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ORIGINAL INVESTIGATION

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# Nicotine improves memory for delayed intentions

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**Abstract** *Rationale:* The present paper asked first whether the cholinergic agonist nicotine improves memory for delayed intentions (prospective memory, ProM) and second whether pharmacological dissociation would support the psychological distinction that is made between strategic (effortful) and automatic (non-effortful) intention activation in prospective memory. *Objectives:* To use nicotine as a pharmacological tool with which to examine the neurochemical bases of prospective memory and to dissociate strategic from automatic components of ProM retrieval. *Methods:* In three experiments, minimally deprived (2 h) smokers either smoked or abstained prior to completing a standard prospective memory study. This involved participants in the simultaneous processing of a ProM task and a cover task (ongoing between the setting and the recall of the intention). Here, the ongoing task involved lexical decision (LDT), while the ProM task required a response to pre-specified target items occurring within the LDT stimuli. Variations in task instructions were used to manipulate the processing requirements of the ProM task, the attention allocated to the ProM task and the balance of importance assigned to the ongoing and ProM tasks. *Results:* In experiment 1, where the ProM processing was automatic, nicotine did not improve ProM accuracy. In experiment 2, where the ProM task involved strategic processing, positive effects of nicotine were observed. In experiment 3, we covaried ProM task instructions, assigned task importance and nicotine conditions. We observed a main effect of nicotine on ProM accuracy, a main effect of task on ProM accuracy and a main effect of assigned task importance on ProM accuracy. There were no interactions between the factors. *Conclusions:* Employing both direct and indirect manipulations of strategic engagement, we demonstrated nicotine-induced enhancement of performance on the ProM task. The results are consistent with the view that relatively small changes in instruction and in task variables engage strategic processing in a ProM task and that when these conditions stretch cognitive resources, nicotine may significantly improve performance.

**Keywords** Nicotine · Prospective memory · Delayed intentions · Attention · Strategic vs. automatic processes

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## Introduction

Whenever we plan, postpone and, at a later date, implement an intention or action, we make use of prospective memory. Prospective memory (ProM) has been defined most simply as the ability to remember to perform a delayed intention (Einstein and McDaniel 1990). It is a central feature of everyday memory. Researchers (McDaniel and Einstein 2000; Ellis and Kvavilashvili 2000; West and Craik 2001) have described ProM as a composite of two memories. First, ProM must include an encoding of what has to be done (effectively an episodic memory trace of the intention). Second, it must include a mechanism for the timely retrieval of that intention (an associative link between that intention and a situational cue for its retrieval). Einstein and McDaniel (1996) in an early paper proposed that the detection of a situational cue in the environment was a relatively automatic process, initiating spontaneous activation of the delayed intention. More recently, ProM research has supported the existence of both strategic and automatic intention retrieval (McDaniel and Einstein 2000; McDaniel et al. 2004). Interest in the distinction between strategic and automatic retrieval of ProM intentions from ProM has focused on demonstrable differences in attention requirements for successful ProM retrieval. If intention retrieval employs strategic or effortful processing, this would absorb attention and would be indicated by a 'cost' to completing the prospective memory task successfully while maintaining an ongoing working-memory task (Marsh and Hicks 1998; McDaniel and Einstein 2000; Kliegel et al. 2001, 2004).

The present study considers the pharmacology of ProM. From the psychological studies, we conclude that prospective memory should engage, to a greater or lesser degree, systems that support attention and working-memory processes. If these strategic and automatic processes reflect separable components, it should be possible to demonstrate a pharmacological dissociation between them. Edginton and Rusted (2003) recently demonstrated selective effects of the cholinergic agonist nicotine on strategic inhibition processes within the retrieval-induced forgetting paradigm. These results are consistent with the long-standing view that the cholinergic system is directly implicated in efficient information processing (Sahakian 1988; Robbins 2002) and the proposition that nicotine selectively improves active, strategic processing of information, but not more automated processes. This has been demonstrated in a variety of paradigms, including semantic processing tasks (Warburton et al. 2001; Rusted et al. 1998), random number generation (Mancuso et al. 1999), the *n*-back task (Ernst et al. 2001; Kumari et al. 2003) and inhibition paradigms (Della Casa et al. 1999; Edginton and Rusted 2003). Interestingly, too, this role for nicotine in modulating strategic or working-memory processes recently has received support from eye movement studies involving visual search (Rycroft et al. 2005) and anti-saccade paradigms (Larrison-Faucher et al. 2004; Rycroft et al. unpublished data).

The present paper addressed two questions. First, it asked whether nicotine can improve prospective memory. Nicotine's cholinomimetic action is shared by the compound galantamine, currently available for the treatment of dementia of the Alzheimer type (DAT). If cholinergic activity can be shown to improve memory for delayed intentions, an essential part of independent living, this would certainly promote the value of cholinomimetics in the treatment of people with DAT. The second question was whether the psychological distinction between strategic and automatic intention activation could be verified by demonstrating selective pharmacological modulation. To this end, the study used nicotine as a pharmacological tool to test for a dissociation between strategic and automatic components of ProM retrieval.

