

Effect of Cigarettes on Memory Search and Subjective Ratings

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WEST, R AND S HACK *Effect of cigarettes on memory search and subjective ratings* PHARMACOL BIOCHEM BEHAV 38(2) 281-286, 1991 —The effects of smoking a nicotine versus a nonnicotine cigarette on performance on Sternberg's memory search task and subjective ratings were examined. Testing sessions were undertaken both before and after a period of 24 hours' abstinence in occasional and regular smokers. Memory search rate was significantly faster after the nicotine cigarette than the nonnicotine cigarette. No significant difference in search rate was found between the results from occasional and regular smokers, and between the effect of a cigarette before and after the period of abstinence. The regular smokers inhaled more smoke from the nicotine and non-nicotine cigarettes than did the occasional smokers, but the amount of smoke inhaled from the test cigarettes did not change significantly from pre- to postabstinence. The nicotine cigarette produced stronger dizziness, tremor and palpitations than the nonnicotine cigarette, the more so after abstinence than before in the regular smokers. The results indicate that smoking a cigarette can produce subjective effects and performance improvements in regular and occasional smokers during the course of normal smoking, and that some subjective effects can be greater after abstinence.

Memory search Nicotine Subjective ratings Withdrawal symptoms Occasional smokers

WHEN asked why they smoke cigarettes, smokers offer a variety of reasons. These include helping to cope with stress, improving concentration and providing pleasurable relaxation (1). Examining the validity of these claims and the extent to which any of the perceived benefits of smoking are attributable to nicotine has provided the impetus for a substantial volume of research [(10), Chap. 6]. However, there is still considerable uncertainty about the nature and extent of any effects [(10), Chap. 6]. The issue is complicated by the possibility of acute tolerance if the effects of a cigarette are tested without smokers having first abstained for a while. If smokers are tested after a period of abstinence then any effects of smoking a cigarette might amount only to relief of a withdrawal decrement. There is also the possibility of chronic tolerance. In theory, nonsmokers could be used as a means of getting around this problem, but they usually cannot inhale tobacco smoke because they have not adapted to its irritancy.

There has recently been a move to test the effects of alternative methods of nicotine delivery which can be used by nonsmokers. These include nicotine tablets [e.g., (11)], nicotine chewing gum [e.g., (6)], nasal nicotine drops (14), and subcutaneous nicotine injections (5). However, the rate of absorption is typically much slower than from inhaled cigarette smoke. This may or may not affect their pharmacological action.

It is possible to address many of the problems of tolerance by testing subjects before and after a period of abstinence and also using both regular and occasional smokers. This latter group appear to have adapted to the cigarette smoke sufficiently that they can inhale it and obtain a substantial nicotine dose (7) but would not be expected to suffer withdrawal effects. The study described in this paper examined the effects of smoking a tobacco cigarette versus a nontobacco cigarette on Sternberg's memory search task

(8) and ratings of subjective effects in regular and occasional smokers, before and after a period of abstinence.

Sternberg's memory search task (8) involves presenting subjects with a short list of digits. This list is known as the "positive set." The digits not in the list are known as the "negative set." The subjects are then shown a series of "probe" digits one at a time and they have to indicate as quickly as possible in each case whether or not it was a member of the original list. This involves them searching their memory of the original list until they find a match, or fail to find one. In his original series of experiments, Sternberg showed that the average time taken to respond to the probes was a simple linear ascending function of the size of the positive set. He concluded that subjects were undertaking an exhaustive serial search through their mental representation of the positive set when each probe was presented. This conclusion has been challenged over the years because of further work carried out with the task (1), but the notion of some kind of memory search still appears to be the most satisfactory interpretation.

The memory search task has been extensively used in tests of the effects of drugs on performance and has been shown in one form or another to be sensitive to the effects of a range of stimulant and sedative drugs [e.g., (9)]. In general, stimulant drugs appear to speed up the search rate and sedative drugs slow it down. It is a task that might be expected to be affected by nicotine on two counts. First, nicotine appears to have a broad CNS and autonomic stimulant action [(10), Chap. 2]. Secondly, the role of cholinergic mechanisms in memory [(10), Chap. 6] suggests that a cholinergic agonist such as nicotine would facilitate retrieval. Sherwood et al. (6) recently reported finding that nicotine chewing gum improved performance on the Sternberg task for a combined group of smokers and nonsmokers, although the

TABLE 1
SUBJECT DETAILS

	Occasional	Regular
N	14	15
N smoking nicotine cig 1st	6	7
N males	5	7
Cigs per day*	1.4	14.6
Age	20.3	20.3
Years of smoking	3.4	4.3
SMQ dependence (max = 18)*	1.5	7.9

*Indicates significantly higher values for regular than occasional smokers

effect was apparently limited to speed of detection of items in the positive set.

