EFFECTS OF SCOPOLAMINE AND NICOTINE ON ENCODING IN CHOICE REACTION TIME TASKS

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ABSTRACT

Background: There has been considerable interest in the role of the cholinergic system in attention and response. This has often involved challenges with scopolamine or nicotine. The present study extended the literature by examining the effects of these two drugs on encoding and response to new information. **Method:** Twenty male university students who were light smokers were recruited. The experiment involved a repeated measures design, with each participant completing five experimental sessions at weekly intervals. Over the five sessions, each participant received one of each of the following: scopolamine vehicle + 0.75 mg nicotine; scopolamine vehicle + 1.5 mg nicotine; 1.2 mg scopolamine + nicotine vehicle; 1.2 mg scopolamine +1.5 mg nicotine; and scopolamine vehicle + nicotine vehicle. In each session, participants carried out a pre-drug baseline and post-drug test. The performance tasks involved choice reaction times with focused attention and categoric search. **Results:** Relative to placebo, the scopolamine-induced impairment in response time was restricted to conditions in which the stimulus was different from the previous trial, with the size of the decrement being the same for both focused and search tasks. Nicotine improved response time on both alternating and repeated stimulus trials, with the size of the effect being similar to scopolamine on the focused task but considerably smaller on the search task. In the combined treatment, 1.5mg nicotine reduced but did not eliminate the scopolamine-induced deficit; the deficit was reduced by around 50% in both the search and the focused tasks in the alternated stimulus conditions impaired by scopolamine administration. **Conclusion:** Both scopolamine and nicotine had significant effects on choice reaction time. The profile of the two drugs was different, and nicotine only partially removed the

scopolamine-induced impairments. Such effects may underlie changes in encoding observed in other changes of state, such as the effects of caffeine.

KEYWORDS: Scopolamine; Nicotine; Focused attention; Categoric search; Choice Reaction time; Encoding; Alternations; Repeats.

INTRODUCTION

Scopolamine is in the antimuscarinic family of drugs and works by blocking some of the effects of acetylcholine within the nervous system. Scopolamine impairs performance on several attention tasks: rapid visual information processing (RVIP),[1] dichotic listening,[2,3] selective attention (the Stroop task),[4] and focused attention (digit cancellation).[5] It also produces decrements in performance on psychomotor tasks, such as finger tapping, digit symbol substitution and symbol copying.[5-7]

Nicotine acts as a receptor agonist at most nicotinic acetylcholine receptors. As a stimulant of the cholinergic system, it also has effects on cognitive performance. Nicotine improves performance on the RVIP task;[8-10] letter cancellation,[11,12] finger tapping,[13] and speed and accuracy of motor movement also improve.[14] While few studies have directly examined the relationship between these two compounds, the implication is that the two compounds have opposing effects on the same functions, that scopolamine impairs performance by impairing stimulus selectivity, and that nicotine improves performance by enhancing stimulus selection through increasing electrocortical arousal. However, 'attention' covers a wide and diverse range of functions which are called into play to varying degrees in the battery of tasks described generically as 'attention tasks', and it is quite feasible that while these compounds may act on common components of some of the tasks, they may also have specific and independent effects on others. Increased interest in the cholinergic system and the consequences of receptor activity within this system encourages a more detailed examination of the precise relationship between compounds which act at pharmacologically specific receptor sites.

Broks et al.[15] reported increased RTs to simple and choice RTs with no warning signals with 1.2mg oral scopolamine, but not simple RTs with a warning signal. Preston et al.[6] used the same 4-choice task, taking measures of 'decision' time (time to release central key) and 'motor' time (time to press target key) and found a dose-dependent increase in RTs (total reported, because no difference between decision and motor measures) but this failed to reach

significance. Preston et al.[16] found that the same task showed a significant decrement under scopolamine, again with similar effects on decision and motor time. Kopelman & Corn[17] found impaired performance with an 8-choice RT task but no significant impairment, even with higher doses of scopolamine, for simple, 2, and 4-choice conditions (RTs only).

