Neuropsychopharmacology (2008) 33, 2044

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Reply to Fulton and Barrett

Reply: Response to Letter to the Editor

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Neuropsychopharmacology (2008) **33,** 2044; doi:10.1038/sj.npp.1301546

Sir

This letter is in response to the letter by Fulton and Barrett, which argued that our paper (Sofuoglu *et al*, 2007) does not support nicotine's reinforcing effects. Fulton and Barrett stated that since in our intravenous self-administration model we used an inactive placebo (saline) for nicotine, greater nicotine self-administration over saline could be due to smokers' 'expectations' of receiving nicotine rather than nicotine's reinforcing effects.

Although expectations of drug effects can confound clinical studies (Mooney *et al*, 2004), it is unlikely to explain our findings. First, in our study, nicotine self-administration and subjective nicotine effects were dependent on the nicotine dose (0.1, 0.4, and 0.7 mg). This would be unexpected if self-administration was based solely on 'expectation' of receiving nicotine. Second, if the 'expectation' of receiving nicotine was driving nicotine self-administration, then one would expect that smokers would choose nicotine over placebo for all routes of administration. This has not been the case. Nicotine products that lead to slower nicotine delivery, such as nicotine gum, are not reliably chosen over placebo gum, compared to the intravenous route, which provides faster nicotine delivery and is chosen over placebo (Hughes *et al*, 2000; Harvey *et al*, 2004). The most likely explanation of these findings is greater reinforcement with faster nicotine delivery (de Wit *et al*, 1992). Lastly, there is a wide range of preclinical literature on nicotine's reinforcing effects, including those demonstrating the molecular and behavioral mechanisms of nicotine reinforcement (Picciotto and Corrigall, 2002; Le Foll and Goldberg, 2006). On the basis of this large body of evidence, it is hard to escape the conclusion that—like cocaine, heroin, and alcohol—nicotine is reinforcing.

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