Electronic cigarette-induced dependence: short and long term effects

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Many smokers have recently switched to e-cigarettes (e-cig) as an alternative means of nicotine delivery because they look feel and taste like traditional cigarettes. Smokers using e-cig had less desire to smoke, fewer symptoms associated with abstinence from tobacco, and improved prospective and working memory (Dawkins et al. 2012, 2013). Furthermore, e-cig are increasingly used as a means of reducing or stopping smoking despite the contrary recommendation of the World Health Organization (World Health Organization, 2008).
Humans experience a withdrawal syndrome (WDW) whose severity closely correlates to smoking relapse, that emerges within hours or days after cessation of cigarette smoking. Nicotine WDW in rodents is characterized by similar somatic signs and affective changes (including increased anxiety, anhedonia and irritability) (Paolini and De Biasi, 2011). However until now, data on the short and long term effects of e-cig WDW are not available. Cigarettes represent also a gateway to the use of other drugs of abuse, particularly cannabis (Dierker et al, 2008).
The aim of this study was to validate a rodent model of e-cig exposure, based on previous nicotine inhalation system (George et al., 2010), that induced high urinary and brain levels of cotinine (the major nicotine metabolite) and mimics the intermittence and route of nicotine administration in humans. We compared the effects of inhaled e-cig vapour (containing 5.6 mg of nicotine/session for a total of 16.8 mg/day delivered for three 30-minute sessions/day for seven weeks), with that of standard cigarette smoke containing the same amount of nicotine on: neurochemical (nicotine and cotinine brain levels, nAChR up-regulation), physiological (body weight and food intake), behavioural (memory function and emotional profile after mecamylamine precipitated or spontaneous WDW), starting from 24 hours to 90 days after nicotine withdrawal. Susceptibility to motivational effects of Δ(9)-tetrahidrocannabinol (0.01-0.3 mg/kg) was also evaluated using the Conditioned Place Preference task (CPP).
Intermittent non contingent exposure to e-cigarette vapour or cigarette smoke had the same effects on brain nicotine and cotinine concentrations and nAChR up-regulation, but cigarette smoke led to more severe mecamylamine-precipitated WDW and more evident cognitive deficits (spatial memory) 24 hours after cessation, whereas e-cig vapour elicited more severe anxiety and compulsive behaviour up to two months after spontaneous withdrawal. Mice previously exposed to cigarette smoke and e-cig were more sensitive to Δ(9)-tetrahidrocannabinol rewarding effects than those exposed only to air and this sensitivity war still present even when CPP was tested 30 or 60 days after nicotine WDW.
These findings demonstrate, for the first time, that e-cig vapour induces addiction-related neurochemical, physiological and behavioural alterations. The fact that inhaled cigarette smoke and e-cig vapour have partially different dependence-related effects indicates that compounds other than nicotine contribute to tobacco dependence.

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