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Effects of Cigarette Smoking on Resting EEG, Visual Evoked Potentials and Photic Driving

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GOLDING, J. F. *Effects of cigarette smoking on resting EEG, visual evoked potentials and photic driving.* PHARMACOL BIOCHEM BEHAV **29**(1) 23–32, 1988.—The effects of smoking a cigarette (1.3 mg nicotine delivery) versus sham smoking were studied using EEG, visual evoked potentials (VEP), photic driving (PD) and heart rate (HR) in thirty young healthy male and female habitual cigarette smokers. Heart rate (HR) and exhaled carbon monoxide (CO) level were significantly increased by real as opposed to sham smoking. Real versus sham smoking significantly increased relative power in the beta bands, reduced alpha and theta activity to a small but significant extent, but had no effect on delta activity. Dominant EEG alpha frequency was significantly increased by real as opposed to sham smoking. Smoking produced no significant mean change in PD or VEP. However, correlational analysis indicated that variables such as basal CO level, residual butt filter nicotine, basal electrocortical response level and personality, predicted to varying degrees the magnitude and direction of the effect of smoking on VEP, PD and EEG.

EEG Evoked potentials Photic driving Heart rate Carbon monoxide Nicotine Smoking Tobacco Addiction Withdrawal Arousal modulation Psychological tool Stimulus filter Personality

CIGARETTE smoking has been shown to produce a variety of effects on electrocortical activity. Thus both increased and decreased tonic activity or response has been observed on EEG [11, 23, 27, 28, 33, 36, 44, 47, 52, 58] and for evoked potentials [8, 9, 16, 18, 19, 26, 37, 39, 40, 57, 59, 61, 64]. Although many of these reports appear contradictory at first sight, there is evidence in animals and humans that nicotine, the postulated primary reinforcer for the smoking habit [42,49], has both stimulant and depressant effects. Moreover, the effects of nicotine appear to be dependent on dosage, with stimulant effects predominating at low doses and depressant effects at higher doses [3, 8, 25]. Additionally, individual differences in personality [9, 11, 16, 45] together with situational factors such as induced stress [23] are important intervening variables determing the effects of cigarette smoking on electrocortical activity. These latter factors may both indirectly reflect variation in sensitivity of the CNS to a given dose of nicotine, and also may be critical in determining the vigour with which the cigarette is smoked, degree of inhalation and consequently the dose of nicotine absorbed [5,42]. The importance of such factors is not unique to cigarette smoking but has also been observed to be important in determining the direction of effects of another smoked substance, cannabis [7].

The purpose of the present study was twofold: first, to examine the effects of smoking on a variety of electrocortical measures in habitual smokers, previous investigations having concentrated separately on either the phasic or the tonic aspects of electrocortical activity. With regard to the latter, little systematic data is available on the effects of smoking on EEG bands apart from the alpha band as has been noted [29]. In addition, for both EEG and evoked potential measures, many of the previous studies have utilised relatively long periods of tobacco deprivation, and a question arises as to whether such findings can be generalised to more naturalistic periods of smoking deprivation [5, 23, 42]. The second objective was to examine the relative importance of factors such as personality, pre-smoking electrocortical activity levels, vigour of cigarette smoking and habitual daily cigarette consumption in determining the outcome of smoking, previous studies having concentrated only on one or other of these variables.

METHOD

Smoking Materials, Butt Nicotine and Carbon Monoxide (CO)

Filter-tipped experimental cigarettes (unventilated) were of 1.3 mg nicotine, 14 mg tar, 12 mg carbon monoxide (CO) delivery as assessed by standard machine smoking. Butt filtration efficiency (nicotine) was 37% and tar/nicotine ratios were similar to equivalent popular brands of cigarettes.

For butt analysis, each filter tip was dissected from the residual cigarette butt prior to nicotine assay (BAT Group Research and Development Laboratories). Nicotine delivery (mouth) was calculated from butt nicotine and filtration efficiency using the standard formula [51].