The present study examined the separate and combined effects of scopolamine and nicotine on attention tasks developed by Broadbent[18, 19] to provide a more detailed breakdown of the components of attention involved in a two-choice reaction time task. These tasks have been widely used in research investigating the effects of changes in state on attention and reaction time.[20-29] The aim was to examine the extent to which nicotine and scopolamine affected the same or distinct components of performance. This was done by examining both reactions to stimuli, which were the same as the previous ones (repeats) and those that were different (alternations). Reaction times to alternations are slower than to repeats, the extra time reflecting the encoding and preparation of response of new information.

METHOD
The study was approved by the local ethics committee and carried out with the informed consent of the participants.

Participants
Twenty male university students aged between 18 and 30 years and weighing between 65 to 85 kg. They were all light smokers. Exclusion criteria were mental health problems, drug use and taking any centrally acting medication.

Design
The experiment involved a repeated measures design, with each participant completing five experimental sessions at weekly intervals. Over the five sessions, each participant received one of each of the following:
• Scopolamine vehicle + 0.75 mg nicotine
• Scopolamine vehicle + 1.5 mg nicotine
• 1.2 mg scopolamine + nicotine vehicle
• 1.2 mg scopolamine +1.5 mg nicotine
• Scopolamine vehicle + nicotine vehicle

Both drugs were administered orally. Scopolamine was prepared in a 0.9% saline solution, such that 10 ml provided a 1.2mg dose. Nicotine was administered on a milk of magnesium tablet. A drop of hot chilli sauce was placed on the same side as the nicotine to disguise the taste. The placebo tablets were produced in a similar way. The order of dosing was counterbalanced, and all treatments were administered double-blind.

Baseline performance was assessed at the beginning of each session. Post-drug performance was tested once 90 minutes after completion of the baseline session. The scopolamine/placebo solutions were given immediately after the completion of the baseline session, and tablet 80 minutes later. Volunteers held the tablet in their mouths for 5 minutes to allow it to dissolve slowly. Testing sessions began at 9.30 or 10.15.

Each participant completed both the focused and the search tasks. The presentation order of the tasks was counterbalanced so that half the volunteers received the focused task first, and half received the search task first. The attention tasks were always presented after a series of verbal recall tasks and took approximately 30 minutes to complete.

Focused attention choice reaction time task
Broadbent developed this selective attention task.[18,19] Target letters appeared as upper-case A's and B's. In each trial, three warning crosses were presented on the screen, and the outside crosses were separated from the middle one by either 1.02 or 2.60 degrees. Participants were told to respond to the letter presented in the centre of the screen and ignore any distractors presented in the periphery. The crosses were on the screen for 500 msecs and were then replaced by the target letter. The central letter was either accompanied by 1) nothing, 2) asterisks, 3) letters that were the same as the target, or 4) letters that differed. The two distractors were identical, and the targets and accompanying letters were always A or B. The correct response to A was to press a key marked A on the left-hand side of the response box, while the correct response to B was to press the key marked B on the right-hand side of the response box. Participants were given ten practice trials followed by five blocks of 64 trials. In each block, there were equal numbers of near/far conditions, A or B responses and equal numbers of the four distractor conditions. The nature of the previous trial was controlled.

Categoric search choice reaction time task
Broadbent[18,19] also developed this task to measure aspects of selective attention. Each trial started with the appearance of two crosses in the positions occupied by the non-targets in the

focused attention task (i.e. 2.04 or 5.20 degrees apart). Participants did not know which of the crosses would be followed by the target. The letter A or B was presented alone on half the trials and was accompanied by a digit (1-7) on the other half. Again, the number of near/far stimuli, A versus B responses and digit/blank conditions were controlled. Half of the trials led to compatible responses (i.e. the letter A on the left side of the screen or the letter B on the right), whereas the others were incompatible. Participants were given ten practice trials followed by five blocks of 64 trials. In each block, there were equal numbers of near/far conditions, A or B responses and equal numbers of the four distractor conditions. The nature of the previous trial was controlled.

RESULTS

Analyses of covariance with the baseline variables as covariates and the post-drug scores as dependent variables were carried out. Drug manipulations had limited effects on the different components of this task. The significant effects were limited to stimulus encoding, with interactions between treatment and stimulus type (repeated vs alternated target stimulus) for both the focused ($F = 2.70$, $p < 0.005$) and the search conditions ($F = 2.43$, $p < 0.01$). These effects are shown in Tables 1 and 2; although the absolute size of the effects was small, they show a highly consistent pattern.

