Psychopharmacology (2001) 153:258–263
DOI 10.1007/s002130000565

ORIGINAL INVESTIGATION

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Improved incidental memory with nicotine after semantic processing, but not after phonological processing

Received: 28 June 2000 / Accepted: 10 August 2000 / Published online: 23 November 2000

Abstract *Rationale:* A number of lines of evidence suggest that a nicotinic cholinergic system is mediating attentional processing. However, the evidence is less clear for a nicotinic system being involved in mnemonic processing. *Objectives:* The present study investigated the effects of nicotine on memory using a depth of processing paradigm. *Methods:* A double-blind design was used with participants (n=40) smoking either a nicotine containing cigarette (n=20) and a denicotinized cigarette (n=20). After smoking, each set of these participants was further subdivided into two groups (n=10 for each). One group were presented with a series of trials each beginning with the presentation of a “decision word” which they had to say whether it represented something which was living or non-living (semantic-orienting). The second group had to say whether the word had one syllable or two syllables (phonological or non-semantic orienting condition). This decision was followed by a word in coloured ink whose colour participants were required to name as quickly as possible. On completion of the whole task the participants were given an unexpected free recall test. *Results:* The nicotine-containing cigarette reduced the latencies for decision-making and colour naming in comparison with the denicotinized cigarette. The free recall test showed that nicotine-containing cigarette increased the number of words remembered, but only for the semantic-orienting condition and not the non-semantic condition. *Conclusions:* There is a nicotinic cholinergic system that mediates effortful processing. It can be deployed for attentional processing, including the associative processing required for memory encoding.

Keywords Nicotine · Cigarette · Attention · Memory · Mental effort

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Introduction

Cholinergic pathways in the brain have been implicated in cognitive processing for over 25 years (Warburton and Rusted 1993). Laboratory and clinical studies have argued for its involvement in attentional processing (Warburton and Brown 1971) and mnemonic processing (Drachman and Leavitt 1974; Drachman 1977). While the laboratory data for the involvement of cholinergic systems in human attentional processing are robust (Levin 1992; Warburton and Rusted 1993), studies of the facilitation of mnemonic processing by cholinergic agents have yielded less consensus in the literature.

In animals, nicotine has also been found to improve learning memory on a variety of tasks (Levin 1992). Positive evidence for facilitation with lower yielding nicotine cigarettes (0.4–1.38 mg) was found for paired-associate learning by Mangan (Mangan 1983; Mangan and Golding 1983), for recognition memory (Warburton et al. 1986) and for free recall of words (Peeke and Peeke 1984; Warburton et al 1986; Colrain et al 1992). Negative results for the effect of nicotine and smoking have obtained, but most commonly for immediate memory (Andersson and Hockey 1977; Peters and McGee 1982; Kusendorf and Wigner 1985; Spilich et al. 1992). However, there have been positive effects on immediate memory (Kleinman et al. 1973; Peeke and Peeke 1984; Warburton et al. 1986, 1992a; Sherwood et al. 1992). The reasons for the negative findings on delayed recall are unclear (e.g. Williams 1980). The results of experiments using acetylcholinesterase inhibitors can be explained in terms of the adverse effects of nausea on performance. Studies using nicotine delivery systems and smoking do not have such a ready explanation, except with the testing with high yield nicotine cigarettes (e.g. 2 mg nicotine cigarettes of Mangan and Golding 1983).

It is known that memory encoding is affected by many factors. Two important ones are that if attentional resources are focussed completely on the to-be-remembered material and if these attentional resources are directed to its meaning rather than to more superficial attributes (Baddeley 1990). From this conclusion, it has been argued that studies in which memory is improved by nicotine the memory task had a strong attentional component (Warburton 1990).

In a typical memory task, attention to the words is controlled by instruction. The list is short and so attention does not play a part. However, the list in the Warburton et al. (1986) study was 48 items long, and that in the Peeke and Peeke (1984) study was 50 words long. In contrast, there were only eight word lists in the Andersson and Hockey (1977) study and the nine-digit list of Williams (1980), for example. In this regard, it is interesting that nicotine did produce a slight improvement in the Andersson and Hockey study when participants had to remember words, word order and location on the computer screen, i.e. 24 items.

