

Directed Forgetting, Event-Related Potentials and Nicotine

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Fifteen male users of oral snuff performed a directed forgetting task after over-night abstinence and after administration of oral snuff. Directed forgetting tasks use cues to classify items for differential reporting at test, emphasizing the need for strategic encoding. Recognition was better after nicotine administration, but we found no evidence for greater strategic control, as hypothetically reflected in successful compliance with the directed forgetting instruction. Reaction time decreased after nicotine administration. Performance among 15 controls was unaffected over two sessions. Copyright © 1999 John Wiley & Sons, Ltd.

KEY WORDS — nicotine; oral snuff; memory; ERPs; reaction time

INTRODUCTION

Studies of nicotine effects on cognitive functions in man are remarkably variable in results and interpretation (Heishman *et al.*, 1994). Memory effects have been one of the central issues. Animal studies show a fairly consistent picture of modest working memory improvement (Levin, 1992), for instance a decrease in radial maze errors after chronic nicotine administration to rats (Levin *et al.*, 1996). Human studies of long-term memory performance after pre-trial nicotine administration have, however, been less conclusive (Heishman *et al.*, 1994). Studies have, over varying retention delays, shown improvement (Peeke and Peeke, 1984; Warburton *et al.*, 1992a,b; Rusted *et al.*, 1995 [Exp. 4]), no change (Parrott and Winder, 1989; Foulds *et al.*, 1996), or impairment (Houston *et al.*, 1978; Spilich *et al.*, 1992). When improvement has been found, it has usually been modest (Heishman *et al.*, 1994).

In the study by Warburton *et al.* (1992b), the results indicated that nicotine emphasized performance patterns found in abstinence; subjects with strong primacy effects enhanced that effect after nicotine administration, with the corresponding

result for recency effects. In discussing these findings Warburton *et al.* suggested that the performance improvements reflect a strategic deployment of resources, facilitated by nicotine, an idea that seems closely related to the concept of nicotine as a cognitive enhancer (Warburton, 1992). However, if this pattern is not merely due to an accentuated, but stable, personal performance characteristic, nicotine administration should facilitate the compliance with encoding manipulations, such as directed forgetting (see, for example, Paller, 1990; Johnson, 1994). Directed forgetting experiments employ an encoding cue, e.g. colour, to designate test items into one group to be remembered and reported as old at test (R-words), and one to be forgotten and reported as new (F-words). At the test stage, this procedure can be regarded as an exclusion task (see, for example, Jacoby *et al.*, 1993) within a standard recognition task (see Wilding and Rugg, 1997, for a similar design in a non-pharmacological context). The exclusion paradigm demands that certain old items be reported as new. One might then apply a dual-process conceptualization of recognition (Jacoby, 1991), where both familiarity (a sense of having encountered the item recently) and recollection (a retrieval of context, pinpointing the item in time) will play a part. The estimation of these components is currently under vigorous debate (Mulligan and Hirshman, 1997; Curran and Hintzman, 1997; Jacoby *et al.*, 1997), but for the present

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study, it is sufficient to note that the correct classification of an old word in a directed forgetting task cannot solely rely on familiarity, as recollection of context information is necessary to decide whether the word belongs to the R- or F-class. New words, on the other hand, can be classified on the basis of less familiarity. Hence, one might assume that strategic resource deployment in this task would comprise a more elaborate encoding, taking advantage of whatever contextual information the subject can generate to facilitate classification at test.

The analysis of the recognition data in this experiment is based on two signal detection measures: d'_{new} , calculated from R-words and new words, and d'_{old} , encompassing the R- and F-words. The critical test of strategic resource deployment is then arguably an increase of d'_{old} after nicotine administration, as this would call for more extensive context retrieval, whereas d'_{new} reflects recognition without any more precise classification.

Given that a differential encoding takes place, event-related potentials might elucidate the encoding process. A classic ERP signature in a colour-guided selection task is the frontal P205, a positive deflection in the response to items of the target colour (Hillyard and Münte, 1984; Wijers *et al.*, 1989). However, in this study all items required further processing and it is therefore likely that the P205 effect would be attenuated. Instead, one might hypothesize that the R-words should be accompanied by an increased late positivity, akin to the Dm effect described by Karis *et al.* (1984), as an indication of more elaborate encoding.

The ERP repetition effect, that previously encountered stimuli elicit a more positive-going wave (see, for example, Rugg, 1996), would imply larger late positivities following R-words in the recognition test, compared to both F-words and new words. It is then possible that the difference amplitude reflecting the signal detection indices, i.e. R-F and R-new, would increase after nicotine administration.