In ProM paradigms, participants traditionally have to work on two tasks simultaneously—the ProM intention and the 'cover' task (ongoing between the setting and the recall of the intention). In experiment 1, we used a paradigm devised by Brandimonte et al. (2001) to examine the effects of nicotine on ProM under two conditions. In one condition, volunteers were directed to maintain the ProM task in mind during the completion of an ongoing lexical decision task (vigilance condition, engaging attention). In the second condition, the ProM task was presented as an incidental or secondary requirement to the ongoing task (prospective condition, engaging 'automatic' or spontaneous ProM retrieval). If nicotine improves only active or strategic processing, nicotine would not be expected to improve ProM performance in the prospective condition. To the extent that the vigilance instruction engages strategic processing, nicotine would be expected to improve performance in the vigilance condition. In this paradigm, however, the ProM task (respond to a specified word target) was an example of what Kliegel et al. (2001, 2004) have described as a 'non-strategic' ProM task since the requisite processing of the ProM target was accomplished within the processing needs of the ongoing task. According to their argument, nicotine would have no effect on ProM task accuracy in either condition since the vigilance instruction changes the volunteers' attention to the ProM task but not the processing effort engaged. The results of experiment 1 adjudicate between these two positions.

In experiment 2, we substituted into the Brandimonte et al. 2001 paradigm a ProM task that was distinctive from the ongoing task, thereby forcing strategic processing in that task (after Kleigel et al. 2001, 2004).

In experiment 3, we examined the relationship between ProM processing requirements and task importance. We anticipated that nicotine would enhance performance of tasks that were effortful, determined either by the nature of the task or the importance assigned to them. We anticipated that nicotine would not modulate automatic/non-effortful processes.

In these three studies, then, we hoped to elucidate both the neurochemistry of ProM and the dissociability of its component processes.

In these studies, nicotine was delivered through smoking, and the volunteers were moderate smokers (5–15 cigarettes per day) who were minimally (2 h) abstinent prior to testing. As a delivery system for nicotine in habitual users, smoking offered some advantages over the more recently available systems such as nasal spray (Myers et al. 2004), nicotine patch (Poltavski and Petros 2005) and gum (Harris et al. 2004). The dose of nicotine was self-titrated and therefore more likely to match the 'optimal' dose, avoiding negative side effects, such as nausea, and avoiding too the experiential differences associated with unfamiliar delivery systems, which can significantly change the outcome (Dar and Frenk, 2004). We recognise that smokers may have a profile that differs from naive users of nicotine. We anticipated, however, that the minimal deprivation procedures used here minimised subjective experience of 'withdrawal' or 'craving' during the test session and thus militated against an interpretation of any cognitive effects in terms of deprivation reinstatement (see Heishman et al. 1994; Heishman 1998 for reviews and discussion).

## Materials and methods

### Experiments 1, 2, 3: volunteers

One hundred and sixty-eight habitual smokers (5–15 cigarettes per day) were recruited from the Psychology subject pool at the University of Sussex (mean age 21 years; range 18–25); 60 completed experiment 1, 44 completed experiment 2 and 64 volunteers completed experiment 3.

All volunteers were required to abstain from smoking for 2 h before the test session, and compliance was monitored with a CO smokerlyser measure on arrival in the laboratory. The criterion for participation was a CO score of less than 15 ppm on arrival at the laboratory; four volunteers were re-booked for experimental sessions in response to high CO scores on arrival. All participants volunteered under a written informed consent procedure and for participation were entered into a lottery draw for a prize. The Sussex University School of Life Sciences Ethics Committee approved the studies.

*Smoker characteristics: comparability of volunteers across conditions*

For each of the experiments, nicotine dependence measures [using the Fagerström Tolerance Questionnaire (FTQ); Fagerström 1978] and pre-session CO scores were analysed across groups (smoke/abstain during the test session) and condition (prospective/vigilance instruction). The results, presented in Table 1, were as follows:

Experiment 1: there were no significant differences or interactions between groups on FTQ scores or pre-session CO scores ($F < 1$). Post-cigarette CO measures were significantly increased for those volunteers who smoked prior to the experimental task, but did not differ between volunteers allocated to the prospective vs vigilance condition ($F<1$).

Experiment 2: there were no FTQ differences across groups, and no CO differences on arrival at the lab following a 2-h abstinence ($p$s>0.05). Participants allocated to the smoking conditions had significantly higher CO scores post smoking, independent of instruction condition.

Experiment 3: mean CO measures on arrival at the laboratory were low (<7 ppm), and all groups had a comparable range of scores (2–13 ppm), but mean CO score for volunteers in the abstaining group was significantly lower than mean CO score for volunteers in the smoking group [2.3 vs 3.9 ppm, respectively; $F_{(1,49)}=6.96$, $p<0.01$]. CO scores for the group who smoked prior to the tasks increased significantly following the cigarette.

## Experiment 1

### Materials

The task was adapted from Brandimonte et al. (2001) and comprised an ongoing computerized lexical decision task (LDT) with an embedded prospective memory (ProM) task. In the LDT task, each volunteer completed 192 trials comprising 50% word, 25% legal non-words and 25% illegal non-words trials. The 192 trials were presented in four blocks of 48 trials. Each stimulus appeared once in each of the four blocks in a computer-generated random sequence. Each stimulus was presented on the centre of the screen in white upper case letters on a black background, following the offset of a focal asterisk. The stimuli remained on screen for 500 ms, and the volunteer was required to press one of two designated buttons: 'yes' for a word, 'no' for a non-word.