In a test of this hypothesis, Rusted and Eaton-Williams (1991) examined the effects of nicotine on a free recall memory task with lists 10 and 30 items long. It was found that nicotine improved free recall, but these effects were significant only for the 30-item word lists but not for the ten-item word list. Another study examined the part of a 32-item word list, where there was better recall with nicotine (Warburton et al. 1992b). It was found that more words were recalled from the latter part of the list, while smoking during presentation of the list. It would be expected that attention would be declining towards the end of a long list. These results support the proposition that inconsistencies in the literature about the effects of nicotine on memory are due, at least in part, to the differences in attentional requirements of the tasks.

Further evidence for an attentional component to improved encoding after smoking or nicotine doses (Rusted and Warburton 1992). They showed post-trial administration of nicotine enhanced recall of a 24-word list after a 10-min delay. If participants were given an attentional, distractor task (rapid visual information processing) during the 10-min delay period, the nicotine-induced enhancement of memory was abolished. However, performance on the 10-min attentional task was improved by nicotine. These data were interpreted as evidence that the post-trial administration of nicotine is increasing attentional resources, which could either be used for rapid visual information processing or memory encoding, by rehearsal. In a later study (Rusted et al. 1995), pre-trial nicotine improved the recall of sets of semantically-related words, irrespective of whether the there was a distractor task to prevent rehearsal or there was no distractor task. These results were explained nicotine improving attention to encoding, with no additional effects on post-trial rehearsal.

If nicotine-enhanced, attentional resources are being deployed for strategic processing of the word lists, for example rehearsal, then these effects could be best revealed by studies in which this form of processing was promoted. A number of nicotine and smoking studies have instructed the participants to form associations. For example, Mangan (1983) asked participants to associate pairs of words and smoking facilitated learning of the pairs. In a second study, Mangan and Golding (1983) studied the effects on memory of a single cigarette smoked immediately after presentation of the paired-associates. Once again, recall was better for those smoking.

In the 32 word-list studies of Warburton (Warburton et al. 1992a, two studies; Warburton et al. 1992b) the participants were presented with the list in blocks of four words and instructed to rehearse the words and form associations. In the smoking studies, (Warburton et al. 1992a) they took a puff on the cigarette and rehearsed for 10 s. Smoking improved memory for the words. In the other study (Warburton et al. 1992b), more words were recalled after the participants had nicotine tablets.

In a subsequent study (Rusted et al. 1998), semantically related words were recalled better than unrelated words, even when participants were explicitly instructed to focus on the unrelated word list. A second study in the same paper showed improvement for semantically-related (hot-cold), but not word pairs which together denote an item (e.g. fishing rod), and where the second word is a primary associate of the first, but has no consistent associate of its own. This finding implies nicotine's effects are mediated through active processing of some associative link between related items.

In summary, these studies are consistent with the hypothesis that memory is improved by nicotine when attention of participants was explicitly directed to the meaning of the words. The present study was designed to test this hypothesis by using a “levels of processing” paradigm (Parkin 1979). This paradigm was devised to examine the proposal that there is a memory-encoding dimension from shallow to deep associative processing. Orthography represents the shallowest level, phonology intermediate and semantics as the deepest (Craik and Lockhart 1972). The specific tasks were a decision about whether the word was one syllable or two syllables (phonological-orienting) or living or non-living (semantic-orienting). It was predicted that nicotine would improve memory more in the semantic-orienting condition, in comparison with the phonological-orienting condition.

Materials and methods

Participants

Forty volunteers (16 men and 24 women) were recruited from the students of Reading University (age range 18–23 years). Participants were compensated for the time and trouble involved in the study. All of them were smokers and smoked more than ten cigarettes per day. While all participants abstained from beverage alcohol and caffeinated drinks for 12 h prior to the study, they were only requested to refrain from smoking for 1 h prior to testing in the afternoon (minimal deprivation). In addition, a group of 20 non-smokers were tested for comparison with the smokers in the non-smoking condition. The Ethics Committee of Reading University did not disallow the study. All participants gave written informed consent to participate.

Drug administration

Subjects smoked either a nicotine cigarette (machine-estimated yield of 0.6 mg nicotine and 6 mg of total particulate matter) or a trace nicotine product (yield of 0.01 mg nicotine and 6 mg of total particulate matter). Pilot studies revealed that the two products could not be discriminated reliably. The two cigarettes were assigned to volunteers according to a double-blind design.