Table 1: Effects of drug condition in the alternation and repeat reaction times (msec) in the focused attention task.

Condition	Alternation	Repetition
Placebo/placebo	386	357
Scopolamine/placebo	400	350
Scopolamine/1.5mg nicotine	395	352
Placebo/ 1.5 mg nicotine	373	341
Placebo/0.75mg nicotine	378	342

Table 2: Effects of drug condition in the alternation and repeat reaction times (msec) in the categoric search task.

Condition	Alternation	Repetition
Placebo/placebo	428	400
Scopolamine/placebo	440	402
Scopolamine/1.5mg nicotine	435	392
Placebo/ 1.5 mg nicotine	418	392
Placebo/0.75mg nicotine	429	398

Relative to placebo, the scopolamine-induced impairment in response time was restricted to conditions in which the stimulus was different from the previous trial (alternated stimulus),

with the size of the decrement being similar for both focused and search tasks. Nicotine improved response time on both alternating and repeated stimulus trials, with the size of the effect being like that of scopolamine on the focused task but considerably smaller on the search task. In the combined treatment, 1.5mg of nicotine reduced but did not eliminate the scopolamine-induced deficit. In contrast, nicotine improved reaction times to both alternations and repetitions, suggesting that it did not influence the stages of processing involved in encoding new stimuli and preparing the response to them. Nicotine partially removed the scopolamine-induced impairment, which suggests there is some partial overlap between the types of processing influenced by the two drugs.

DISCUSSION

The present study examined the role of the cholinergic system in the encoding and response in choice reaction time tasks. The design has been frequently used before and examined the effects of scopolamine and nicotine, both alone and in combination. The effects of scopolamine were restricted to alternating stimuli in the focused attention and categoric tasks. This suggests that scopolamine impairs the encoding of new stimuli or possibly the preparation of the response to those new stimuli. Nicotine improved reaction times to both repeats and alternations. It also partially removed the impairments induced by scopolamine.

Much of the interest in the cholinergic system has been related to memory impairments seen in the cognitive decline of the elderly. The present results are probably more relevant to changes in state, such as those related to the ingestion of caffeine. Two effects of caffeine have been identified.[30] The first is the reduction of impairments seen in fatigued individuals.[30] Such effects have been shown to reflect changes in the noradrenergic system.[31] Other effects of caffeine, such as those found with cognitive vigilance tasks, are observed in alert individuals and may reflect changes in the encoding of new information due to cholinergic stimulation.[32,33] The present effects could be important in many types of tasks, and further research is needed to examine the cholinergic mechanisms linking different changes of state.

CONCLUSION

There has been extensive previous research on the cholinergic system and attention and response. This has often involved experiments with scopolamine or nicotine. The present study examined the effects of these two drugs, alone and in combination, on encoding and response. The experiment had a repeated measures design, with each participant completing

five conditions. Each participant received one of each of the following: scopolamine vehicle + nicotine vehicle; 1.2 mg scopolamine + nicotine vehicle; scopolamine vehicle + 0.75 mg nicotine; scopolamine vehicle + 1.5 mg nicotine; and 1.2 mg scopolamine +1.5 mg nicotine. In each session, there was a pre-drug baseline and post-drug test. Focused attention and categoric search choice reaction times were performed. Relative to placebo, the scopolamine-induced impairment in reaction time was restricted to conditions in which the letter was different from the previous trial. The size of the scopolamine decrement was similar in both focused and search tasks. Nicotine improved response time on both alternating and repeated stimulus trials. On the focused task, the size of the nicotine effect was like that of scopolamine. However, the nicotine effect was considerably smaller on the search task. In the combined treatment, the scopolamine-induced deficit was reduced, but not eliminated, by 1.5mg of nicotine. Nicotine reduced the deficit by around 50% in the alternated stimulus conditions impaired by scopolamine administration in both the categoric search and the focused attention tasks; scopolamine and nicotine both had significant effects on choice reaction time. The profile of the two drugs was different, and nicotine only partially removed the scopolamine-induced impairments. Such changes in the cholinergic system may underlie changes in encoding observed in other changes of state, such as those seen in alert individuals given caffeine.

ACKNOWLEDGEMENT

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