For the ProM task, two 'target' items were identified from the LDT stimuli, one word ('history') and one legal non-word ('bolin'), each of which would appear, like all

**Table 1** Mean (SD) dependence and end tidal CO measures for volunteers in experiments 1, 2 and 3

| Instruction/ProM task | Assigned condition | FTQ | Pre-session end tidal CO | Post-cigarette end tidal CO |
|---|---|---|---|---|
| Experiment 1 | | | | |
| Prospective/word | Abstain | 3.0 (1.3) | 6 (3) | |
| | Smoke | 4.0 (1.2) | 8 (5) | 14 (6) |
| Vigilance/word | Abstain | 3.2 (0.8) | 7 (3) | |
| | Smoke | 3.3 (1.4) | 8 (5) | 15 (9) |
| Experiment 2 | | | | |
| Prospective/letter | Abstain | 3.3 (2) | 4.4 (3) | |
| | Smoke | 2.7 (1) | 4.8 (2) | 9.0 (3) |
| Vigilance/letter | Abstain | 2.9 (2) | 4.5 (3) | |
| | Smoke | 3.7 (2) | 4.9 (2) | 9.6 (2) |
| Experiment 3 | | | | |
| ProM-important/word | Abstain | | 3.9 (2) | |
| | Smoke | | 4.5 (1) | 11.1 (2) |
| LDT-important/word | Abstain | | 2.3 (1) | |
| | Smoke | | 3.3 (2) | 9.1 (2) |
| ProM-important/letter | Abstain | | 2.3 (1) | |
| | Smoke | | 3.5 (2) | 9.4 (3) |
| LDT-important/letter | Abstain | | 2.7 (1) | |
| | Smoke | | 4.5 (2) | 13.0 (4) |

other items, four times within the test period (once per block). Volunteers were instructed that if they saw either of the target items during the presentation, they should withhold the LDT response for that stimulus.

A practice set of 24 items, with the same proportion of words, legal non-words and illegal non-words, was devised.

### Design

Nicotine condition (abstain/smoke prior to task) and instruction type (vigilance/prospective, defined in the Procedure section) were between-subjects factors, producing a 2×2 factorial design, with volunteers randomly assigned to one of four groups: vigilance/abstain, vigilance/smoke, prospective/abstain, prospective/smoke. Dependent measures included LDT performance (median reaction times[1] and error data) and ProM task performance (error data).

### Procedure

Each volunteer was instructed to smoke as normal in the morning but to abstain from smoking for the 2-h period prior to the test session. This procedure was designed to preclude overnight nicotine deprivation and to ensure minimal deprivation of nicotine. Carbon monoxide levels were measured on arrival (using a Bedfont Pico smokerlyser) to confirm compliance with instructions. Participants were randomly assigned to either smoke one of their own brand cigarettes prior to the experimental task or to continue to abstain from nicotine until the end of the testing session. Prior to nicotine intake, volunteers received instructions for the LDT/ProM task, derived from Brandimonte et al. (2001), as follows. All were instructed to complete the LDT task as quickly and accurately as possible, but with the caveat that they should withhold the LDT response for all exemplars of the two ProM targets provided. For volunteers in the vigilance condition (half of the abstainer and half of the smoking group), the importance of not responding to those target items was reiterated prior to the practice set (which included target exemplars) and again on completion of the practice set. For the prospective instruction volunteers (all remaining volunteers), the importance of the ProM task was not restated, and the practice set did not contain target exemplars. This instructional difference precisely mirrored the Brandimonte paradigm, in which it was demonstrated that relative to the prospective instruction, the vigilance instruction improved ProM outcome and slowed LDT responses (consistent with the notion of continued attention to the ProM task only in the vigilance instruction condition).

Following the LDT/ProM task, at the end of the session, a subset comprising half of the test trials was re-presented as a straightforward LDT task to establish a 'baseline' measure of LDT performance in the absence of the concurrent ProM task for all volunteers.

## Experiment 2

### Design

Nicotine condition (abstain/smoke prior to task) and instruction type (vigilance/prospective, defined in the Procedure section) were between-subjects factors, producing a 2×2 factorial design, with volunteers randomly assigned to one of four groups: vigilance/abstain, vigilance/smoke, prospective/abstain, prospective/smoke. Dependent measures included LDT performance (median reaction times and error data) and ProM task performance (error data).

### Procedure

Procedures were exactly as in experiment 1, with vigilance/prospective instruction again a between-subjects factor. The only modification was in the detail of the ProM targets. In experiment 2, the target items were letters within the stimuli, following Kliegel et al. (2004), rather than the whole-word targets employed in the original Brandimonte et al. 2001 paradigm. According to Kliegel et al. (2004), the letter task cannot be completed using the same cognitive processes as the ongoing LDT task, which is relatively automatic; accurate ProM performance will require strategic allocation of attention. Specifically, volunteers were asked to respond in experiment 2 to any words that contained both the letters 'M' and 'E'. As in experiment 1, there were eight target cues in total with four word and four non-word targets presented during the test period (once each per 48-trial block, in approximately the same positions as targets in experiment 1). The stimuli containing these target letters were novel to each block since repetition would allow the task to become a 'whole-word' process on the second occasion, thus defeating the purpose of the manipulation.

## Experiment 3

### Design

Nicotine condition (abstain/smoke prior to task), ProM task type (word/letter targets: following experiments 1 and 2) and importance instructions (LDT/ProM priority: defined in Procedure) were between-subjects factors, producing a 2×2×2 factorial design, with volunteers randomly assigned to one of eight groups. Dependent measures included LDT performance (median reaction times and error data), and ProM task performance (error data).