Materials

The test materials consisted of two sets of one and two syllable words, which were either living or non-living (from Parkin 1979, experiment II). Each set of words consisted of a total of 48 words, in 16 groups of three words, an associated stimulus-response pair (e.g. "bed", "sleep") and a second, unrelated stimulus-response pair (e.g. "key", "sleep"). The latter word was matched for semantic category (in this case non-living), word frequency, the same number of syllables and letters (plus or minus one).

For each participant, a word list consisted of 64 words in total, (16 living, associate pairs; 16 living, non-associate pairs; 16 non-living, associate pairs; and 16 non-living, non-associate pairs intermixed randomly). Within each class of 16 words, there were equal numbers of monosyllabic and disyllabic words. There were long, monosyllabic words (e.g. adult) and short, disyllabic (e.g. zebra). A second list was also constructed from the same 64 pairs, but with half of the pairs reversed. A practice list of 26 pairs was also constructed.

Design

Ten participants were allocated at random to each of the four conditions. These conditions were 1) nicotine and semantic processing, 2) nicotine and phonological processing, 3) trace nicotine and semantic processing and 4) trace nicotine and phonological processing.

Procedure

They were informed that the experiment was investigating the effects of smoking on a simple reaction time task. The emphasis in the instructions was on answering as quickly and as accurately as possible. Because of the stressful nature of the procedure, participants were told that they could stop at any time if felt uncomfortable or unable to continue. All participants were given a practice session with the 26 pairs, in order to familiarise them with the procedure. It also allowed adjustment of the sensitivity of the voice key to the individual's voice.

The words in white print were presented sequentially in the centre of a computer screen. For the Semantic Condition, the participants were asked to press the YES or NO button to indicate whether the stimulus word (e.g. zebra) represented a living or a non-living thing. In the Phonological Condition, the participants indicated whether the stimulus word (e.g. zebra) had one or two syllables, by pressing one of the two buttons.

Pressing the key triggered presentation of the second word of the pair, which was either associated or not associated. The second word was printed in colour (red, green, yellow or blue) and participants were asked to name the colour of the word by speaking into a small microphone attached to a voice-key. The voice-key activated a 500 ms warning tone, which was followed 500 ms later by the next stimulus word.

After completion of this task, the participants were given an unannounced, 10-min free-recall test in which they were required to list any words from the practice or main test.

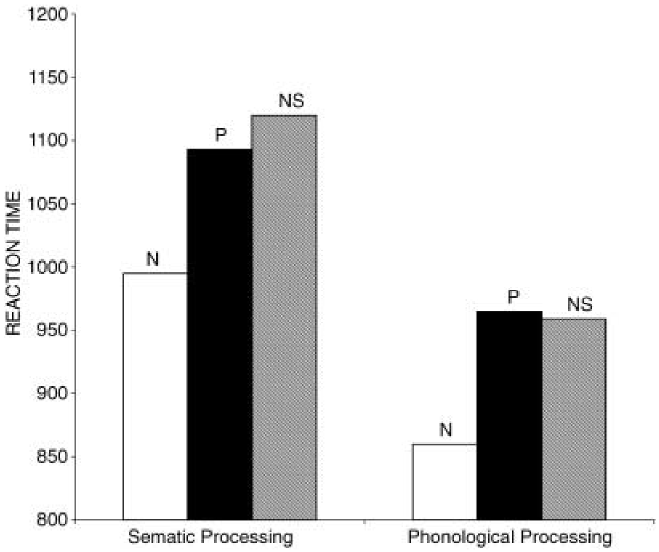

Fig. 1 Speed of phonological and semantic processing of smokers with nicotine (*N*) and without nicotine (*P*), and of non-smokers (*NS*)

Results

None of the participants withdrew and so failed to complete the study. Therefore there were full data on reaction times and word recall for all four conditions.

Decision latencies

The decision time data were for the presentation of the stimulus word (the first word of the pair) and so one would not expect any difference the associate and control trials (see Parkin 1979). Thus, it was possible to combine the associate and control trials and compare nicotine's effects on the phonological and semantic processing. The data are presented in Fig. 1. For comparison purposes, the reaction times for a set of non-smokers have been included. A 2×2 factorial analysis of variance of the decision time data gave a significant difference [$F(1,36)=7.89$, $P<0.01$] between phonological processing (mean±SD=962±128) and semantic processing (mean±SD=1101.5±127.9). The mean±SD difference was not significantly different [$F(1,36)=2.63$, $P>0.05$] between smokers (1029.4±113.33) and non-smokers (1039.5±104.6).