METHOD

Subjects

Eighteen male users of oral snuff (mean age 27.4, S.D. 4.0 years) were tested. All were users for at least 2 years (mean 10.4, S.D. 5.0 years). Average daily consumption of oral snuff was 32.8, S.D.

18.4 g/day. Data from three of these were excluded due to admitted non-compliance with abstinence in one case, and excessive reaction to blood sampling in two cases. No other nicotine users reported any discomfort by the blood sampling. Seventeen male non-users of nicotine (mean age 24.9, S.D. 3.8 years) were tested in a similar manner. They did not receive nicotine and for practical reasons did not undergo blood sampling, as the main point of the control group was to provide a reference in terms of performance and ERPs in this type of task. Two control subjects were excluded due to technical fallacies.

Procedure

Subjects came to the laboratory for two sessions, separated by a week. Experiments were run at 8.00 a.m. or 10.00 a.m., and both sessions were run at the same hour. Subjects had been instructed to refrain from nicotine, alcohol, or caffeine for 12 h. In one of the sessions, nicotine users applied oral snuff of their own preferred brand for 20 min, after which the study test was run (see below). Nicotine use was balanced over sessions. Subjects were placed in a comfortable armchair. Subjects were instructed about the purposes of the experiment, and gave their written informed consent.

Directed forgetting task

The experiment was run using PsyScope 1.0.2 (Cohen *et al.*, 1993). The subjects read five consecutive lists of 40 nouns each, with a short subject-terminated pause between each list. There were four counter-balanced sets of five lists. The nouns were selected from a pool of common nouns, sampling categories such as animals, vehicles, tools, etc. Words were randomly allocated to lists and categories. Words were shown in blue or red typeface, with instructions that blue words should be remembered (R-words) and red forgotten (F-words). Every list started and ended with two R-coded buffer words that were not included in the recognition test. Every list comprised 15 words of either the R- or F-class, later included in the recognition test, along with three flower names of each colour. The flower names were included to ensure that subjects read all stimuli. The complete list of names of nine common flowers was shown to subjects beforehand. The subjects were instructed to read each word, and press a response button on a dedicated device (PsyScope ButtonBox) as soon

as they encountered a flower name. Words were shown for 2000 ms, and the inter-trial interval was 800 ms. When the study task was completed, the subjects performed a distracter task (a choice reaction time task, data not reported), lasting approximately 7 min.

Immediately following the distracter task, a recognition test was run, where all of the R- and F-words were presented (buffer words and flower names were excluded), together with 75 new words, also selected from the initial pool of nouns. All words were shown in black typeface. The subjects were to respond to R-words by pressing a designated response button, and to F-words and new words by pressing another button. Words were shown for 2000 ms, with a response window of the same duration and an 800 ms inter-trial interval.

Data recording

Continuous EEG was recorded using a NeuroScan system. EEG was sampled at 250 Hz from the F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, and Oz derivations, with earlobes as reference. Oculo-motor artifacts were monitored using electrodes placed below the right eye, and at the outer left canthus, and were corrected off-line using NeuroScan software. EEG was converted into epochs starting 160 ms before stimulus onset and ending 1000 ms after onset. The pre-stimulus segment was used to correct the base-line of each epoch. Data was digitally band-pass filtered at 0.3 and 20 Hz with a 24 dB roll-off. Epochs were excluded if EEG amplitudes exceeded $\pm 100 \mu\text{V}$ after correction for oculomotor artifacts.

Data analysis

In the encoding task, the average amplitude in the 500–750 ms interval, corresponding to the late positive component, was calculated at the Cz and Pz leads. For the recognition data, average amplitudes in the 350–550 ms interval, corresponding to the N400-like negativity, and the 550–850 interval, corresponding to the late positive component, were calculated for the Fz, Cz, and Pz electrodes. Mean reaction times were calculated for correct responses, and the signal detection index d' was formed including R- and F-words, d'_{old} , and for the R-words and new words, d'_{new} . Non-responses (mean 6%, S.D. 6%) were excluded from the calculation of the d' indices. ERP difference

measures corresponding to the d'_{old} , R-F, and d'_{old} , R-new, were formed.

Nicotine analysis

Blood samples were drawn from an antecubital vein before the start of the encoding task, and after the recognition task. Blood samples were immediately put on ice, and stored at -18°C until analysis. Determination of nicotine was performed by capillary gas chromatography after a single-step liquid–liquid extraction of the plasma sample.