[1] Following Brandimonte et al. (2001), we used LDT median reaction times for each participant to avoid distortion by outliers in the reaction time data.

Procedure

Procedures were as in experiment 1. The only modifications were in the ProM targets and the priority instructions; both were derived following Kliegel et al. (2004). Volunteers were allocated for their ProM task either whole-word targets, as in experiment 1, or letter targets, as in experiment 2. In addition, half of each group was told to prioritise the ProM task and half to prioritise the LDT task. Explicitly, the instructions were either 'It is much more important that you perform the LDT task correctly than the other task (remembering NOT to press when you see the target items)' or 'It is much more important that you perform well on the ProM task (remembering NOT to press the button when you see the target items) than the other task (the LDT task)'. The assumption was that instructions would determine strategic allocation of attention between the LDT and the ProM task, respectively. Although there are superficial similarities between these priority instructions and the Brandimonte instructions used in experiments 1 and 2, there are critical differences. The Brandimonte prospective condition was designed to discourage participants from maintaining the intention in an active state, hence the ProM task was not referred to again after initial instructions were given. In contrast, the vigilance instruction was designed explicitly to keep the intention in mind, and a reminder was given immediately before the experimental trials. In experiment 3, neither priority instruction was intended to reduce conscious maintenance of the ProM intention, and both incorporated the later reminder of the ProM task, but the instruction explicitly directed that emphasis be placed on either the ProM or LDT task. This very act of prioritising one task over another implies awareness of the other task and induces an active 'dual-task' interplay between the two.

## Results

Data from three of the studies are presented together in Tables 1, 2, 3, 4 for comparison. Analyses are presented separately. For all studies, data from volunteers who failed to make any ProM response throughout the session were removed, on the basis that they had failed to register the requirement for the ProM task[2]. Data were also removed from volunteers who produced more than 30% incorrect responses on the lexical decision task. In total, this amounted to two and one volunteers, respectively, in experiment 1; in experiment 2, four and one, respectively; in experiment 3, three and four, respectively.

Prior to analyses, the outcome variables were tested for normality of distribution. For each analysis including within-subjects factors with more than two levels, Mauchly's Test of Sphericity was performed; these were non-significant in all cases. For comparisons of means, Levene's Test for Equality of Variance was used. These were insignificant in all but two cases (both in experiment 2); an assumption of non-equality of variance did not change the significance of the comparisons under review, and the adjusted $t$ values are reported.

## Experiment 1

1. Costs of performing a concurrent ProM task (Table 2)
   A 2×2 (abstain/smoke prior to task; ProM LDT/baseline LDT) between-subjects ANOVA on error data in the LDT task revealed a main effect of ProM task [$F(1,55)=47.7$, $p<0.01$] but no other significant differences or interactions between these factors. Error rates were higher when there was a concurrent ProM task than in the baseline LDT.
   A similar analysis of median RT data incorporated the additional within-subject factor of stimulus type (word, legal or illegal non-word). There were no effects of nicotine condition. Main effects of ProM task [$F(1,55)=88.8$, $p<0.01$] and stimulus type [$F(2, 110)=91.2$, $p<0.01$] also significantly interacted [$F(2,110)=18.2$, $p<0.01$], but there were no other interactions. Reaction times to make a lexical decision were slower with a concurrent ProM task, and the usual increased RTs to legal non-words were apparent in the data. The legal/illegal non-word difference was less pronounced in the baseline LDT than when there was a concurrent ProM task.
2. Prospective memory task analysis
   (a) Accuracy of LDT performance (Table 3)
   Mean error rates were low (7% of trials). A two-way factorial ANOVA (prospective/vigilance instruction; abstain/smoke prior to task) on error data for the LDT task indicated no effect of instructions or nicotine condition, and no interaction [$F$s $(1,53)<1$].
   (b) Speed of LDT performance
   A three-way (prospective/vigilance instruction; abstain/smoke prior to task; stimulus type) ANOVA demonstrated a significant difference in response times for words and non-words [$F(2, 106)=109.9$, $p<0.01$], but no other main effects or interactions.
   (c) Accuracy of ProM (Table 4)
   A two-way between-subject ANOVA (prospective/vigilance instruction; abstain/smoke prior to task) revealed a marginal effect of instruction [$F(1,53)=3.3$, $p<0.07$], but no effect of nicotine and no interactions. ProM accuracy was increased by the vigilance instruction.

[2] Volunteers were not asked to confirm/disconfirm their ProM task compliance, as post-test statements are often biased by subjective assessment of performance accuracy or experimenter intentions. Arguments can be found for both techniques (omitting non-responders; using post-session confirmation as the basis for omission) in the ProM literature.

