Acute Nicotine Exposure Produces Only Mild Impairments of Adult Rat Serial Pattern Performance

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Introduction

Rats are sensitive to the structural organization of serial patterns in sequential learning, frequently making more errors at points in the pattern where structure changes (e.g., chunk boundary and violation elements) than on within-chunk elements in acquisition. Previous work examining the effects of ACh agonists and antagonists have shown mild to severe impairments in acquisition and retention, specifically at structural changes in the pattern, suggesting that central cholinergic systems are necessary for making correct responses at these points in the pattern. We examined effects of nicotine, a nicotinic cholinergic agonist, on performance of a well-learned serial pattern. Prior data have shown mild impairments due to nicotine in this task; however, multiple acute exposures to nicotine have not been assessed in the adult rat in this sequential learning paradigm.

Method

Subjects. 7 male hooded rats implanted with bipolar electrodes for hypothalamic brain-stimulation reward (BSR) served as subjects.

Acquisition. Rats were trained to press levers in a sequential pattern for BSR in a discrete-trial procedure with correction. The rats learned a pattern composed of eight 3-element chunks:

123-234-345-456-567-678-781-818

where the digits represent the clockwise positions of levers in a circular array, dashes indicate 3-s pauses ("phrasing cues"), and other intertrial intervals were 1 s. The first element of each chunk is termed a "chunk boundary", with the following elements in each chunk designated as "within-chunk elements". The last element of the pattern is called a "violation" element as it violates the rule followed in the previous seven chunks of "turn left" *after* phrasing cues. Rats were trained on 50 patterns per day.

Nicotine Effects on Pattern Performance. Once rats reached a criterion of less than 10% errors throughout the pattern, they received an i.p. injection of saline to establish baseline performance. Following baseline, all rats received a relatively high dose of nicotine (0.4 mg/kg i.p.) 30 min prior to training for three consecutive days.

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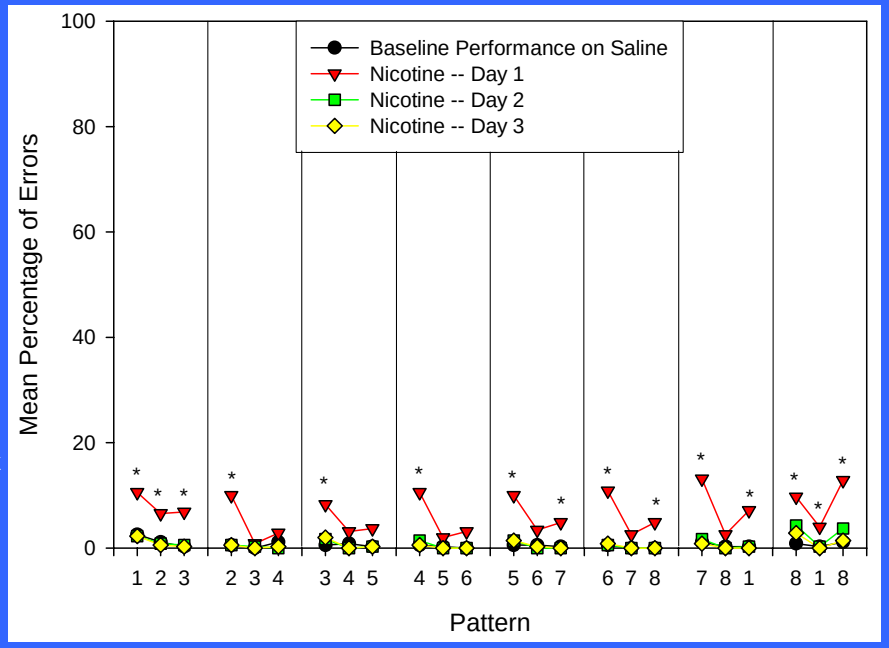

Results: Nicotine Effects on Pattern Performance

- Nicotine, an ACh nicotinic receptor agonist, caused small but significant impairments on chunk-boundary and violation elements performance on Day 1 of nicotine exposure. Analysis of error types indicate rats primarily made "back 2 levers" errors (e.g., 123-**1** rather than 123-**2**) at chunk boundaries and "overextension" errors (e.g., 81**2** rather than 81**8**) at the violation element.
- Within-chunk elements remained relatively unaffected by the drug treatment compared to the effects at chunk boundary and violation elements on Day 1.
- Performance on all elements returned to baseline on Days 2 and 3 of nicotine exposure, suggesting the possibility of tolerance.

Discussion

These results show that nicotinic cholinergic systems may play a small supportive role in the maintenance of sequential responses. Prior evidence suggests that muscarinic cholinergic systems are more critical for acquiring and retaining correct responses in sequential patterns, particularly where structure changes. These results provide further evidence that multiple memory processes may be involved in the performance of well-learned sequential tasks. In particular, the processes required for performance of higher-order rules (i.e., at chunk boundaries) are more sensitive to central cholinergic manipulations than those necessary for performing responses consistent with lower-order rules (i.e., within-chunk elements).

It is interesting to note that the impairments due to nicotine in this paradigm, although small and limited to the first exposure day, are unexpected given prior research that shows improvements in performance under acute nicotine exposure in working memory tasks (e.g., radial arm maze), spatial learning tasks (e.g., Morris water maze), and fear conditioning tasks (e.g., passive avoidance) (Picciotto, Caldarone, King, & Zachariou, 2000). However, some evidence has shown that if proactive interference is introduced into these paradigms, nicotine can impair learning. This suggests that the nicotine-induced effects reported here, and possibly serial learning impairments we observed in our earlier studies involving cholinergic drugs, may reflect impairments in rats' ability to manage interference when they encounter changes in pattern structure.

Reference

Picciotto, M. R., Caldarone, B. J., King, S. L., & Zachariou, V. (2000). Nicotinic receptors in the brain: Links between molecular biology and behavior. *Neuropsychopharmacology, 22,* 451-465.