Statistical analysis

To counterbalance order effects, nicotine users were randomly assigned to receive nicotine in their first or second testing session. To achieve the same counterbalancing in the control group, each control subject was yoked in a pair with a nicotine subject, and his first and second session were assigned to a pseudo-nicotine and a pseudo-abstinence condition, in parallel with his counterpart. Separate analyses are reported for the groups. Signal detection measures are analysed by a two session repeated measures ANOVA. Reaction time was analyzed by a 2 sessions \times 3 word classes ANOVA. A similar ANOVA, adding electrodes as a further within subjects factor, was used in the ERP analyses. Greenhouse-Geisser correction was applied when necessary.

RESULTS

Nicotine levels

The mean nicotine concentration in the abstinence pre-test samples was 3.36 ng/ml (S.D. 1.19), and in the post-test samples 2.93 ng/ml (S.D. 1.00). In the nicotine session, pre-test samples contained 11.06 ng/ml (S.D. 2.92), and post-test samples 14.95 ng/ml (S.D. 5.54).

Encoding task

Performance. The identification of catch trial words was quite high (Table 1), and unaffected by nicotine administration [$F(1, 14) = 1.2$, $p = 0.30$], and similar for R- and F-coded words [$F(1, 14) < 1$, n.s.]. There was no interaction between nicotine administration and stimulus class [$F(1, 14) < 1$, n.s.]. All comparisons in the control group were non-significant [all $F(1, 14) < 1$, n.s.].

Table 1. Encoding control test

Hit rate (%)	Abstinence		Nicotine	
	M	SD	M	SD
<i>R-code</i>				
Nicotine ($n = 15$)	90.7	16.1	94.7	12.6
Control ($n = 15$)	96.9	4.3	97.8	4.1
<i>F-code</i>				
Nicotine ($n = 15$)	92.4	11.5	92.4	18.7
Control ($n = 15$)	98.2	4.7	98.2	3.1

Table 2. Average amplitude in μV of the late positive component in the encoding task, collapsed over electrodes

	Abstinence		Nicotine	
	M	SD	M	SD
<i>R-word</i>				
Nicotine group ($n = 15$)	0.82	1.52	0.58	2.06
Control group ($n = 15$)	1.46	1.45	0.26	2.05
<i>F-word</i>				
Nicotine group ($n = 15$)	1.10	1.44	0.62	1.55
Control group ($n = 15$)	1.34	1.75	1.02	1.79

Event-related potentials. Average amplitudes for the late positive component can be found in Table 2.

The administration of nicotine had no effect on the amplitude of the late positive component [$F(1,14) < 1$, n.s.], nor was there any significant

difference between R- and F-stimuli [$F(1,14) < 1$, n.s.], or any interaction [$F(1,14) < 1$, n.s.] (Figure 1).