**Table 2** Comparison of mean (SD) baseline and ProM-task session performance for volunteers in experiments 1, 2 and 3

| Assigned condition | LDT error rate (%) | | LDT median RTs (ms) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | With ProM task | Baseline | | | With ProM task | | |
| | | | Word | Legal non-word | Illegal non-word | Word | Legal non-word | Illegal non-word |
| Experiment 1 | | | | | | | | |
| Abstain | 4.78 | 10.26 | 515 (58) | 606 (127) | 533 (84) | 550 (62) | 668 (126) | 560 (71) |
| Smoke | 5.90 | 12.03 | 509 (59) | 586 (85) | 518 (52) | 557 (72) | 668 (105) | 508 (59) |
| Experiment 2 | | | | | | | | |
| Abstain | 4.17 | 7.72 | 551 (77) | 628 (94) | 532 (58) | 781 (204) | 883 (220) | 713 (162) |
| Smoke | 4.24 | 9.05 | 531 (61) | 627 (87) | 521 (46) | 723 (174) | 809 (174) | 651 (167) |
| Experiment 3 | | | | | | | | |
| Abstain | 2.64 | 9.39 | 571 (137) | 591 (107) | 542 (100) | 720 (268) | 728 (224) | 646 (227) |
| Smoke | 4.62 | 9.76 | 518 (59) | 577 (105) | 508 (58) | 633 (132) | 716 (194) | 605 (135) |

## Results: experiment 2

1. Costs of performing a concurrent ProM task (Table 2)
   Baseline LDT error rates were analysed in a two-way (abstain/smoke prior to task; ProM LDT/baseline LDT) ANOVA; error rates were less than 10% throughout. There was a main effect of the concurrent ProM task [$F(1,37)=25.7$, $p<0.01$], with fewer errors in the baseline LDT task than with a concurrent ProM task. No other effects or interactions were significant. Reaction times were analysed in a three-way ANOVA (abstain/smoke prior to task; ProM LDT/baseline LDT; word/legal non-word/illegal non-word). There was a main effect of ProM task [$F(1,72)=60.8$, $p<0.01$] and of stimulus type [$F(2,72)=104$, $p<0.01$], and an interaction between these factors [$F(2,72)=12.8$, $p<0.01$]. Relative to legal non-words, illegal non-words were rejected more quickly in the ProM LDT (when there was a concurrent ProM task) than in the baseline LDT. There were no differences or interactions associated with nicotine condition.
2. Prospective memory task analysis
   (a) Accuracy of LDT performance (Table 3)
   In the two-way (prospective/vigilance instruction; abstain/smoke prior to task) ANOVA, there were no effects of nicotine and no effect of instruction on LDT errors when there was a concurrent ProM task ($F$s<1).
   (b) Speed of LDT performance
   Median RT data was analysed [2×2×3 (prospective/vigilance instruction; abstain/smoke prior to task; word/legal non-word/illegal non-word) mixed

**Table 3** Mean LDT (SD) performance measures during the ProM-task session for volunteers in experiments 1, 2 and 3

| Instruction and ProM task | Assigned condition | LDT errors (%) | LDT median RTs (ms) | | |
|---|---|---|---|---|---|
| | | | Word | Legal non-word | Illegal non-word |
| Experiment 1 | | | | | |
| Prospective/word | Abstain | 10.7 (8) | 535 (66) | 652 (129) | 547 (83) |
| | Smoke | 12.6 (10) | 542 (80) | 654 (91) | 564 (70) |
| Vigilance/word | Abstain | 9.9 (9) | 561 (59) | 680 (128) | 570 (60) |
| | Smoke | 11.5 (12) | 573 (64) | 682 (119) | 559 (64) |
| Experiment 2 | | | | | |
| Prospective/letter | Abstain | 5.6 (3) | 875 (223) | 983 (245) | 812 (163) |
| | Smoke | 11.1 (8) | 631 (107) | 747 (112) | 574 (77) |
| Vigilance/letter | Abstain | 9.1 (10) | 721 (176) | 819 (186) | 650 (131) |
| | Smoke | 7.5 (6) | 792 (186) | 855 (200) | 708 (194) |
| Experiment 3 | | | | | |
| ProM-important/word | Abstain | 14 (8) | 751 (364) | 760 (306) | 667 (300) |
| | Smoke | 7 (6) | 576 (70) | 673 (167) | 554 (61) |
| LDT-important/word | Abstain | 12 (6) | 680 (276) | 698 (197) | 630 (229) |
| | Smoke | 8 (3) | 557 (106) | 589 (72) | 523 (61) |
| ProM-important/letter | Abstain | 6 (2) | 721 (91) | 699 (84) | 629 (61) |
| | Smoke | 14 (20) | 727 (153) | 836 (213) | 710 (185) |
| LDT-important/letter | Abstain | 7 (2) | 729 (324) | 758 (289) | 658 (293) |
| | Smoke | 9 (2) | 670 (126) | 763 (227) | 626 (118) |

**Table 4** Mean (SD) ProM errors (maximum possible=8) for volunteers in experiments 1, 2 and 3

| Instruction/ProM-target | Assigned condition | ProM errors |
|---|---|---|
| Experiment 1 | | |
| Prospective/word | Abstain | 2.4 (1.9) |
| | Smoke | 2.6 (1.6) |
| Vigilance/word | Abstain | 1.8 (1.0) |
| | Smoke | 1.7 (1.7) |
| Experiment 2 | | |
| Prospective/letter | Abstain | 2.4 (2.5) |
| | Smoke | 3.3 (1.7) |
| Vigilance/letter | Abstain | 3.5 (2.2) |
| | Smoke | 1.0 (1.3) |
| Experiment 3 | | |
| LDT-important/word | Abstain | 4.9 (1.6) |
| | Smoke | 3.9 (1.3) |
| ProM-important/word | Abstain | 4.4 (1.5) |
| | Smoke | 2.3 (1.4) |
| LDT-important/letter | Abstain | 4.1 (1.1) |
| | Smoke | 3.8 (2.1) |
| ProM-important/letter | Abstain | 2.3 (1.6) |
| | Smoke | 0.9 (1.6) |

ANOVA]. Predictably, stimulus type influenced RTs [$F(1,35)=29.5$, $p<0.01$] but did not interact with instruction or nicotine condition. There was no main effect of either of these factors, but there was a significant interaction between the two [$F(1, 35)=7.3$, $p<0.01$]. *T* tests revealed a significant effect of smoking on median RTs under prospective instructions, i.e. abstainers were more than 200 ms slower than smokers [$t(8.3)=2.8$, $p<0.02$], but not under vigilance conditions [$t(21)<1$]. Vigilance instructions produced slower median RT times than did prospective instructions for smokers [$t(19)=2.30$, $p<0.05$], but not for abstainers (Fig. 1).

