cannabis, and tobacco (4). In any case, I believe that caution is warranted when extrapolating from rodent behavioral findings to the clinical treatment setting.

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Article Information

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References

1. Spencer S, Neuhofer D, Chioma VC, Garcia-Keller C, Schwartz DJ, Allen N, *et al.* (2018): A model of Δ^9-tetrahydrocannabinol self-administration and reinstatement that alters synaptic plasticity in nucleus accumbens. Biol Psychiatry 84:601–610.
2. Gray K, Carpenter M, Baker N, DeSantis S, Kryway E, Hartwell K, *et al.* (2012): A double-blind randomized controlled trial of N-acetylcysteine in cannabis-dependent adolescents. Am J Psychiatry 169:805–812.
3. Gray KM, Sonne SC, McClure EA, Ghitza UE, Matthews AG, McRae-Clark AL, *et al.* (2017): A randomized placebo-controlled trial of N-acetylcysteine for cannabis use disorder in adults. Drug Alcohol Depend 177:249–257.
4. Duailibi MS, Cordeiro Q, Brietzke E, Ribeiro M, LaRowe S, Berk M, Trevizol AP (2017): N-acetylcysteine in the treatment of craving in substance use disorders: Systematic review and meta-analysis. Am J Addictions 26:660–666.

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