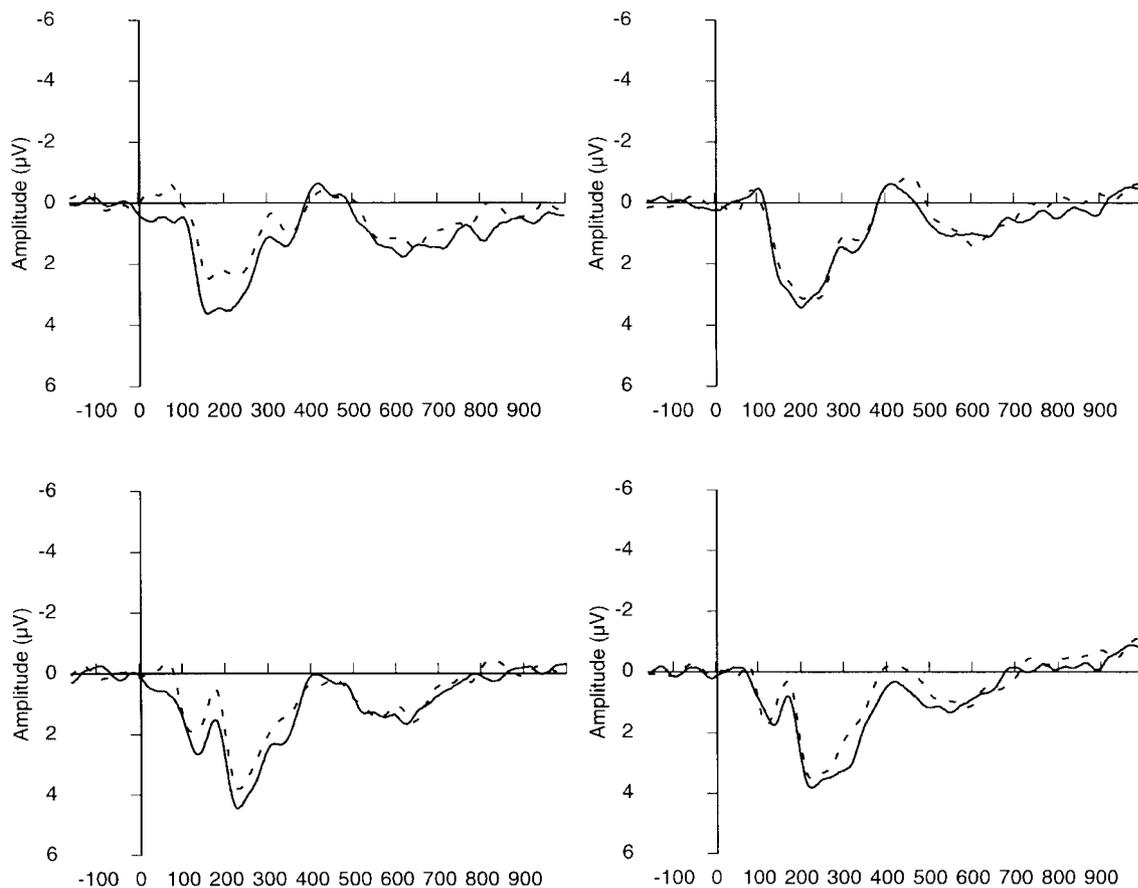


Figure 1. Grand averages from the encoding task for the nicotine group. Left panels depict abstinence, right panels the nicotine session, upper panels Cz, lower Pz. Solid lines = R-words, dash = F-words

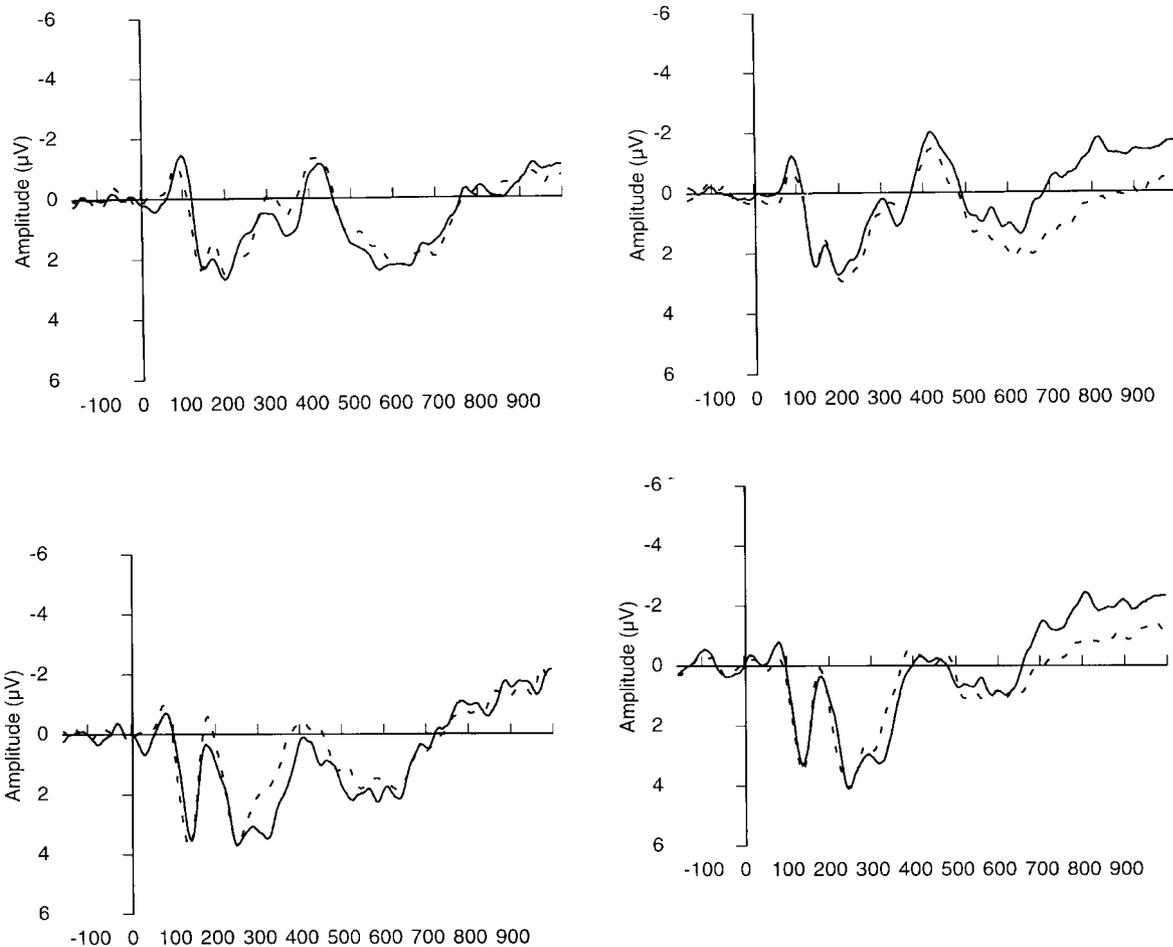


Figure 2. Grand averages from the encoding task for the control group. Left panels depict pseudo-abstinence session, right panels pseudo-nicotine session, upper panels Cz, lower Pz. Solid lines = R-words, dashed = F-words