The ratings of subjective effects used in this study included those which have been shown to be affected by smoking and/or nicotine in previous studies: dizziness/lightheadedness, tremor, nausea, and palpitations [e.g., (3,13)]. We also wished to know how pleasurable the smokers would find their cigarettes. A previous study had found that a significant proportion of heavy smokers who smoked a cigarette after 24 hours' abstinence found it unpleasant despite having been craving it strongly in preceding hours (13).

This study used cigarettes as the means of nicotine delivery because there is as yet no other acceptable method of dose administration which mimics their absorption profile. The disadvantage was that we could not control the dose obtained because individuals differ in the amount they puff on and inhale smoke from their cigarettes. This means that conclusions regarding the extent of tolerance to particular effects can only be expressed in very broad terms.

The rationale for including occasional smokers was that any effects of smoking a cigarette after a period of abstinence could not reasonably be interpreted as relief of withdrawal symptoms because these smokers should not experience any. We checked this assumption by measuring withdrawal symptoms using a questionnaire which has already been shown to be sensitive to cigarette withdrawal (12,13).

Most data on withdrawal symptoms currently available have come from heavy smokers who wish to give up. This study provided an opportunity to examine withdrawal symptoms in young regular smokers whose cigarette consumption was closer to the national average and who had no intention of giving up.

METHOD

Subjects

The subjects were all college students none of whom expressed a desire to give up smoking. They were recruited by advertisement and personal contact. Fourteen were occasional smokers and 15 were regular smokers. Occasional smokers were defined as smoking fewer than 20 cigarettes per week and not smoking for at least one day every week. Table 1 gives the subject details. It is clear that the occasional smokers did indeed smoke very little. They also scored as minimally dependent on the Smoking Motivation Questionnaire dependence scale [see (12)]. They had been smoking for a similar length of time to the regular smokers.

Design

The occasional and regular smokers underwent two testing

TABLE 2
STUDY DESIGN

Preabstinence Session	Postabstinence Session
Baseline	Baseline
CO + mood quest + Stern	CO + mood and craving quest + Stern
Cigarette 1	Cigarette 1
Posttest 1	Posttest 1
Stern + CO + Smoking effect quest	Stern + CO + Smoking effects quest
Cigarette 2	Cigarette 2
Posttest 2	Posttest 2
Stern + CO + Smoking effects quest	Stern + CO + Smoking effects quest

Note: CO = expired-air CO measure, Stern = Sternberg task. Cigarette 1 was a nicotine cigarette for half the subjects and a nonnicotine cigarette for the remainder. Cigarette 2 was a nicotine cigarette for those who had previously smoked a nonnicotine cigarette and vice versa.

sessions in the laboratory. The first was in the afternoon of a normal day during which they had smoked or not as they wished, and the second was after 24 hours complete abstinence. Table 2 shows the main features of the design of the study. Each testing session consisted of a series of baseline measures followed by the subjects smoking either a nicotine or nonnicotine cigarette (cigarette 1). This was followed by a further set of measures (posttest 1). Then those who had previously smoked the nicotine cigarette smoked the nonnicotine cigarette and vice versa (cigarette 2). The time between completing the first cigarette and starting the second was approximately 20 minutes. Then a final set of measures was taken (posttest 2). Occasional and regular smokers were randomly allocated to receive either the nicotine cigarette first or the nonnicotine cigarette first. If they smoked the nicotine cigarette first in the preabstinence testing session, they also smoked it first in the postabstinence testing session.

Materials and Measures

The nicotine cigarette was Benson & Hedges King Size (FTC ratings: tar 18 mg, nicotine 1.5 mg, CO 19 mg). The nonnicotine cigarette used was a brand called "Free" derived from wheat, cocoa and citrus plants.