A 2×2 factorial analysis of variance of the decision time data of the smokers gave a significant difference [$F(1,36)=7.56$, $P<0.01$] between phonological (912.3±75.69) and semantic processing (1039±97.96). The mean difference also significant [$F(1,36)=4.47$, $P<0.05$] for cigarette type (nicotine cigarette mean 926.8±95.74 and trace nicotine mean 1028.7±88.70). Finally, the interaction between type of processing and cigarette type was not significant [$F(1,36)=3.97$, $P>0.05$]. In summary, the nicotine cigarette improved processing speed, but this effect was not significantly greater for either condition; the mean difference for phonological processing was 105 ms, in comparison with 98 ms for semantic processing.

Colour naming latencies

Inspection of the latencies of colour naming of some participants revealed some spurious data, i.e. data that seem to have been generated by processes other than those under investigation. There were some extremely brief reaction times, a little as 10 ms, and some unusually slow reaction times, as measured by the voice key. The brief reaction times were due to coughing or sneezing and the slow reaction times were the result of the person having to repeat the response, if the first response had not been loud enough for the voice key.

In order not to bias the accuracy of the mean reaction time, a technique was needed to remove these extreme values from the affected data sets. There are many different outlier procedures in use, which usually used without explicit reasons being given for the special procedure (Ulrich and Miller 1994). For our data, examination of the data revealed that the problem was confined to seven participants and so any procedure could not be applied to all individuals, e.g. truncation to remove the top and bottom 5% of the reaction time data of each participant. Instead, Grubb's Outlier Test was used detect the outliers in the individual's set of reaction times. These values were replaced using a derivative of trimming, truncation and standard deviation methods called windsorizing (Barnett and Lewis 1978). In windsorizing, the extreme values are not eliminated from the data, but are replaced by the value of the cut-off criterion, the largest or smallest non-outlier. The technique of windsorizing is a compromise between the two goals of eliminating the strong influence of extreme values on the mean, while at the same time using all of the information in the data set.

A 2×2 factorial analysis of variance of the colour-naming latencies gave a significant difference between phonological and semantic processing [$F(1,36)=11.65$, $P<0.01$]. The difference also significant for cigarette type [$F(1,36)=6.88$, $P<0.03$]. Finally, the interaction between type of processing and nicotine was not significant [$F(1,36)=3.93$, $P>0.05$].

In summary, the nicotine cigarette improved processing speed on the colour naming, but this effect was not significantly greater for nicotine condition. It also confirmed that when there was semantic orienting, participants took longer to name the print colour, when the second word was associated with the preceding decision word, whereas association had no effect on colour naming in the phonological orienting condition.

Incidental memory

The number of words, which were recalled from the two lists, was compared and decision words, colour words and words from the practice list. Only a few participants had intrusion errors and so these were disregarded. The mean number of words recalled for lists one and two were 10.5 and 9.4 respectively and a *t*-test revealed no significant difference [$t(38)=0.699$, $P>0.05$]. The number of words for the four conditions is shown in Fig. 2, together with the data for non-smokers for memory after phonological and semantic processing. A 2×2 factorial analysis of variance showed a difference between the number of words, which were recalled after the two types of processing for smokers and non-smokers. The mean±SD was significantly greater [$F(1,36)=22.08$, $P<0.001$] (mean for phonological=7.45±1.27 versus mean for semantic=10.8±1.19), but there was no significant difference [$F(1,36)=3.98$, $P>0.05$] for the means for non-smokers (9.16±1.53) and smokers (9.15±1.38).

For the smoking condition, the effect of the type of processing on words recalled was significant [$F(1,36)=22.08$, $P<0.001$] after semantic processing (12.85±1.33) compared with after phonological processing (7.32±0.84). The effect of cigarette type on word recall was significant [$F(1,36)=5.57$, $P>0.025$] (nicotine cigarette mean=11.16±1.21 and trace nicotine mean=9.15±0.78) A significant interaction between nicotine and type of processing was found [$F(1,36)=7.62$, $P<0.01$]. Figure 2 shows the interaction between the variables with the participants in the nicotine condition recalling more words in the semantic processing condition than those in the non-nicotine condition do. Nicotine had no effect on the number of words recalled in the phonological processing condition, but nicotine has enhanced recall in the semantic processing condition.

