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Nicotine chewing gum (2 mg, 4 mg) and cigarette smoking: comparative effects upon vigilance and heart rate

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Abstract. Sixteen male smokers, abstinent the morning before testing, were assessed under four conditions: placebo chewing gum, 2 mg nicotine chewing gum, 4 mg nicotine gum, and cigarette smoking. Placebo gum was administered in the cigarette condition, while sham smoking occurred in the gum conditions. Pre-drug administration and post-drug difference scores were calculated for each assessment measure: rapid visual information processing (RVIP), memory for new information, and heart rate. Nicotine raised heart rate in a significant monotonic dose-related manner ($P<0.001$): placebo +0.2; 2 mg gum +5.1; 4 mg gum +9.8; cigarette +17.5 bpm. Rapid visual information processing target detections were also significantly related to dose ($P<0.01$), with this increased vigilance significant under 4 mg nicotine gum and cigarette smoking. Memory task performance was not significantly affected. Self-reported feelings of alertness/energy were higher while smoking than under placebo or 4 mg gum. Complaints about the taste of the 4 mg nicotine gum were frequent.

Key words: Nicotine – Smoking – Psychological performance – Attention – Heart rate

Nicotine has a range of psychological and physiological effects (Mangan and Golding 1983; Wesnes and Warburton 1983a). Heart rate is increased by injected nicotine (Lucchesi et al. 1967; Hopkins et al. 1984), and cigarette smoking (Herxheimer et al. 1967; Woodson et al. 1986), although not by nicotine-free cigarettes (Herxheimer et al. 1967). Central nervous system effects include increased alertness (Knott and Venables 1977; Waller and Levander 1980), improved letter cancellation (Williams 1980), Stroop test (Wesnes and Warburton 1978), and divided attention task performance (Leigh et al. 1977). Withdrawal from smoking leads to impaired vigilance performance (Tarriere and Hartmann 1964), and reduced feelings of concentration (West et al. 1987). In an extensive review, Wesnes and Warburton (1983a) concluded that nicotine can maintain performance on monotonous tasks, increase the speed and accuracy of information processing, and improve aspects of learning and memory when state dependent effects are controlled. One task is particularly sensitive to nicotine: rapid visual information processing (RVIP), (Wesnes and Warburton 1983b, 1984a, b, c). RVIP target detection varies with the nicotine strength of cigarettes (Wesnes and Warburton 1983b, 1984b, c), and nicotine dose in sucked oral tablets (Wesnes and Revell 1984; Wesnes and Warburton 1984a). RVIP was therefore selected as the main performance measure here.

Nicotine chewing gum has been introduced as an aid for smoking cessation (Jarvis et al. 1982; Schneider and Jarvik 1984; West et al. 1984). The rate of success is significantly improved, although many return to smoking or report cigarette craving despite gum use (Jarvis et al. 1982; West et al. 1984). Less nicotine is delivered by the gum than by cigarettes. West et al. (1984) reported plasma nicotine with 2 mg gum to be around 33% of smoking levels. Nemeth-Coslett et al. (1987) found significantly raised plasma nicotine following 8 mg and 4 mg gum, although not after 2 mg gum. Physiologically, significant tachycardia has been demonstrated following nicotine gum (Nyberg et al. 1982; Schneider et al. 1984), but its effects upon psychological performance and subjective mood do not seem to have been investigated. This study was therefore undertaken to investigate the effects of 2 mg and 4 mg gum upon psychological and physiologial functions known to be sensitive to nicotine: vigilance, memory, and heart rate.

Methods

Subjects. Sixteen male smokers (age range 18–26) volunteered for the study. All reported that they smoked 15+cigarettes per day, and inhaled the smoke. Subjects signed informed consent forms, agreed to refrain from smoking each morning before testing, and were paid for participation.

Drug conditions. The four drug conditions comprised: 2 mg nicotine gum, 4 mg nicotine gum, placebo gum, and cigarette smoking. In the smoking condition subjects were given placebo gum. Sham smoking (manipulation of an unlit cigarette) occurred in the gum conditions. The nicotine chewing gum squares (AG LEO, Sweden) were packaged in identical labelled envelopes; gum administration was therefore double blind. The manufacturer's written instructions for gum chewing were given: "Put the gum in your mouth and chew it slowly leaving a few seconds between each chew. Do this for about ten chews then leave the gum under your lip or cheek for a minute or two. Carry on chewing for another ten chews then rest the gum again." In the cigarette

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condition each subject smoked their normal brand of cigarette (Benson and Hedges = 6, Silk Cut = 4, Marlboro = 4, Old Holborn = 2).