Expired-air CO was measured using a Bedfont Instruments CO analyzer into which subjects exhaled having held their breath for 20 seconds. Expired-air CO measured in this way provides a very accurate indication of percent carboxyhaemoglobin (COHb) which is elevated by smoke inhalation. Used as a means of estimating the smoke intake from a single cigarette it performs less well (Pearson's $r = .7$ with COHb) but, nevertheless, provides an approximate indication (2).

The Sternberg task was implemented on a BBC Model B microcomputer using a modified version of a program provided by Professor Hindmarch of Surrey University, UK. The task involved presenting subjects with a short list of digits (the positive set) for three seconds. Subjects were then presented with a series of probe digits one after the other and they had to indicate in each case whether the probe digit was or was not a member of the positive set. They responded by pressing one key on the computer keyboard if the digit was a member of the positive set and another key if it was not. They used the index finger of their right hand in the former case and the index finger of their left hand in the

latter case. Their fingers were resting on or just above their respective keys at all times. The subjects were instructed to respond as quickly as possible but it was stressed that they should make as few errors as possible. Response times were recorded in milliseconds. The Sternberg task took about 5 minutes to complete.

In each of the three testing periods (baseline, posttest 1 and posttest 2), the subjects were allowed one practice trial with positive set size 2 and one with positive set size 5. Each trial consisted of presentation of a positive set followed by 16 probe digits, eight randomly chosen from the positive set and eight randomly chosen from the negative set. After the practice trial, the subjects underwent four trials with positive set size 2 and four with positive set size 5. The trials were randomly interspersed.

The subjects' mean response times for correct responses were calculated separately for set sizes 2 and 5. The memory search rate was indexed as the difference between the two. In addition to memory search rate and expired air CO, three measures were taken

1. After each cigarette, subjects completed a smoking effects questionnaire in which they rated the extent to which the cigarette had led to certain subjective effects: dizziness, nausea, tremor and palpitations. In each case they indicated whether this effect had occurred definitely (3), probably (2), or not at all (1). The subjects also rated how pleasurable they had found the cigarette on a scale of 1 (very unpleasant) to 5 (very pleasant), with 3 as the midpoint (neither pleasant nor unpleasant)
2. At the start of the preabstinence and postabstinence sessions, all subjects completed a mood questionnaire. This included five-point ratings of depression, irritability, restlessness, hunger and poor concentration [see (13)]
3. At the beginning of the postabstinence session, the subjects completed a craving questionnaire containing six-point ratings of difficulty not smoking, and strength and duration of urges to smoke (12).

Procedure

Before the subjects arrived for the first session, they were instructed that they should maintain their normal smoking pattern up to the time of arrival. On arrival at the laboratory, the subjects were instructed as to the procedure to be adopted. They then undertook the regimen shown in Table 2, as explained in the Design section. When they smoked the test cigarettes, they were permitted to smoke at their own pace so as to maintain as far as possible generalizability to normal smoking patterns. At the end of the first session, they were instructed to ensure that they smoked no cigarettes nor used any other tobacco product until the session the following day. This took place 24 hours later. Abstinence was checked by means of the first expired-air CO reading of the post-abstinence session

RESULTS

As shown in Table 3, the occasional smokers experienced no discernible withdrawal symptoms following their period of abstinence, confirming that they were not physically dependent. The regular smokers, by contrast, showed a significant increase in irritability [$F(1,26)=8.8$, $p<0.01$, for comparison between occasional and regular smokers] and hunger, $F(1,26)=4.6$, $p<0.05$. There were no other significant withdrawal-related changes in mood among the regular smokers. The regular smokers also reported much greater difficulty not smoking and urges to smoke during the 24 hours' abstinence compared with the occasional smokers, $F(1,26)=11.6$, $F(1,26)=11.0$ and $F(1,26)=11.6$, re-

TABLE 3
WITHDRAWAL CHANGES IN OCCASIONAL AND REGULAR SMOKERS

	Occasional	Regular
Depression	0 1	0 0
Irritability*	-0 2	0 8
Restlessness	0 2	0 1
Hunger*	-0 2	0 9
Poor concentration	0 1	0 3
Diff not smoking*	1 7	3 3
Time spent with urges to smoke*	1 9	3 2
Strength of urges to smoke*	2 2	3 9

Note Values for depression, irritability, restlessness, hunger and poor concentration were computed from ratings made after 24 hours' abstinence minus ratings made before abstinence. Difficulty not smoking to strength of urges to smoke were ratings at 24 hours' abstinence.