(c) Accuracy of ProM (Table 4)
On the ProM task, a two-way (prospective/vigilance instruction; smoke/abstain prior to task) ANOVA revealed no significant main effects, but a significant interaction between instruction set and nicotine condition [$F(1, 35)=7.57$, $p<0.01$]. *T* tests revealed better performance by the smokers relative to the abstainers following vigilance instructions [$t(15.5)=3.29$, $p<0.003$], but not following prospective instructions ($t<1$). Vigilance instructions only produced significantly better ProM performance for volunteers who smoked prior to task [$t(19)=3.65$, $p<0.01$] (Fig. 2).

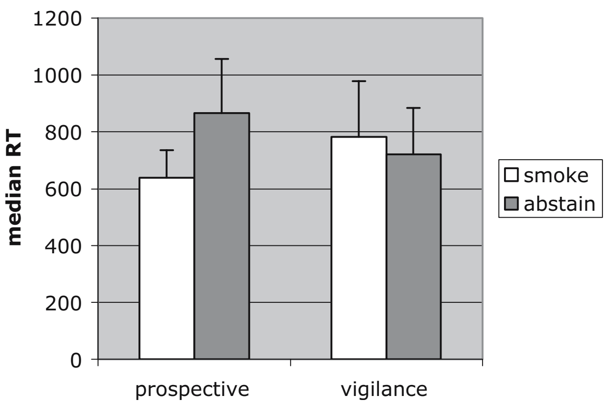


**Fig. 1** Median RTs for the LDT task, by nicotine and instruction; experiment 2

## Results: experiment 3

1. Costs of performing a concurrent ProM task (Table 2)
LDT error rates were analysed in a two-way (abstain/smoke prior to task; ProM LDT/baseline LDT) ANOVA; error rates were less than 12% throughout. Error rates were lower for the baseline LDT than when there was a concurrent ProM task [$F(1,55)=59.2$, $p=0.001$); there were no effects of nicotine condition on error rates and no interactions between factors.
Reaction times were analysed similarly. There was a main effect of ProM task [$F(1,55)=39.9$, $p<0.01$] and of stimulus type [$F(2,110)=34.8$, $p<0.001$]. Stimulus type also interacted independently with ProM task [$F(2,110)=8.45$, $p<0.01$] and with nicotine condition [$F(2,110)=4.72$, $p<0.01$]. Illegal non-words were rejected relatively more quickly when there was a concurrent ProM task than in the baseline LDT; both word and illegal non-word decisions were made more quickly by the smoking group relative to the abstainers.
2. Prospective memory task analysis
(a) Accuracy of LDT performance (Table 3)
A three-way ANOVA (smoke/abstain prior to task; letter/word ProM task; LDT/ProM importance instruction) on error rate in the ProM LDT task also found no main effects of nicotine, instruction or task. There was a significant interaction between nicotine condition and ProM task, however, [$F(1,49)=5.01$, $p<0.03$]. There were more errors as-

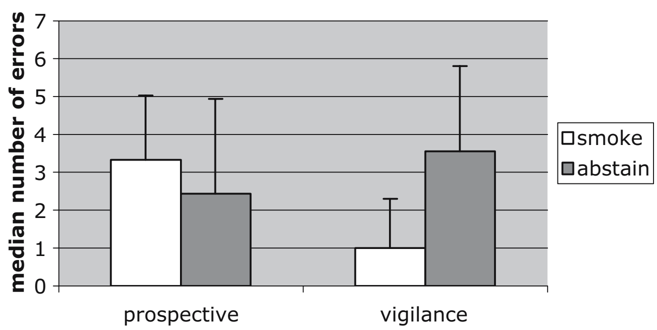


**Fig. 2** Mean number of ProM errors, by nicotine and instruction; experiment 2

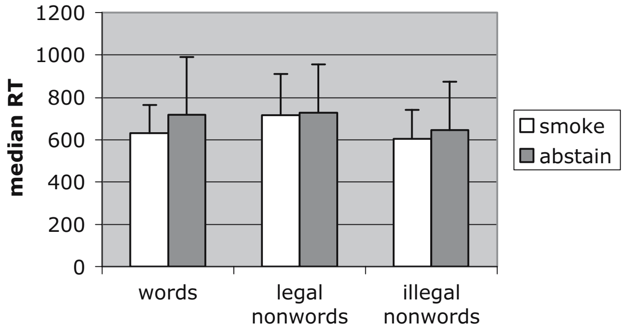


**Fig. 3** Interaction between nicotine and stimulus type for LDT RTs; experiment 3

sociated with the letter ProM task in the smoking group, and more errors associated with the word ProM task in the abstaining group.

