

Beyond Nicotine Gateway Hypothesis

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“A gateway drug is a drug that lowers the threshold for addiction to other agents.”¹

Psychological studies involving humans suggested that addiction is a form of learning and that relapse is a persistent memory of the drug experiences.² It is the gene transcription factor cyclic AMP response-element-binding protein (CREB) acting as a switch, converting short-term memory to long-term memory, referred to as the acetylation of chromatin structures.³

For nicotine gateway hypothesis, data from a group of students, aged 15.7 to 34.2 years, showing the majority of cocaine users (75.2%) were smoking during the month they began using cocaine⁴, and the rate of cocaine dependence was highest (20.2%) among users who started using cocaine after having smoked cigarettes, in contrast to dependence among persons who had begun using cocaine before they

started smoking (6.3%) and among those who had never smoked more than 100 cigarettes (10.1%).⁵

Combining epidemiologic and biologic studies suggest a model in which nicotine exerts the priming effect on cocaine by means of HDAC inhibition and provide a molecular explanation of the unidirectional sequence of drug use observed in mice and in human populations. Nicotine acts as a gateway drug through global acetylation in the striatum, creating an environment primed for the induction of gene expression. Long-term exposure to nicotine presumably lessens constraints on dopaminergic neurons in the ventral tegmental area and leads to the enhanced release of dopamine.⁶

Of note, the current debate about electronic e-cigarettes as a tool to stop smoking and reduce the harmful effects of combustible tobacco use in the population by eliminating some of the morbidity

associated with combustible tobacco, is especially in regard to the heat-not-burn electronic cigarettes while disregarding the nicotine-liquid electronic cigarettes *per se*.⁷ Therefore, tobacco harm reduction by noncombustible tobacco cigarettes is beneficial and conclusively beyond nicotine gateway effect.⁸

References

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