The different pharmacokinetic profiles of nicotine delivered through smoke inhalation (rapid), and gum chewing (gradual), necessitated the following procedure. After the pre-test all subjects were administered gum which was chewed for 9 min. In the three gum conditions the chewing then continued for a further 12–13 min. In the smoking condition, the gum was discarded, and a cigarette was lit. After two inhalations the post-test commenced, with further smoke inhalation each minute (or sham smoking). Half-way through the post-test cigarettes were extinguished/discarded, and the final test period (post-test 2, which continued without break from post-test 1), was free from smoking.

Assessment measures. Four assessment measures were given: rapid visual information processing (RVIP), memory for new information, heart rate, and profile of mood state questionnaire (POMS-BI). In RVIP (Wesnes and Warburton 1983b, 1984a, b) a series of single digits were displayed on a VDU at the rate of 100 digits/min. Targets comprised either three consecutive odd digits or three consecutive even digits, with eight targets/min. Following target detection, a single response button was pressed. Target detection, commission error, and response time were automatically calculated (BBC-B computer).

The memory test comprised a shortened presentation of the Ghoneim and Mewaldt (1975) task (Parrott 1986). Each memory list contained 16 words, controlled for word length and frequency of occurrence. The printed list was presented for 30 s. Immediate written recall was then required. Delayed recall was assessed after the interpolated RVIP task. Different lists were used at each test session. Correct recall and commission error were scored.

Heart rate was monitored throughout using a Tunturi meter with an electrode attached to the ear. Readout was recorded each minute, and the average values from 5-min blocks calculated: pre-test (5 min), 0–5 min gum, 5–10 min gum, 10–15 min gum (or during cigarette), 15–20 min gum (or post-cigarette).

Subjective feeling state was assessed using the bipolar version of the Profile of Mood State Questionnaire (POMS-BI), (McNair et al. 1980). Mood areas were covered by 12 feeling state adjectives, each scored on a 0–3 response scale (max score = 36).

Design and procedure. Subjects were assessed under each drug condition, the order of drug administration being determined by a balanced Latin square. As far as possible, subjects were tested at the same time each day between 0930 and 1230 hours. Three 10-min RVIP practice sessions were given before the trial.

The procedure each test day was as follows: word list 1 presented; immediate recall of word list 1; RVIP pre-test (5 min); delayed recall of word list 1; gum administration and chewing for 9 min; light cigarette and discard gum or sham smoke and continue with gum; word list 2 presented; immediate recall of word list 2; RVIP post-test 1 (5 min); cigarette discarded; RVIP continues without interruption as post-test 2 (5 min); delayed recall of word list 2; mood state questionnaire; gum discarded; comments from subjects.

Analysis. Each measure was analysed by latin square analysis of variance (ANOVA; Edwards 1968, p 183). Orthogonal polynomials were calculated to investigate monotonic trends for the dose order: placebo, 2 mg gum, 4 mg gum, cigarette. Duncan's multiple range test was used to compare treatment means.

Results

There were no significant differences between pre-drug conditions for any assessment measure; subsequent analyses were therefore conducted upon pre-test/post-test difference scores. Group mean difference scores are presented in Tables 1 and 2. ANOVA drug effects, linear dose trends, and Duncan multiple range test comparisons are also presented.

Table 1. Pre-post drug difference scores for rapid visual information processing (RVIP); memory immediate recall and delayed recall

Assessment measure		Drug condition				Anova drug effect	Linear dose effect	Duncan multiple comparison					
		Placebo (P)	2 mg Nicotine gum (2)	4 mg Nicotine gum (4)	Cigarette (C)			P/2	P/4	P/C	2/4	2/C	4/C
RVIP target	Post 1	0.8	1.2	0.6	3.7								+
Detection (TOT)	Post 2	−2.2	0.2	1.9	2.2	*	**		*	*			
RVIP response	Post 1	−2	14	29	2	*			*				*
Time (ms)	Post 2	−2	11	22	3								
Memory recall (TOT)													
Immediate		0.0	0.3	−0.4	0.9								
Delayed		0.6	1.6	1.1	1.6								
Memory commission													
Error (TOT)													
Delayed		0.5	1.1	0.4	0.5								
Immediate		0.0	0.0	0.2	−0.1								