(b) Speed of LDT performance
A four-way (smoke/abstain prior to task; letter/word ProM task; LDT/ProM importance instruction; word/legal non-word/illegal non-word) mixed ANOVA showed speed of response was not affected by instruction or by type of ProM task. There was a main effect of stimulus type [$F(2,98)=33.3$, $p<0.01$], qualified by an interaction with nicotine condition [$F(2,98)=4.90$, $p<0.01$]. Smoking improved decision speed for words and illegal non-words, but not for the (harder to reject) legal non-words (Fig. 3). There were no other main effects or interactions.

(c) Accuracy of ProM (Table 4)
ProM performance itself was analysed with a three-way between-subject ANOVA (smoke/abstain prior to task; letter/word ProM task; LDT/ProM importance instruction). There was a main effect of instruction [$F(1,49)=17.39$, $p<0.01$], a main effect of ProM task [$F(1,49)=6.71$, $p<0.02$] and a main effect of nicotine condition [$F(1,49)=8.89$, $p<0.004$]. There were fewer errors when the instructions emphasised the ProM task (means 2.4 and 4.19, respectively, for important vs unimportant). There were fewer errors when the ProM task was letter-based than when it was word-based (means 2.68 and 3.79, respectively), and there were fewer errors from volunteers who smoked at the start of the session (means 2.59 and 3.93 for smoking vs abstaining volunteers). On the three-way ANOVA, there were no interactions between factors.

## Discussion

### Tests of paradigm robustness

Baseline data from all three experiments confirmed that the volunteer responses in these experimental paradigms were consistent with earlier literature. There was a cost to the embedding of a ProM task within the LDT task, such that the LDT baseline speed and accuracy measures were better than LDT performance when there was a concurrent ProM. Similarly, performance was affected by stimulus type, with words responded to more quickly than legal non-words and with decisions to illegal non-words fastest of all. As RT to the lexical decisions were speeded with practice, there was a tendency for reaction times to the illegal non-words to get faster over time relative to the decision times for rejection of legal non-words. With one exception, these baseline performance effects were unaffected by the nicotine manipulation. The exception was experiment three, where, consistent with the attention-enhancing effects of nicotine, there was a tendency for nicotine to speed lexical decisions to illegal non-words and to words, while rejection times for the more difficult legal non-words remained unchanged. This effect appeared only in experiment 3, however, so it is possible that the effect emerges only when task manipulations stretch the volunteers.

### Experiment 1

The first study was essentially a replication of the original Brandimonte et al. (2001) study with a nicotine condition. In the original study, the vigilance instruction, designed to maintain focus on the ProM task, produced greater ProM accuracy at the expense of ongoing task accuracy. The ProM task (response to a word target) was, however, an example of what Kliegel et al. (2004) would consider an 'automatic' condition, where the requisite processing of the PM target is accomplished within the processing needs of the ongoing task and where cue recognition is relatively automatic. Accordingly, they would have argued for no effect of instruction or of nicotine on ProM task accuracy. Indeed, in their paper, they demonstrated no effect on ProM accuracy with a similar task when volunteers were explicitly instructed to prioritise the ProM task. Our results replicated the original Brandimonte result, demonstrating better ProM accuracy following vigilance than following prospective instructions. However, we found no effect of nicotine. Since the paradigm clearly demonstrated a ProM advantage under vigilance instruction, it seems reasonable to conclude that the vigilance instruction altered processing in a way that was distinct from changes induced by either a priority instruction (Kliegel et al. 2004) or by nicotine. We will return to this suggestion in the general discussion.

### Experiment 2

Employing the same paradigm as experiment 1, experiment 2 increased the demands of the ProM task by making the processing requirements for identification of the target stimulus distinct from the processing demands of the ongoing LDT. Under these conditions, ProM performance should have reflected strategic processes under both prospective instructions and vigilance instructions. Consistent with this suggestion, there was no advantage for vigilance over prospective instructions for the control group (abstaining smokers). Positive effects of nicotine on performance were observed under both prospective and vigilance conditions; the improvement, however, was observed on ProM accuracy under vigilance instructions and on the ongoing LDT reaction times under prospective instructions.

We suggest that when the ProM task engaged strategic processing, this increased the overall resource needs of the paradigm, relative to experiment 1. Under these conditions, and in line with expectations, nicotine improved performance. Specifically, the pattern of results indicated that when processing resources are stretched, nicotine improved performance on the particular task under focal attention, as determined by the instruction manipulation. If nicotine acted to increase attentional resources available, then these resources appear only to be available for allocation to the task under focal attention.

## Experiment 3

Experiment 3 introduced the instruction manipulation used by Kliegel et al. (2004), assigning importance to either the ProM task or to the LDT task. In essence, this was an explicit manipulation of priorities in a situation where resources were likely to be stretched. Instruction was combined with a ProM task manipulation (word vs letter targets) and nicotine manipulations (smoke/abstain prior to task). Kliegel et al. (2004) reported that the importance instruction augmented performance on a letter-based task (additional processing required for identification of the ProM target) but not on a word-based task (automatic activation of target item as part of the ongoing task). Their interpretation, that increased attention only benefited the strategic task, was supported by the fact that improved ProM performance was mirrored by impaired performance on the ongoing task. In experiment 3, a concurrent ProM task generally slowed RT in the lexical decision task and produced more errors. There was a positive effect of instruction; ProM accuracy improved when that task was prioritised, evidencing benefits from increased attention to the ProM task. Unlike Kliegel et al. (2004), however, we did not see better ongoing task performance when volunteers were instructed to prioritise the LDT task.