Exhaled carbon monoxide (CO) levels were measured using a Grubb Parsons model IRGA20 non-dispersive infrared (IR) gas analyser set to the appropriate wavelength and

TABLE 1

MEAN CHANGES (POST-PRE) REAL VS. SHAM SMOKING, WITH CONFIDENCE INTERVALS AND *t*-TESTS (n=15 SUBJECTS IN EACH GROUP)

Variable	Smoking Group	Mean Change (Post-Pre) Smoking	95% Confidence Interval	Unpaired *t*-Test of Real vs. Sham 2-Tailed *t*	*p*
carbon monoxide	real	+ 9.3	6.3 to 12.3	6.7	0.0001
(p.p.m.)	sham	− 0.2	−0.7 to 0.3		
heart rate	real	+11.4	6.4 to 16.4	5.2	0.0001
(beats per min)	sham	− 1.3	− 2.6 to 0.0		
photic driving 16 Hz	real	+ 0.002	− 0.23 to 0.23	0.9	ns
(log (μV × μV/Hz))	sham	− 0.111	− 0.28 to 0.06		
photic driving 26 Hz	real	+ 0.136	− 0.01 to 0.28	1.9	ns
(log (μV × μV/Hz))	sham	− 0.101	− 0.33 to 0.13		
photic driving balance	real	+ 0.128	− 0.08 to 0.33	0.1	ns
(ratio)	sham	+ 0.109	− 0.15 to 0.37		
VEP N65	real	− 0.9	− 3.3 to 1.6	0.8	ns
(μV)	sham	+ 0.6	− 2.2 to 3.4		
VEP N65P100	real	+ 1.5	− 3.9 to 7.0	1.0	ns
(μV)	sham	− 1.5	− 5.5 to 2.5		
VEP P100N130	real	+ 2.9	− 1.5 to 7.4	1.8	ns
(μV)	sham	− 1.4	− 4.3 to 1.5		
VEP N130P200	real	+ 5.5	1.2 to 9.9	1.0	ns
(μV)	sham	+ 2.6	− 2.1 to 7.3		
alpha frequency	real	+ 0.60	0.33 to 0.87	4.0	0.0001
(Hz)	sham	− 0.03	− 0.25 to 0.18		
delta, eyes closed	real	− 2.6	− 8.6 to 3.5	0.4	ns
(rel. power %)	sham	− 1.2	− 5.3 to 2.8		
delta, eyes open	real	− 4.5	−12.5 to 3.5	0.3	ns
(rel. power %)	sham	− 5.9	−11.5 to −0.4		
theta, eyes closed	real	− 1.7	− 3.4 to 0.0	2.2	0.05
(rel. power %)	sham	+ 0.4	− 0.8 to 1.5		
theta, eyes open	real	− 0.7	− 2.4 to 0.9	0.8	ns
(rel. power %)	sham	+ 0.1	− 1.5 to 1.7		
alpha, eyes closed	real	− 1.9	− 7.2 to 3.3	1.4	ns
(rel. power %)	sham	+ 2.5	− 1.7 to 6.6		
alpha, (eyes open)	real	− 6.4	−13.4 to 0.6	3.7	0.001
(rel. power %)	sham	+ 7.4	3.6 to 11.2		
beta 1, eyes closed	real	+ 2.2	0.2 to 4.2	2.6	0.05
(rel. power %)	sham	− 0.8	− 2.1 to 0.6		
beta 1, eyes open	real	+ 5.1	2.8 to 7.4	3.0	0.01
(rel. power %)	sham	+ 0.0	− 2.8 to 2.8		
beta 2, eyes closed	real	+ 4.0	0.9 to 7.1	2.8	0.01
(rel. power %)	sham	− 0.8	− 2.9 to 1.3		
beta 2, eyes open	real	+ 6.5	2.3 to 10.7	3.2	0.01
(rel. power %)	sham	− 1.6	− 5.0 to 1.8		

Note: *t*-test df=28; numbers are rounded; see text for details of variables.

sensitivity ranges. The IR gas analyser was left in 'stand-by' mode between experiments to eliminate drift and physically located in a room separate to those used for EEG equipment and subjects. Calibration gas was 145 ppm CO in dry nitrogen (Air Products), calibrations being carried out before, and rechecked after each experiment. Additional filters were fitted to the gas analyser to suppress any possible artefacts from carbon dioxide, water vapour and (although not applicable to the present subject sample) exhaled Ketones and alcohols. External filters consisted of quartz wool plugged U tubes filled with sodium hydroxide (20 g self-indicating 'Carbasorb', 10–16 mesh, BDH Chemicals), activated carbon (20 g of MF3) and finally two 'Cambridge Filter' pads. Filter constituents were renewed according to the method of Reynard [53] at intervals judged by visual inspection (Carbasorb, Cambridge Filters) and after every 7 samples (activated carbon). A theoretical correction factor of 0.87 to allow for carbon dioxide and water vapour removal can be applied to all sample gas CO values, based on (resting) normative data for partial pressures of these gases in expired alveolar air. However, since the literature concerning CO and smoking is not unanimous, and is more commonly silent concerning this point, uncorrected figures are given. Exhaled CO (ppm) relates linearly to blood COHb (%) with