Positive scores indicate: more target detections, shorter response time, greater memory recall, less commission errors. *Two-tail*: $^{+}$ $P<0.10$; * $P<0.05$; ** $P<0.01$. *One-tail*: * $P<0.05$; * $P<0.025$; ** $P<0.005$

Table 2. Pre-post drug difference scores for heart rate. Post drug scores for profile of mood state questionnaire (POMS)

Assessment measure	Drug condition				Anova drug effect	Linear dose effect	Duncan multiple comparison					
	Placebo (P)	2 mg Nicotine gum (2)	4 mg Nicotine gum (4)	Cigarette (C)			P/2	P/4	P/C	2/4	2/C	4/C
Heart pre-post (0–5 min)	0.6	3.5	2.9	−0.5	***		*	*			**	**
Rate pre-post (5–10 min)	0.1	4.6	6.3	−0.8	***		**	**			**	**
(BPM) pre-post (10–15 min)	−0.7	3.9	9.5	17.4	***	***	*	**	**	*	**	**
Pre-post (15–20 min)	0.2	5.1	9.8	17.5	***	***	*	**	**	*	**	**
Profile of Mood State (POMS)												
Composed-anxious	21.6	23.1	20.8	23.0								
Energetic-tired	17.6	18.8	15.6	21.0	*				+			**
Agreeable-hostile	23.6	24.5	23.2	24.8								
Elated – depressed	21.1	22.7	20.8	23.3								
Confident – unsure	20.1	21.0	18.7	21.6	*					+		**
Clearheaded – confused	20.2	21.1	19.0	21.8								

Two tail: $^{+}$ $P<0.10$; * $P<0.05$; ** $P<0.01$; *** $P<0.001$. *One tail*: $^{+}$ $P<0.05$; * $P<0.025$; ** $P<0.005$; *** $P<0.0005$
Note: *** Level not calculated for Duncan test

Each ANOVA also generated period (test session) and replication (Latin square row) effects; none of these was significant. Heart rate and RVIP target detection are also presented graphically (Figs. 1, 2).

RVIP target detection pre-test baselines were similar across conditions (23.0–23.5). With pre-test/post-test 1 difference scores, the drug effect was non-significant, but the cigarette/4 mg gum comparison bordered on significance, reflecting comparatively better performance under smoking ($P<0.10$, two-tail; $P<0.05$, one-tail; Table 1). With RVIP target detection pre/post-test 2 difference scores, both ANOVA drug effect and linear dose effect were significant ($P<0.05$, $P<0.01$; Table 1). Compared to pre-drug, target detections were decreased under placebo (−2.2 targets), almost unchanged under 2 mg nicotine gum (+0.2 targets), improved under 4 mg gum (+1.9 targets), and improved to the greatest extent under smoking (+2.2 targets). Target detections under smoking and 4 mg gum were each significantly higher than under placebo (Table 1, Fig. 1). Post-test 1/post-test 2 RVIP target detection differences also showed a significant drug effect ($P<0.05$); this reflected the significant differences between 4 mg gum (where performance improved with further chewing), and placebo (where performance declined: placebo/4 mg gum, $P<0.01$, Dunnet-*t* test), and post-cigarette (where performance also declined: cigarette/4 mg gum, $P<0.10$, two-tail, Dunnet-*t* test).

RVIP commission errors were not significantly affected by any drug condition (Table 1). RVIP response times showed a significant drug effect, with faster times following 4 mg gum, compared to placebo and cigarette smoking ($P<0.05$; Table 1). However, this may be an artefact of the comparatively longer pre-test response times in the 4 mg condition. Group mean pre-test values were: placebo 442 ms; 2 mg gum, 455 ms; 4 mg gum 459 ms; cigarette 442 ms. These pre-test differences were not significant, but may have contributed to the significance of the pre/post difference scores. An analysis of the post-test scores revealed no significant drug effect. On the memory tests there were no significant differences between drug conditions (Table 1).