The ProM letter task was more demanding than the word task and, unsurprisingly, produced better ProM accuracy than the word task, independent of other manipulations. In the original study by Kliegel et al. (2004), effects of importance were limited to conditions involving the letter target, that is, explicit attention to the ProM task only promoted ProM performance if the task invoked strategic processing of the ProM cue. Their study, then, supported the contention that word targets automatically cued ProM retrieval and were immune to instructional bias towards or away from the ProM task. In contrast, the main effect of instruction in experiment 3 indicated that prioritising the ProM task benefited both the word and the letter version.

The nicotine manipulation also produced a main effect. All conditions showed improved ProM performance under nicotine, and in the present study, the effects of nicotine were not modulated either by instructions to prioritise a particular task or by the processing requirements of the ProM task. Nicotine also speeded the reaction time to respond in the ongoing LDT task.

The absence of interactions between instruction, task and nicotine condition was unexpected. The relationship between task and importance instruction, however, is not straightforward. Older adults, for example, respond differently to younger adults when requested to prioritise one task in a dual-task paradigm (Kleigel, personal communication). The instructional emphasis is critical. In the present study, a parsimonious interpretation of the data is that the priority instruction induced a dual-task situation, where both tasks (ProM and LDT) were maintained and processed within the balance of available resources. Thus, nicotine-induced increases in resources benefited both tasks. This contrasts with the Brandimonte paradigm, where the vigilance instruction induces a narrowing of the attentional spotlight to the primary task at the expense of the second task. The latter scenario characterised experiment 2, and in these conditions, we saw nicotine effects only on the focal task.

## General discussion

These three studies explored the potential for nicotine to enhance prospective memory. The studies were prefaced on the assumption that nicotine can induce changes in performance on cognitive processes that are effortful or strategic in nature. Our results confirm the view that ProM can involve strategic processing, although they demonstrate, too, that across ProM paradigms, critical differences in engagement of strategic processes can result from relatively small changes in instruction and in task variables.

First, we demonstrated that a vigilance instruction does not necessarily engage additional resources; if the requisite ProM processing is explicit in the ongoing task, ProM retrieval is relatively automatic (as shown in experiment 1). Hence, nicotine does not modulate performance. When the ProM task demands are distinct from the ongoing task, however (as shown in experiment 2), additional resources are engaged. Under these circumstances, the task under focal attention (as determined by instruction emphasis) improves under nicotine. Finally, when instruction set makes division of resources explicit (experiment 3), strategic processes are employed by default and independent of the nature of the ongoing task. Under these conditions, nicotine-induced enhancement is measurable independent of the demands of the ProM task, and these effects may be additive with task importance.

The mechanism of action of nicotine on ProM seems most likely to be an increase in resources available for task processing. Hence, the beneficial effects emerge only when conditions stretch attentional resources, such as when cue detection requires an additional component analysis of word stimuli or when the volunteer engages in simultaneous management of two independent tasks. An alternative possibility, that nicotine has its effects on ProM performance through enhanced task focus and improved concentration to the task in hand, is not supported since we observed no effect of nicotine in the basic vigilance manipulation in experiment 1. Indeed, the failure of nicotine to benefit attentionally mediated cue detection per se supports our general conclusion that it enhances performance only when resources are limited. Clearly, further work needs to be completed to test directly this working-memory hypothesis (for example, by including a direct manipulation of working-memory load) and to test the effects of nicotine across different routes of delivery (to target pharmacological effects of nicotine and generalise to non-smoking populations).

In relation to previous work with nicotine on retrospective memory paradigms, the link with effortful processing is consistent. As summarised in the introduction, nicotine has been associated with improvements in working memory and effortful engagement of cognitive processes, rather than simply sustained attention, although a distinctive neural basis for effects on memory and on attention has yet to be established. Kumari et al. (2003) reported an fMRI study involving a small group of healthy volunteers who were administered placebo or subcutaneous nicotine on two separate occasions and were tested on the working-memory '*n*-back' task under different memory loads. They demonstrated positive effects of nicotine on both accuracy and latency for correct performance, independent of load. Performance changes correlated with increased activity in the midbrain and brain stem regions associated with increased arousal and only limited increases in activity in prefrontal regions associated specifically with working-memory processes. Indeed, a load-dependent effect of nicotine on response latency (nicotine increased latency in the 0-back condition and decreased latency in the 3-back condition) suggested an arousal explanation for the performance improvements in that study. Ernst et al. (2001) had not, however, previously recorded positive effects of nicotine on performance of the same *n*-back task, and further work is needed to establish robust nicotinic effects on this paradigm.

The results reported in the current study provide the first evidence that nicotine can promote improved performance on tasks of prospective memory. They further confirm the multi-process framework (McDaniel and Einstein 2000; McDaniel et al. 2004) as the best account of the effects of procedural and instructional variations reported across the literature. The modulatory effect of nicotine on the ProM task variations employed here confirms that ProM performance may engage attentional resource, but it also indicated that attentional demand, and by implication strategic processing, is not categorically determined by either task or vigilance or priority rating. The complexity of these interrelationships undoubtedly limits the predictive value of the current psychological models of prospective memory and, in so doing, also limits the application of that knowledge to interventions aiming to reduce prospective memory failure in everyday situations. A detailed exploration of these interactions provides a challenging target for the next phase of development in this topical field of cognitive psychology.

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