Controls were stable over sessions [$F(1, 14) = 1.7, p = 0.22$], and there was no main effect of word classes [$F(1, 14) = 1.5, p = 0.25$]. All other comparisons were non-significant [$F(1, 14) < 3.8, p > 0.07$] (Figure 2).

Recognition task

Performance. Performance data can be found in Table 3. The task was difficult, with low identification of R-words, especially. Nicotine administration did not affect d'_{old} [$F(1, 14) = 2.3, p = 0.15$], but d'_{new} was significantly higher after nicotine administration [$F(1, 14) = 12.9, p = 0.003$], indicating better recognition. Both measures were unaffected in the control group [$F(1, 14) < 1, n.s.$].

In the nicotine group, reaction time decreased significantly after nicotine administration [$F(1, 14) = 6.1, p = 0.03$] (Table 4). There was no difference between word classes, nor any interaction [$F(2, 28) < 1.8, p > 0.19$ in both cases].

Controls were stable over sessions [$F(1, 14) = 1.4, p = 0.26$], and there was no word class difference, nor any interaction effect [$F(2, 28) < 3.1, p > 0.10$].

Event-related potentials. Average amplitudes for the late negativity and the late positivity can be found in Table 5. Grand averages for the mid-line electrodes are shown in Figures 3 (nicotine group) and 4 (controls).

Late negativity. The administration of nicotine had no effect on the amplitude of the late negativity

Table 3. Recognition test performance

	Abstinence	Nicotine	<i>t</i> (14)	<i>p</i>
<i>Hit rate R-word (%)</i>				
Nicotine	46.4	53.2	2.3	0.04
Control	43.8	46.5	0.52	n.s.
<i>False alarms F-word (%)</i>				
Nicotine	32.1	31.5	0.14	n.s.
Control	25.5	25.3	0.06	n.s.
<i>False alarms new word (%)</i>				
Nicotine	20.7	15.0	2.85	0.01
Control	12.3	11.5	0.19	n.s.
<i>d' old</i>				
Nicotine	0.42	0.61	1.5	0.15
Control	0.54	0.69	0.64	n.s.
<i>d' new</i>				
Nicotine	0.86	1.21	3.6	0.003
Control	1.23	1.36	0.45	n.s.

Table 4. Reaction time in the recognition test

	Abstinence		Nicotine	
	M	SD	M	SD
<i>R-word</i>				
Nicotine (<i>n</i> = 15)	1118	157	1044	132
Control (<i>n</i> = 15)	1107	126	1094	161
<i>F-word</i>				
Nicotine (<i>n</i> = 15)	1146	178	1081	174
Control (<i>n</i> = 15)	1129	166	1091	140
<i>New word</i>				
Nicotine (<i>n</i> = 15)	1130	183	1001	178
Control (<i>n</i> = 15)	1056	171	1038	167

[$F(1,14) < 1$, n.s.], and there was no significant difference between word classes [$F(1, 14) = 1.1$, $p = 0.34$]. The interaction between word class and electrode was significant [$F(4, 56) = 3.3$, $p = 0.04$]. However, when re-scaled (McCarthy and Wood, 1985) to compensate for problems with non-additivity, this was attenuated [$F(4,56) < 1$, n.s.]. All other terms were non-significant ($p > 0.19$). Both difference measures, analogous to d'_{old} and d'_{new} , were unaffected by nicotine administration [$F(1,14) < 1$, n.s.].

Controls were stable over sessions [$F(1,14) < 1$, n.s.], and there was no main effect of word class [$F(1,14) < 1$, n.s.], and no interaction between session and word class [$F(1,14) < 1$, n.s.]. The amplitude decreased from anterior to posterior leads [$F(2, 28) = 5.9$, $p = 0.01$]. All other

Table 5. Event-related potential parameters for the recognition task, collapsed over electrodes