*Indicates regular smokers have significantly higher values than occasional smokers

spectively, $p<0.005$. In general, the occasional smokers reported no discernible withdrawal symptomatology, whereas the regular smokers reported a fair degree of discomfort.

The start-of-session CO was 16.9 ppm in the regular smokers at the start of the preabstinence session. This showed that they had been smoking at a reasonable rate on that day. This value dropped to 7.4 ppm after abstinence, with no subjects exceeding the 10 ppm threshold for detection of abstinence violation. In the occasional smokers the expired-air CO remained virtually unchanged (4.5 ppm versus 4.6 ppm).

As shown in Table 4, the mean CO boost from the nicotine cigarette was 2.9 ppm in the occasional smokers before abstinence, and 2.4 ppm after abstinence. For the regular smokers the corresponding figures were significantly higher at 5.5 ppm and 6.6 ppm, $F(2,52)=7.4$ and $F(2,52)=10.6$, respectively, $p<0.02$. Similar increases in CO were obtained from the nonnicotine cigarettes (Table 4). Thus the regular smokers obtained more CO and, therefore, almost certainly more nicotine from the nicotine cigarettes than did the occasional smokers. However, the CO intake from the cigarette postabstinence was not significantly different from preabstinence in either group.

The nicotine cigarette caused significantly more dizziness, tremor, and palpitations overall than did the nonnicotine cigarette, $F(1,26)=66.5$, $F(1,26)=37.4$ and $F(1,26)=47.6$, respectively, $p<0.001$, see Table 4. There was evidence for stronger dizziness and tremor from the nicotine cigarette after abstinence than before only in the regular smokers, $F(1,26)=9.3$ and $F(1,26)=9.1$, respectively, $p<0.01$. The nicotine cigarette produced slightly greater nausea in the occasional smokers than the regular smokers, whereas in the regular smokers the nonnicotine cigarette was judged to produce slightly more nausea than the nicotine cigarette, $F(1,26)=4.3$ for the interaction, $p<0.05$.

The rated pleasure from the nicotine cigarette was significantly greater overall than the nonnicotine cigarette, $F(1,26)=27.2$, $p<0.001$. Given that a rating of 3 meant "neither pleasant nor unpleasant," the difference was due to the nonnicotine cigarette being judged mildly unpleasant rather than the nicotine cigarette being judged pleasant (see Table 4). The regular smokers rated the nonnicotine cigarette after abstinence as significantly more unpleasant than did the occasional smokers, $F(1,26)=7.5$, $p=0.01$.

TABLE 4
EFFECTS OF NICOTINE AND NONNICOTINE CIGARETTES

	Occasional				Regular			
	Preabst		Postabst		Preabst		Postabst	
	Nic	Non	Nic	Non	Nic	Non	Nic	Non
CO boost‡	2.9	3.5	2.4	4.9	5.5	6.1	6.6	6.2
Nausea§	1.8	1.6	1.6	1.4	1.4	2.0	1.6	1.7
Dizz*†	2.6	1.6	2.6	1.4	2.3	1.4	2.9	1.4
Palp*	1.8	1.2	1.8	1.1	1.7	1.2	2.1	1.1
Trem*†	1.8	1.4	1.8	1.1	1.7	1.2	2.4	1.3
Pleasure¶	2.9	2.3	3.3	2.6	3.3	2.1	3.4	1.7
Stern 2	0.00	-0.03	0.00	0.00	-0.06	-0.05	-0.01	-0.02
Stern 5*	-0.19	-0.08	-0.04	-0.01	-0.09	-0.05	-0.04	0.00
Search time diff*	-0.19	0.11	-0.04	-0.01	-0.03	0.00	-0.03	0.02

Note: Stern 2 means change in response time for positive set size 2 in the Sternberg task, Stern 5 means change in response time for positive set size 5 in the Sternberg task. Search time diff means difference between Stern 5 and Stern 2.

*Values for nicotine cigarette were significantly higher than for nonnicotine cigarette.

†Postabstinence nicotine cigarette resulted in significantly higher ratings than did the preabstinence cigarette among the regular smokers but not the occasional smokers.

‡Regular smokers had significantly higher levels than did occasional smokers.

§Occasional smokers had significantly higher scores from nicotine cigarettes, whereas regular smokers had higher scores from nonnicotine cigarette.