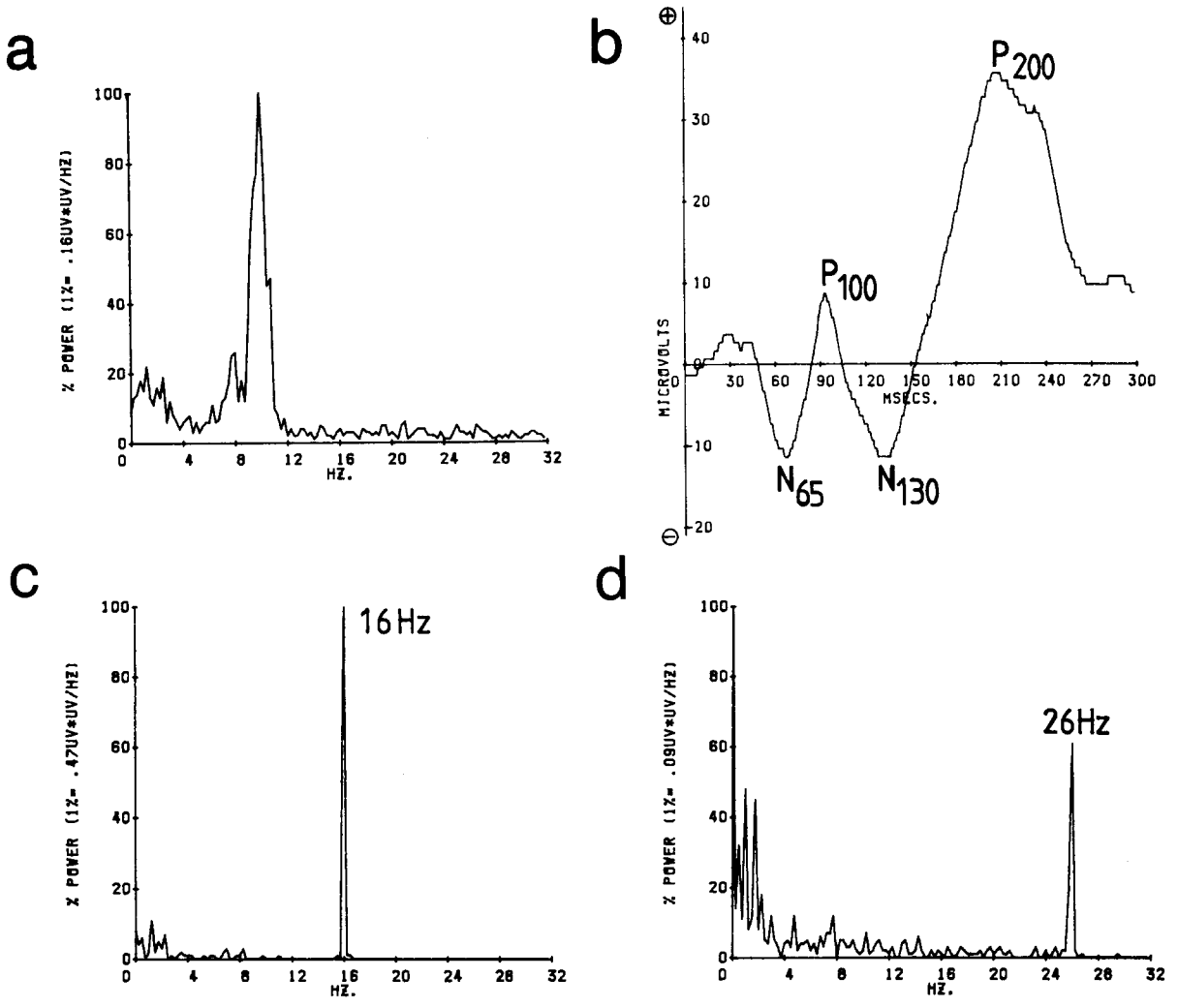

FIG. 1. Specimen traces of: (a) Spectral analysis of EEG with power scaling factor on ordinate; (b) Visual (flash) evoked potential with main components labelled, positive up; (c) Spectral analysis of EEG during photic stimulation at 16 Hz with driving response labelled; (d) Spectral analysis of EEG during photic stimulation at 26 Hz with driving response labelled. See text for details.

correlations around r=0.98 [34].

After breath holding for 20 seconds, to allow alveolar gas equilibration with blood (subjects held their nostrils closed throughout), subjects exhaled through a 3-way valve; successively into 350 ml and 1 litre bags (CO impermeable metathene plastic). The first upper respiratory tract sample was discarded and the second end-tidal air sample was used for CO analysis.