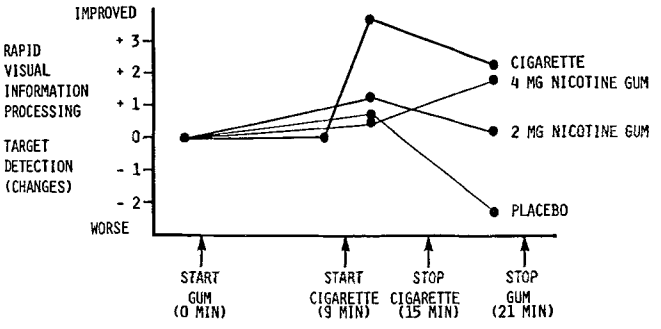

Fig. 1. Rapid visual information processing target detection change under nicotine chewing gum (2 mg, 4 mg) and cigarette smoking

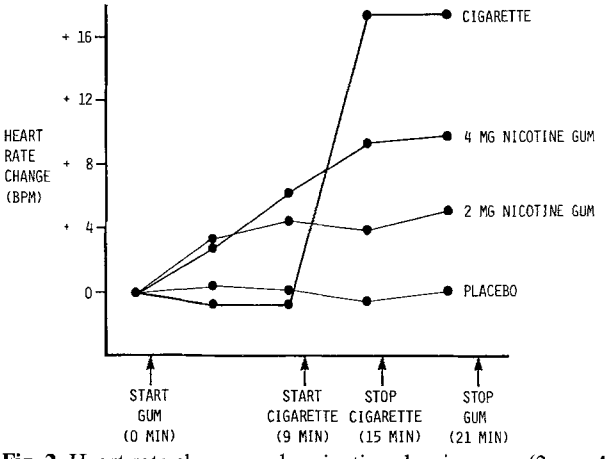

Fig. 2. Heart rate change under nicotine chewing gum (2 mg, 4 mg) and cigarette smoking

Heart rate pre/post difference scores were significant at each post-test, with heart rate increases under all the nicotine conditions (Table 2). Under 2 mg gum, heart rate was significantly raised at each post-test. Under 4 mg gum, values were also raised at each post-test, with the increases

becoming greater following longer periods on the gum; after 10–20 min of chewing, heart rate was significantly higher under 4 mg gum compared to 2 mg gum (Table 2). In the cigarette condition, heart rate was markedly increased ($P<0.01$), and remained significantly elevated for the 5-min period after smoking. Heart rate was significantly higher under smoking compared with each other condition (Table 2, Fig. 2). On the Profile of Mood State questionnaire (POMS-BI), two of the six mood areas produced significant drug effects: energetic-tired, and confident-unsure. The placebo/cigarette comparison for feelings of energy/alertness bordered on significance ($P<0.05$, one-tail), while subjects also felt significantly more energetic and confident in the cigarette condition than under 4 mg gum ($P<0.01$; Table 2). Under 4 mg nicotine gum, subjects disliked its taste: "like mustard", while seven subjects also reported feeling unwell (e.g., nausea, burping, burning sensations).

Discussion

The main findings were the significant dose-dependent effects of nicotine chewing gum and cigarette smoking upon heart rate and vigilance. Increased heart rate has been demonstrated following various forms of nicotine administration (Herxheimer et al. 1967; Lucchesi et al. 1967; Woodson et al. 1986), with the degree of increase closely related to plasma nicotine (Hopkins et al. 1984). In the present study, both doses of nicotine chewing gum led to significantly raised heart rate; 4 mg gum had a significantly greater effect than 2 mg gum, while cigarette smoking produced a significantly greater increase than either dose of gum (Table 2; Fig. 2). Nyberg et al. (1982) reported significant tachycardia with 4 mg gum in non-smokers (+8 bpm; similar to the increase found here). Nemeth-Coslett et al. (1987) reported unchanged heart rate with 2 mg, 4 mg and 8 mg gum, but their subjects were nicotine deprived for only 50 min. Long-term gum use also produces tachycardia (Schneider et al. 1984; West and Russell 1985). The tachycardia while smoking was within the expected range, an increase of 10–20 bpm generally being reported following the first cigarette of the day (Mangan and Golding 1984, p 116); this suggests high compliance to the "no smoking before testing" instruction given here.