¶Regular smokers found nonnicotine cigarette significantly more unpleasant postabstinence than occasional smokers.

The increase in memory search rate was significantly greater after the nicotine cigarette than the nonnicotine cigarette among the occasional and regular smokers combined and before and after abstinence, $F(2,52) = 3.26, p < 0.05$. There was no significant interaction with abstinence and no significant difference between the occasional and regular smokers. The effect was not significantly different for the positive and negative set responses. Figure 1 shows the result graphically, with search rate calculated as 3 divided by the difference between response time in seconds for positive set size 5 and response time for positive set size 2. When

the nicotine cigarette was smoked first there was an increase in search rate after the first cigarette, and when the nicotine cigarette was smoked second there was an increase in search rate after the second cigarette. This increase in search rate resulted from a decrease in the response time for positive set size 5, $F(2,52) = 2.9, p < 0.05$, and not an increase in response time for positive set size 2. It, therefore, reflected a genuine improvement in performance. This was not offset by an increase in the number of errors as in all conditions subjects performed with 2 or fewer errors in each block of 16 trials.

DISCUSSION

Both the occasional and regular smokers obtained significant intake of smoke from the test cigarettes as indicated by the rise in CO levels. However, the regular smokers inhaled more smoke than did the occasional smokers. Smoking a nicotine cigarette resulted in an increase in memory search rate. This did not differ significantly according to whether the subjects abstained from smoking before smoking the test cigarette or whether they were occasional or regular smokers. The regular smokers reported increased irritability and hunger after 24 hours' abstinence, and they reported difficulty not smoking and strong urges to smoke. The occasional smokers reported no such problems with abstinence. Smoking a nicotine cigarette resulted in some dizziness, tremor and palpitations. The dizziness and tremor were greater in the regular smokers when the nicotine cigarette was smoked after abstinence than before. The occasional smokers found the nicotine cigarette to produce more nausea than the nonnicotine cigarette, whereas the reverse was true for the regular smokers. The nicotine cigarette was judged on average to be neither pleasant nor unpleasant but the nonnicotine cigarette was judged slightly unpleasant, more so by the regular smokers after abstinence.

The difference in CO boost from the test cigarettes between the occasional and regular smokers does not accord with the find-

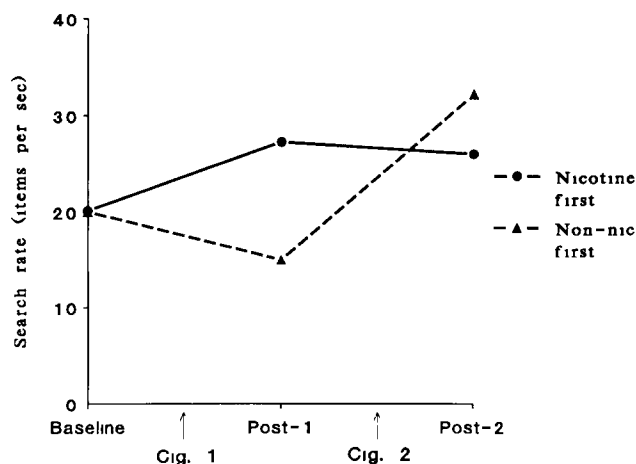


FIG 1 Mean search rates before and after smoking nicotine and nonnicotine cigarettes. Search rate was calculated as 3 divided by the difference in search time in seconds between response times for positive set size 5 and positive set size 2.

ing of Shiffman et al. (7) They reported a study in which occasional smokers inhaled as much smoke from each cigarette as regular smokers. There are several possible explanations. First of all, our "occasional smokers" were more occasional than those in Shiffman et al.'s study. We required our occasional smokers to go at least one day per week without smoking at all, whereas they required that their occasional smokers should smoke for at least four days per week. We chose a stringent definition of occasional smokers because we felt that having at least one day per week without cigarettes was important in establishing a prima facie case for nondependence. A second possible explanation is that we did not require our occasional smokers to have been smoking in this way for any particular period of time. Therefore, they may have been at an early stage in a developing smoking career, or they may even have been trying to give up. However, by self-report they were not interested in giving up or even limiting their smoking. Also, they had been smoking for a similar length of time to the regular smokers. Thirdly, our subjects were all college students and were, therefore, young and from particular socio-economic backgrounds. It may be that, although the occasional smokers had no intention of giving up, they were a kind of smoker who would give up once they finished college and their social circumstances took on a different character. Finally, it is possible that Shiffman's sample of occasional smokers were atypical in that they were recruited by advertisement. It will be important to establish which of these explanations holds true because of the implications for our understanding of why some smokers can apparently continue smoking without becoming dependent.

