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Pharmacological modulation of farnesyltransferase subtype I attenuates mecamlamine-precipitated nicotine withdrawal syndrome in mice

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Abstract

This study was designed to investigate the effect of FTI-276 trifluoroacetate, a selective inhibitor of subtype I, on the development of the mecamlamine-induced nicotine withdrawal syndrome. Mice were administered nicotine (2.5 mg/kg, subcutaneously) four times daily for 7 days. To precipitate nicotine withdrawal, mice were administered one injection of mecamlamine (3 mg/kg, intraperitoneally) 1 h after the last nicotine injection on the test day (day 8). Behavioral observations were made for a period of 30 min immediately after mecamlamine treatment. FTI-276 trifluoroacetate treatment markedly and dose-dependently attenuated the precipitated nicotine withdrawal syndrome, measured by a composite withdrawal severity score, jumping frequency, hyperalgesia in the tail flick test, and anxiety-like behavior in the elevated plus maze test. The results suggest that FTI-276 trifluoroacetate can inhibit the development of a precipitated nicotine withdrawal syndrome, and thus that farnesyltransferase subtype I may be a viable pharmacological target to tackle the problem of nicotine addiction.

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