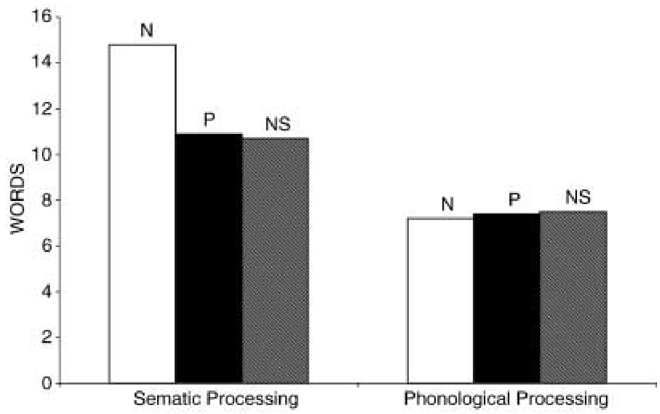

Fig. 2 Memory for words after semantic and phonological processing for smokers with nicotine (*N*) and without nicotine (*P*), and of non-smokers (*NS*)

Discussion

The results of this study confirmed the finding of Parkin (1979) of longer decision times for processing semantic information, in comparison with phonological information. It also established that when there was semantic orienting, participants took longer to name the print colour, when the second word was associated with the preceding decision word, whereas association had no effect on colour naming in the phonological orienting condition. A comparison was made between the mean reaction times for a set of non-smokers and a group of minimally deprived smokers and there were no significant differences between the two groups.

The nicotine cigarette reduced decision times in both the phonological and semantic condition, but there was no difference between conditions. This absence of a difference between smokers and non-smokers suggests that nicotine may not merely be restoring performance, which has been degraded by abstinence. The finding of shorter decision latencies and colour naming latencies with nicotine is consistent with a recent study on nicotine and lexical decision making. In this experiment, nicotine increased the response speed on a task, which required the making of a rapid decision about whether a given letter was actually a word or non-word (Hale et al. 1999). These data provide further support for the large body of evidence that nicotine can improve the overall efficiency of information processing (Warburton 1990).

In a previous study, we used the nicotine patch to investigate the cognitive processes underlying the changes in attentional performance (Mancuso et al. 1999). We examined the effects of nicotine on attention with tests, which assessed the intensity and selectivity features of attention. These were Random Letter Generation, the Stroop Test and the Flexibility of Attention Test. Briefly, nicotine improved speed of production in the random letter generation, but did not affect stereotypes significantly. On the Stroop Test, nicotine increased the rate colour naming in both the conditions, but the Stroop Effect was not different. However, nicotine had no effect on the attentional switching the Flexibility of Attention Test.

The present results and the results of the Mancuso et al. (1999) study are compatible with the hypothesis that nicotine mainly improves the intensity feature of attention, rather than the selective feature. This possibility is consistent with the State Model for mental effort (Warburton 1986). In this model, information processing is being modulated by a cholinergic system. For tasks, which require mental effort, like number generation and colour naming performance, there will be activation of the cholinergic pathways, resulting in cortical arousal. Nicotine helps to maintain this desynchronized state for more efficient performance, i.e. it “locks” the brain into the attentional mode.

In contrast, nicotine improved word recall only in the semantic condition and not the phonological condition in the incidental memory component of the test. The incidental recall data are in agreement with studies that show nicotine can improve memory via improved attentional processing (Rusted and Eaton-Williams 1991; Rusted and Warburton 1992; Warburton et al. 1992a, 1992b. This effect is thought to depend on the allocation of resources for continued processing of material for storage, e.g. the associative processing of rehearsal. This study forced the participants to process the material associatively and non-associatively and nicotine only improved performance in the associative (semantic) condition and not the non-associative (phonological) condition. Of course, it cannot be assumed that the only semantic processing, which occurs, is restricted to the orienting instructions. A clear demonstration of the inaccuracy of this assumption is seen in Stroop studies, in which the Stroop Effect results from semantic processing, even though the orienting instructions are to name the print colour.

As we pointed out earlier mnemonic encoding is effective if attentional resources are focussed completely on the to-be-remembered material and if these attentional resources are directed to its meaning rather than to more superficial attributes (Baddeley 1990). Semantic orienting has focussed attentional resources on the words and so has produced a more richly encoded memory trace with a greater number of associations with the input word. Nicotine modulates these associations and enhances storage, even though it was not intentional.

Acknowledgements This study was supported in part by Wellcome Grant M/93/789/GM/MB. We thank Dr. J Rusted for her critical comments on an earlier version of the manuscript and to two reviewers for constructive comments on the paper.

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