Acute behavioural responses to nicotine and nicotine withdrawal syndrome are modified in GABA(B1) knockout mice.

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Nicotine is the main active component of tobacco, and has both acute and chronic pharmacological effects that can contribute to its abuse potential in humans. The aim of the present study was to evaluate a possible role of GABA(B) receptors in acute and chronic responses to nicotine administration, by comparing GABA(B1) knockout mice and their wild-type littermates. In wild-type mice, acute nicotine administration (0.5, 1, 3 and 6ămg/kg, sc) dose-dependently decreased locomotor activity, and induced antinociceptive responses in the tail-immersion and hot-plate tests. In GABA(B1) knockout mice, the hypolocomotive effect was observed only with the highest dose of nicotine, and the antinociceptive responses in both tests were significantly reduced in GABA(B1) knockout mice compared to their wild-type littermate. Additionally, nicotine elicited anxiolytic- (0.05ămg/kg) and anxiogenic-like (0.8ămg/kg) responses in the elevated plus-maze test in wild-type mice, while selectively the anxiolytic-like effect was abolished in GABA(B1) knockout mice. We further investigated nicotine withdrawal in mice chronically treated with nicotine (25ămg/kg/day, sc). Mecamylamine (1ămg/kg, sc) precipitated several somatic signs of nicotine withdrawal in wild-type mice. However, signs of nicotine withdrawal were missing in GABA(B1) knockout mice. Finally, there was a decreased immunoreactivity of Fos-positive nuclei in the bed nucleus of the stria terminalis, basolateral amygdaloid nucleus and hippocampal dentate gyrus in abstinent wild-type but not in GABA(B1) knockout mice. These results reveal an interaction between the GABA(B) system and the neurochemical systems through which nicotine exerts its acute and long-term effects.

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