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**Differential roles of  $\alpha 4\beta 2$  and  $\alpha 7$  nAChRs in Nicotine Addiction process: Implications for smoking cessation medication development**


The primary reinforcing actions of drugs of abuse including nicotine and the conditioned motivational effects of environmental stimuli (e.g., smoking) associated with previous drug intake may be mediated by dissociable, yet connected, neurobiological mechanisms. We used animal models of nicotine self-administration and cue-induced relapse of nicotine-seeking behavior to examine effects of pharmacological blockade of specific neurotransmitter receptors on nicotine intake and cue-triggered nicotine seeking. Male Sprague-Dawley rats were trained to intravenously self-administer nicotine (0.03 mg/kg/infusion) on a fixed ratio 5 schedule of reinforcement. To establish a nicotine conditioned cue, an auditory/visual stimulus (5-s tone/20-s lever light on) was associated with each nicotine infusions. After lever responding was extinguished by withholding nicotine and its cue presentation, the cue-induced reinstatement tests were performed. Prior to the self-administration and the reinstatement test sessions, animals were subjected to receptor antagonist treatment to block activation of specific neurotransmitter receptors. Antagonists of the  $\alpha 4\beta 2$  nicotinic acetylcholine receptors (nAChRs) but not the  $\alpha 7$  nAChR

antagonists reduced nicotine self-administration. In contrast, antagonists of the  $\alpha 7$  nAChRs rather than the  $\alpha 4\beta 2$  nAChR antagonists effectively reversed cue-induced reinstatement of nicotine-seeking behavior. These results suggest distinct involvement of the  $\alpha 4\beta 2$  and  $\alpha 7$  subtypes of the nAChRs in nicotine primary and conditioned reinforcement. In addition, although bupropion suppressed nicotine self-administration, its enhanced cue-triggered reinstatement of nicotine-seeking behavior. Taken together, these findings may have implications for clinical effort to develop pharmacotherapies aimed at reducing nicotine consumption in current smokers and preventing environmental cue-triggered relapse in abstinent smokers.

**Speaker Biography**

Xiu Liu is a professor at the University of Mississippi Medical Center, USA. He has a two-decade track record of studying drug addiction, particularly nicotine and alcohol addictive behavior in animal models. His research has been funded by USA National Institute of Health and Food and Drug Administration grants. He has published 60 research papers, 6 book chapters and more than 80 research abstracts. Dr. Liu has served as a member of grant review panels for international and national research funding agencies and an editorial board member of more than a dozen reputed journals.

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