	Abstinence		Nicotine	
	M	SD	M	SD
<i>Late negativity amp. (µV)</i>				
<i>R-word</i>				
Nicotine (<i>n</i> = 15)	-0.11	2.18	-0.69	2.84
Controls (<i>n</i> = 15)	-0.17	2.57	-0.05	2.01
<i>F-word</i>				
Nicotine (<i>n</i> = 15)	0.33	2.13	-0.08	1.63
Controls (<i>n</i> = 15)	0.16	1.82	0.22	1.96
<i>New word</i>				
Nicotine (<i>n</i> = 15)	-0.05	1.67	0.16	1.84
Controls (<i>n</i> = 15)	-0.40	2.28	0.12	1.72
<i>Late positivity amp. (µV)</i>				
<i>R-word</i>				
Nicotine (<i>n</i> = 15)	0.37	2.01	-0.10	2.95
Controls (<i>n</i> = 15)	1.15	2.31	1.56	2.67
<i>F-word</i>				
Nicotine (<i>n</i> = 15)	1.04	1.95	0.77	1.57
Controls (<i>n</i> = 15)	1.34	2.16	1.54	2.09
<i>New word</i>				
Nicotine (<i>n</i> = 15)	1.40	1.42	1.62	1.86
Controls (<i>n</i> = 15)	1.66	2.33	2.16	1.67

comparisons were non-significant ($p > 0.18$). Difference measures were stable over sessions [$F(1,14) < 1$, n.s.].

Late positivity. The administration of nicotine had no effect on the amplitude of the late positivity [$F(1,14) < 1$, n.s.]. There was a difference between word classes [$F(2, 28) = 6.6$, $p = 0.01$], as new words elicited larger amplitudes than old [$F(1, 14) = 9.1$, $p = 0.01$]. The interaction between word class and session was not significant [$F(2,28) < 1$, n.s.]. There was a difference between electrodes [$F(1, 14) = 14.4$, $p = 0.01$], with smaller amplitudes at Fz. All other terms were non-significant ($p > 0.12$). Difference measures were stable over sessions ($F(1,14) < 1$, n.s.).

Controls were stable over sessions [$F(1, 14) = 1.6$, $p = 0.23$], and there was no main effect of word class [$F(1, 14) = 1.1$, $p = 0.33$], and no interaction between session and word class [$F(1,14) < 1$, n.s.]. The amplitude was highest at Cz [$F(2, 28) = 8.8$, $p = 0.01$]. All other comparisons were non-significant ($p > 0.15$). Difference measures were stable over sessions [$F(1,14) < 1$, n.s.].

