

## LETTERS TO THE EDITOR

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### Euphoriant effects of nicotine

To the Editor – The recent “debate” created by the tobacco industry on whether nicotine is addictive has brought to the fore the thorny question of what drug effects constitute addiction. The industry has attempted to mount the case that a) in order to qualify as addictive, a substance, in addition to meeting the standard criteria for tolerance and withdrawal, must also induce a state of intense euphoria; and b) nicotine does not meet this requirement because nicotine has not been shown to produce dose-related euphoriant effects.<sup>1–3</sup>

Setting aside the question of whether euphoriant effects are essential to the concept of addiction, a position no longer widely held outside the tobacco industry, it is not correct that such a dose-response relationship has never been reported. Euphoriant effects of nicotine were clearly demonstrated as early as 1978.<sup>4</sup> Henningfield and colleagues have shown increases in drug liking for both intravenous nicotine and inhaled tobacco smoke that are both blockable by mecamylamine<sup>5</sup> and dose-related.<sup>6,7</sup> We took a somewhat different approach,<sup>8</sup> asking subjects to push a button when a euphoric sensation was experienced and to keep it depressed for the duration of the sensation; and using increase in venous blood nicotine concentrations rather than cigarette strength as an index of dose, because smokers can so easily adjust nicotine intake. These effects were experienced by 19 of the 22 smokers we tested (86%); they were more pronounced fol-

lowing overnight abstinence than following minimal deprivation, in more dependent smokers, and as a function of plasma nicotine increment upon smoking. These sensations are experienced intermittently during the smoking of a cigarette and are therefore easy to miss if smokers are queried at specified, standardised intervals. Once we instituted a subject-initiated procedure, the phenomenon proved quite readily detectable.

During the review process for that paper, one reviewer raised the question of whether the pleasurable effects reported by subjects actually constituted euphoria, pointing out that subjects may have depressed the button in response to feelings of dizziness or intoxication. In response to this critique, we set up two foot-pedals, the right one (the “accelerator”) labelled with a smiling face and the left (the “brake”) with a frowning face. The following instructions were provided: *People sometimes report experiencing pleasurable or euphoric sensations when they smoke that might be described as a rush, a buzz, or a high. Not everybody experiences these sensations. If you happen to experience any of these pleasurable sensations while smoking today, please depress the right foot pedal and hold it down for the duration of the sensation. If you experience an unpleasant sensation, please depress the left foot pedal for the duration of the sensation. Please smoke your cigarette now.* (It should be noted that in all the years we have used this apparatus, not one smoker has ever indicated that s/he was confused or did not know what we were talking about when we described smoking-induced euphoric sensations.)

In a recent study involving 15 male smokers (mean  $\pm$  SD age:  $29.8 \pm 7.5$  years; mean  $\pm$  SD cotinine level:  $222.7 \pm 152.1$  ng/ml, characterising them as moderately heavy smokers), we found that 12 of the 15 smokers (80%) reported at least one euphoric sensation during the smoking of a single cigarette following approximately 12 hours abstinence from smoking. Mean  $\pm$  SD number of sensations was  $3.6 \pm 3.7$ , and total time spent in this state (mean  $\pm$  SD) was  $127.4 \pm 168.4$  seconds. By contrast, only six smokers (40%) experienced any dysphoric sensations, and total time spent in this state

was  $15.6 \pm 39.8$  seconds. There was no significant correlation of either the number ( $r = -0.32$ , NS) or duration ( $r = -0.27$ , NS) of euphoric with dysphoric sensations. Both the number ( $r = +0.62$ ,  $p < 0.05$ ) and duration ( $r = +0.73$ ,  $p < 0.005$ ) of dysphoric sensations were highly correlated with self-reported change in nausea measured using visual analogue scales presented before and 30 minutes after smoking, whereas no such significant correlations were seen for euphoric sensations (number:  $r = -0.19$ , NS; duration:  $r = -0.27$ , NS).

We conclude that smokers experience both euphoric and dysphoric sensations, though many more of the former, and that they have no trouble in distinguishing them from one another. We further conclude that the dysphoric sensations are indicative of nicotine intoxication, whereas the euphoriant effects probably reflect nicotine's actions on reward-relevant brain systems.

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