Target detections on the RVIP task were improved in a dose-related manner (Fig. 1), with significant improvements under cigarette smoking and 4 mg nicotine gum, and a non-significant improvement under 2 mg gum (Table 1). The effects of nicotine gum upon vigilance have not been previously reported. Previous studies with RVIP have shown significant improvement in target detection with cigarettes (Wesnes and Warburton 1983b, 1984b), and with sucked nicotine tablets in one study (Wesnes and Warburton 1984a), although a non-significant improvement occurred in a second study (Wesnes and Revell 1984). Moreover, target detection decrements under the cholinergic antagonist scopolamine (Wesnes and Revell 1984; Wesnes and Warburton 1984a; Parrott 1986) were counteracted by nicotine (Wesnes and Revell 1984; Wesnes and Warburton 1984a). Target detection was improved to a greater extent following high nicotine cigarettes (Wesnes and Warburton 1983b, 1984c), and high doses of nicotine tablet (Wesnes and Warburton 1984a). The present findings therefore not only demonstrated significant vigilance improvements under cigarette smoking/4 mg gum, they also confirmed the sensitivity of the RVIP task to nicotine dose (Fig. 1). Improved vigilance has also been found with other attentional tasks under nicotine: letter cancellation (Williams 1980), divided attention (Leigh et al. 1977), and the Stroop task (Wesnes and Warburton 1978).

The pattern of RVIP target detection over time was interesting. During the first 5 min there was little difference between placebo and the two gum conditions, although smoking performance was comparatively higher. During the second 5-min period, placebo performance deteriorated, 2 mg nicotine gum performance remained unchanged, while 4 mg gum performance improved. In the immediate post-smoking period, target detections remainded elevated, but at a rate lower than that found during smoking (Fig. 1). The effects of nicotine upon vigilance were therefore most evident during the latter part of testing; a pattern of performance which has been previously reported (Wesnes and Warburton 1983b, 1984b). Furthermore, performance levels under nicotine were higher than pre-drug levels (Fig. 1); thus nicotine not only prevents a decline in vigilance, but tends to improve performance, at least in nicotine deprived subjects (Wesnes and Warburton 1983b, 1984b).

RVIP task response times under smoking/nicotine have been improved in some studies (Wesnes and Warburton 1983b, 1984b), but not others (Wesnes and Revell 1984; Wesnes and Warburton 1984a). Response time changes in the present study were complicated by the appreciable differences in pre-drug values between drug conditions (see Results), and must be treated with caution. Commission errors did not differ significantly between drug conditions (Table 1), therefore the improved RVIP target detection performance did not reflect a general increase in responsiveness. Previous studies have similarly demonstrated RVIP commission error to be unaffected by nicotine (Wesnes and Warburton 1983b, 1984a, b, c).

Memory task performance was not significantly affected by nicotine (Table 1). The task used was a brief version of one with demonstrated sensitivity to scopolamine (Ghoneim and Mewaldt 1975; Parrott 1986), and this shortened version may be comparatively less sensitive. However, the literature on nicotine and memory displays considerable variation, with increments, decrements, and unchanged performance each reported (see reviews in: Mangan and Golding 1983; Wesnes and Warburton 1983a). Performance is affected by numerous factors: the aspect of memory (acquisition or consolidation), stimulus material, nicotine/cigarette strength (with biphasic dose dependency), duration of deprivation, and the nicotine state during presentation and recall (state dependency).

Subjective feelings of alertness/energy were higher under cigarette smoking compared to placebo ($P<0.05$, one-tail). No other placebo/drug differences approached significance. Self-reported alertness and confidence were also significantly higher under cigarette compared to 4 mg nicotine gum (Table 2). The low feeling state values in the 4 mg gum condition may have been influenced by the gum's unpleasant taste. The pleasurable effects of the first cigarette of the day are well recognised (Jones et al. 1978). Similarly, the increased feelings of alertness/energy while smoking agree with the increased arousal reported elsewhere (Knott and Venables 1977; Waller and Levander 1980).

In conclusion, with both heart rate and vigilance, the peak effects of 4 mg gum were around 50% of cigarette levels, while peak effects of 2 mg gum were about half those

found with 4 mg gum. These findings broadly agree with the data on plasma levels following nicotine gum (West et al. 1984; Nemeth-Coslett et al. 1987). People entering smoking cessation programs should be warned to expect that vigilance/concentration abilities will probably be reduced when they cease smoking (Tarriere and Hartmann 1964; West et al. 1987). They should also be counselled that nicotine gum will probably aid their concentration/attention, although not to the extent that may have occurred with cigarettes.

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