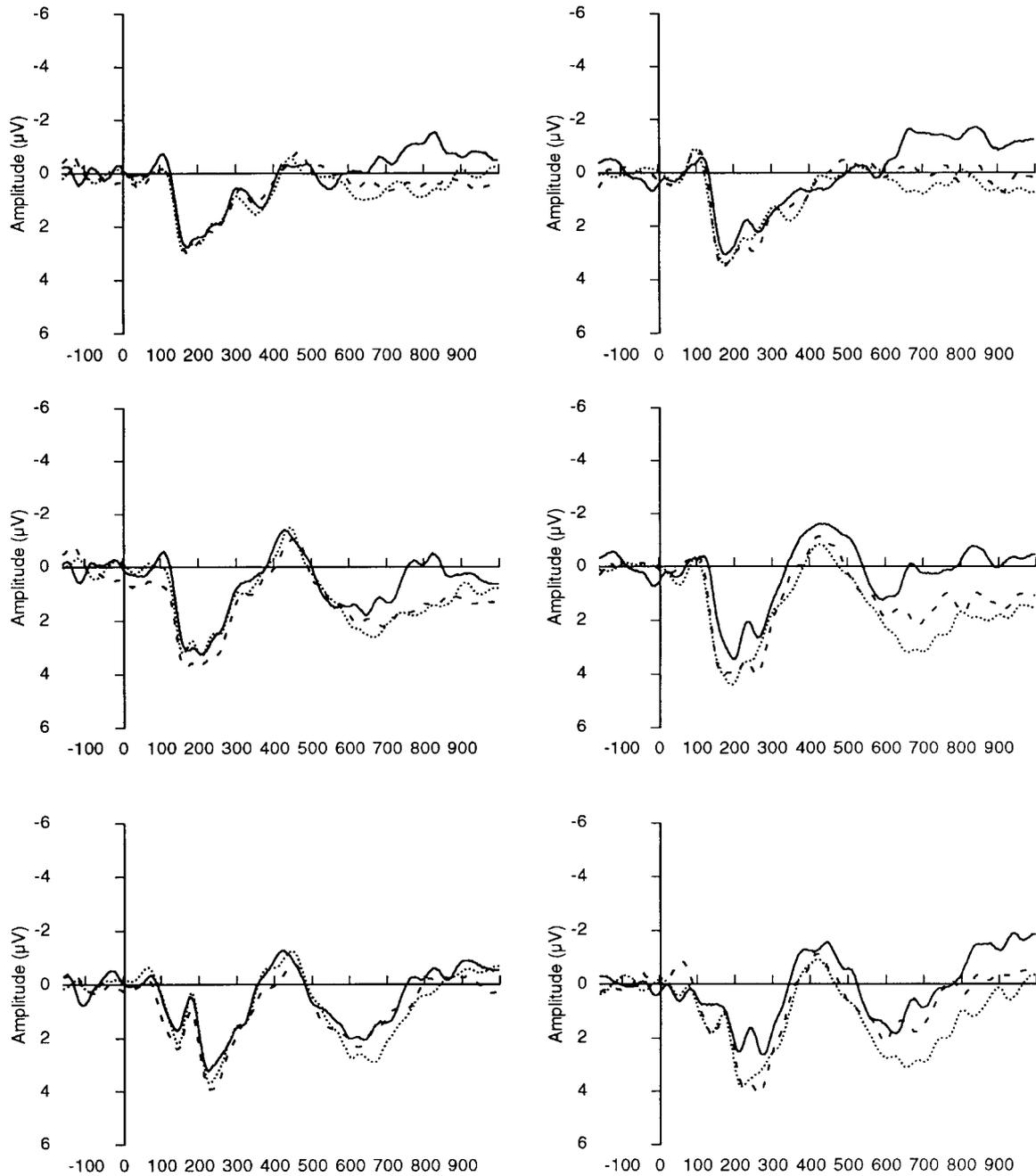


Figure 3. Grand averages formed for correct responses in the recognition task for the nicotine group. Left panels depict abstinence, right panels the nicotine session, upper panel Fz, mid Cz, lower Pz. Solid lines = R-words, dashed = F-words, dotted lines = new words