The absence of withdrawal symptoms among the occasional smokers was expected, but worth confirming. More interesting is the fact that the regular smokers did not report the full gamut of withdrawal symptoms found in studies with smoker's clinic clients and samples recruited by advertisement in stop-smoking studies. The difference may be due to the age of our subjects, the fact that they were not heavy smokers or the fact that they were at a relatively early stage in their smoking careers. This is something which will have to be investigated further because it bears on the issue of how rapidly physical dependence to cigarettes develops.

Perhaps the most important finding of this study was that smoking a nicotine cigarette increased memory search time and that the effect did not appear to depend on prior abstinence in regular smokers. Unlike Sherwood et al. (6), we did not find evidence of a difference in size of effect for positive and negative set responses. The fact that the regular smokers did not obtain a larger effect than the occasional smokers despite greater smoke intake suggests either that there is some degree of chronic tolerance to the effect, or that the dose-response curve flattens off at or below the level of nicotine intake achieved by the occasional smokers. It seems unlikely that there is substantial acute tolerance to the effect at the doses normally obtained with smoking because of the similarity between the effect before and after abstinence. The fact that the effect was observed in regular smokers during the course of a normal smoking day indicates that any chronic or acute tolerance which may have developed was not complete within the dosing profile adopted by our smokers. Further studies will be needed to determine whether nicotine delivery systems

with slower rates of absorption will produce similar effects, and to chart the dose-response curve with differing amounts of prior nicotine exposure. Differences in the rate of absorption may underlie the difference between our finding and that of Sherwood et al. (6) who reported that the increase in search rate was limited to recognition of positive set items.

It was already known that nicotine could induce dizziness, tremor, palpitations and nausea. The interesting feature of the present study was that the regular smokers experienced these effects during a normal smoking day to the same degree as the occasional smokers. This conflicts with the earlier finding of West and Russell (13) that a cigarette smoked on a normal smoking day had no detectable subjective effects of this kind. The difference may be due to the fact that the present study used college students who had only been smoking for three to four years and averaged only 15 cigarettes per day; West and Russell's subjects were smoker's clinic clients who averaged nearly 30 cigarettes per day. This raises the possibility that the extent of acute and/or chronic tolerance to these effects of nicotine varies according to habitual levels of nicotine intake even within the range found in regular smokers. This is something which merits further study. If smokers of 15 cigarettes per day are regularly getting subjective effects from their cigarettes, this may provide a source of motivation to continue to smoke and contribute to the continued development of dependence.

It is interesting to note also that the regular smokers reported more dizziness and tremor from their cigarette after they had been abstinent for 24 hours. This was despite apparently not smoking their postabstinence cigarettes significantly harder. This is consistent with the view that some degree of acute tolerance to nicotine exists with regard to these effects.

It may seem surprising that neither the occasional nor the regular smokers obtained positive pleasure from the nicotine cigarette. However, the result is consistent with West and Russell's (13) study involving heavy smokers. It may be that the pleasure which smokers obtain from cigarettes is heavily dependent on the situation. The fact that our subjects were in a laboratory may have militated against enjoyment of smoking. The mild dislike of the nonnicotine cigarette is unlikely to have been due to noxious taste as these cigarettes were very mild. More likely is the fact that the nonnicotine cigarettes failed to match up, either in taste or pharmacological action, to the subjects' usual cigarettes. Indirect support for this view comes from the finding that the regular smokers disliked the nonnicotine cigarette more than did the occasional smokers only after they had been abstinent for 24 hours. At such a time, they may well have been seeking withdrawal relief from the cigarette.

In conclusion, this study has provided evidence that nicotine cigarettes can speed up memory search time even in regular smokers during the course of a normal smoking day. Regular smokers can also experience dizziness, tremor and palpitations when they smoke cigarettes without having abstained first, although they report that dizziness and tremor are stronger when nicotine cigarettes are smoked after a period of abstinence. Our results provide some support for smokers' claims that cigarettes can improve their performance, but whether memory search speed reflects a more general increased efficiency is unclear.

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