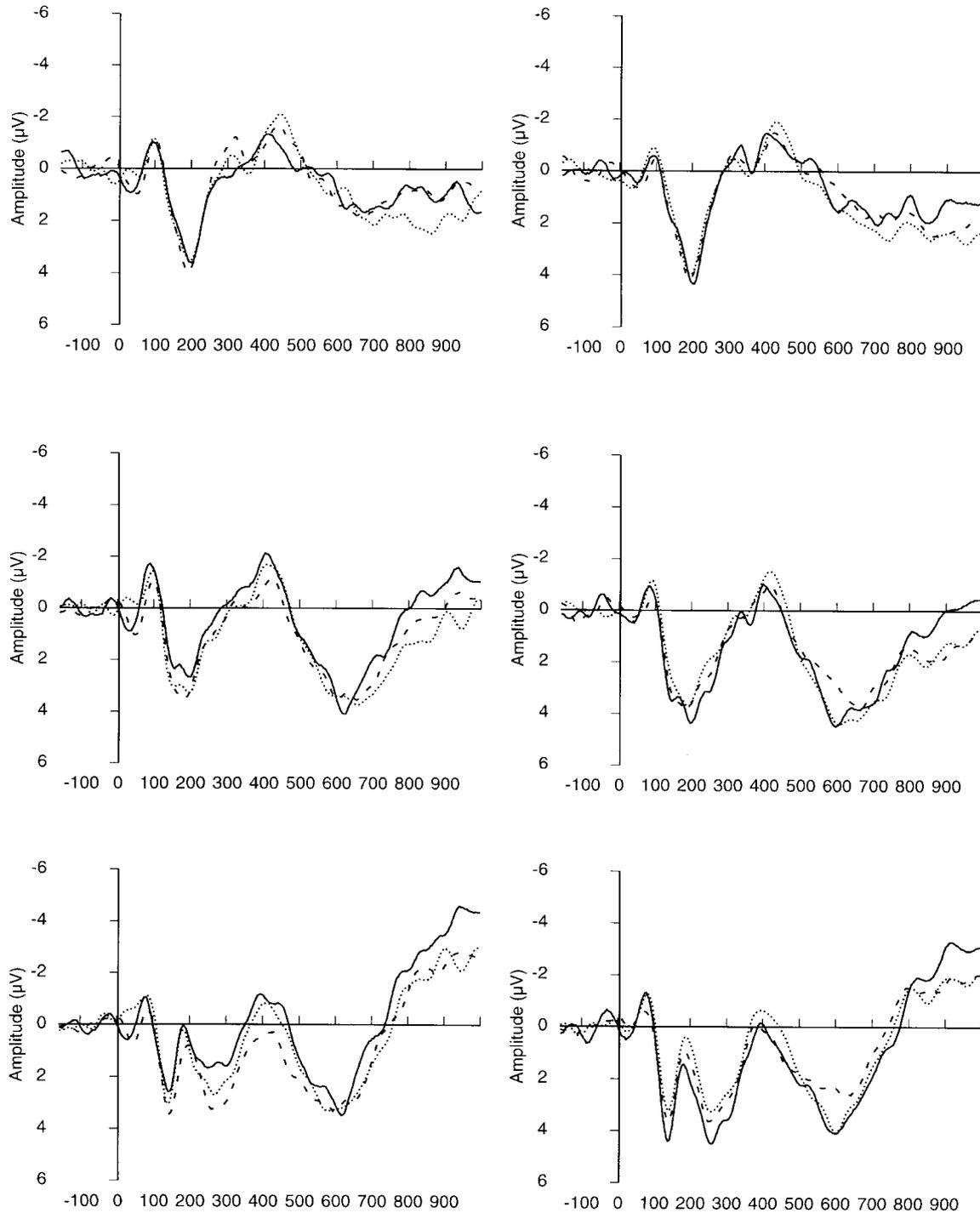


Figure 4. Grand averages formed for correct responses in the recognition task for the control group. Left panels depict pseudo-abstinence session, right panels the pseudo-nicotine session, upper panel Fz, mid Cz, lower Pz. Solid lines = R-words, dashed = F-words, dotted lines = new words

DISCUSSION

The administration of oral snuff improved the discrimination between R-words and new words in the recognition test. The discrimination inherent in the directed forgetting task was not reliably affected. Assuming that a more effective allocation of resources in the study phase would be reflected in an increased d'_{old} , we found no positive support for improved strategic use of cognitive resources. Furthermore, performance after nicotine administration was comparable to that of the control group, indicating that there was no supra-normal improvement of performance.

Event-related potentials in the encoding phase showed no pertinent effects. It is likely that the encoding instruction was insufficient to yield any separation between stimulus classes. Encoding details such as the Dm are also affected by the subject's strategy, e.g. opting for rote rehearsal versus some facilitating organisation of the material (Donchin and Fabiani, 1991). This was not explicitly controlled in the present experiment.

Response time decreased generally after nicotine administration. This is a frequent, if not constant, finding in simple psychomotor task (Sherwood, 1993; Heishman *et al.*, 1994). The present study would seem to have more in common with previous studies of memory scanning, which have frequently employed the Sternberg task. Decreased memory scanning times have been demonstrated (West and Hack, 1991; Sherwood *et al.*, 1991), although not uniformly (Spilich *et al.*, 1992; Foulds *et al.*, 1996).

The task used was difficult and performance fairly low. Wilding and Rugg (1997) reported higher hit-rate than found in the present study, but roughly comparable performance for F-words and new words. They noted that a double encoding classification was necessary to reach a comparatively high discrimination between R- and F-words, whereas a single encoding classification (flower or not?) was used in the present task. The failure to find any pertinent amplitude differences between R- and F-words is probably due to the low discrimination between these categories, as Wilding and Rugg point out in connection with their exclusion task. Furthermore, directed forgetting might give clearer results when used with a recall test, rather than the recognition test chosen in the present study (Golding *et al.*, 1994), although it is quite possible to use the technique with recognition tests.

We expected that previously shown words should elicit larger late positivities in the recognition test, in line with previous findings (Rugg, 1996). In fact, the opposite was found in the nicotine group, as new words elicited the larger positivities, while there was no difference in the control group. In view of the larger proportion of correct responses for new words, it is possible that these have stood out, causing a 'target' effect analogous to the odd-ball P300 (Picton, 1992), which might speculatively have attenuated repetition effects.

When a difficult task such as ours is used, there is always a risk that motivation deficiencies or floor effects affect results. This would mean an increased risk of Type II errors, as results would not reflect subtle changes in performance. Whereas an optimized task certainly should be used in further studies, one must note that performance improvements were found in the nicotine group, thus implicating that our task has been appropriate, though not ideal, to our purpose.

Our design confounds actual nicotine effects with the relief of abstinence. This makes the interpretation of the increased d'_{new} somewhat unclear. However, we tentatively suggest that a relief of abstinence is perhaps the major factor, as performance in the nicotine group after nicotine administration was comparable to the control group.

The possibility of strategic aspects of nicotine use would demand a more systematic mapping of nicotine level, task load and situation to get a satisfactory answer (Perkins, 1995), however, in the present study, the results were not indicative of greater strategic control. Generally, our results instead seem to point towards an alleviation of abstinence, 'normalizing' nicotine users' performance in the relatively easy part of the recognition task, expressed as d'_{new} . The results are in general agreement with earlier findings in our laboratory of nicotine effects on arousal and psycho-motor speed, but not on selective attention (Lindgren *et al.*, 1996, 1998).

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