The measures of smoking used here had the advantage of being non-invasive. It can be argued that measurement of blood nicotine levels has the advantage of being more 'direct.' The disadvantage of such an invasive method is the potential stress involved for the subject, unless cannulation is repeated over several sessions to habituate the subjects to the procedure. Such an effect (stress) may distort results, since stress is know to alter smoking behaviour and CNS response to smoking [23, 41, 49]. In the present experiment, non-invasive measures were chosen, although it is not implied that invasive methods do not also have other advantages.

Recording and Stimulation Equipment

Resting EEG, photic driving (PD) response and visual evoked potentials (VEP) were recorded from Ag/AgCl electrodes (SLE) in contact with hypertonic saline jelly (interelectrode impedance with respect to ground less than 2 kohm after skin scarification). Bipolar electrode positions were midway between C_z–O_z (10–20 system; [35]) with reference to linked mastoids, ground electrode was on forehead midhairline. Signals were amplified and recorded by a Biodata System (time constant=0.2 sec, high frequency cut open except for EEG/PD where a 30 Hz lower band-pass was utilized to prevent aliasing from higher frequency EEG components in spectral analysis [12]). Raw EEG was continuously monitored on oscilloscope. This was used to monitor compliance with instructions to subjects concerning movement artefacts, similar to the procedure employed by Woodson *et al.* [64].

A/D conversion rate was 1 kHz for VEP and 64.1 Hz for EEG. Averaged VEPs were displayed online and together with VEP, EEG, and PD data were stored on magnetic disk

for further offline analysis (Biodata software for VEP and fast Fourier analysis). Photic (flash) stimuli were presented from a Xe flash tube (SLE model PS100, 100 μsec pulse, 0.23 Joule) situated 5 ft from the subject's head. Responses to 30 flash stimuli (2 second inter-stimulus interval) were averaged for VEP, the last 8 seconds of EEG during two 10-second periods of flash stimulation at 16 Hz and at 26 Hz were utilised for spectral analysis of PD response. Two 32 sec samples with eyes open and closed were used for spectral analysis of the resting EEG.

ECG was continuously recorded from disposable self-adhesive electrodes in contact with hypertonic saline jelly on the chest and right clavicle, amplified output was recorded on moving paper chart-recorder.

Subjects

Young healthy male (n=16) and female (n=14) volunteers (mean age 23.6±3.9 years) who were habitual cigarette smokers (16.8±6.9 cigs/day) were allocated to real smoking (1.3 mg nicotine cigarette) or sham smoking (0 mg nicotine cigarette) groups; sex ratio and average daily cigarette consumption were balanced between groups. Each subject attended the laboratory on 2 occasions. The first session enabled familiarisation to the laboratory environment, including photic stimulation. Subjects were given cigarettes of the brand used in the experiment to familiarize them with smoking this brand in the intervening days, and requested to practise inhaling all the smoke that they puffed, i.e., to regulate their smoke intake by puffing rather than regulating intake by (not) inhaling. The second (recording) session was a few days later. Subjects completed an Eysenck Personality Questionnaire [17] at home, which was returned at the second session. Subjects were asked to desist from alcohol for 24 hours prior to experiment and tea, coffee and cigarettes for one hour prior to experiment. All subjects subsequently stated that they had complied with the instructions.

In the second session, subjects were seated in a comfortable upright chair in a well-lit, temperature-controlled room (21°C). Communication was by intercom and observation by a one-way window. Resting EEG (with eyes closed and eyes open fixating a dot); photic driving (PD) response to high and low frequency stimuli (order of presentation randomised between subjects) and visual evoked potentials (VEP) were recorded. CO levels were taken before and after smoking a 1.3 mg nicotine cigarette or sham smoking. Subjects were requested to inhale the smoke that they puffed and this was visually checked. Electrocortical measures were repeated immediately following smoking. Standard payment was made to subjects for expenses and travel.

Data Analysis

EEG power was analysed in the following bands: delta (1–3.5 Hz), theta (4–7 Hz), alpha (8–13 Hz), beta1 (15–22 Hz), beta2 (23–31 Hz). Raw EEG power in these bands ($\mu V \times \mu V/Hz$) was converted to relative power (% of total power 1–31 Hz) [30,32]. Dominant alpha frequency was scored as the frequency of peak power in the 8–13 Hz band. Only the data with eyes closed was utilised, since with the eyes open, as a consequence of the alpha-blocking response, insufficient alpha activity was present to reliably identify dominant frequency across all subjects. Raw PD response ($\mu V \times \mu V/Hz$) was measured using 3 analysis widths; power at exact photic driving frequency 'point' frequency, and powers in the bands ±0.5 Hz and ±1.0 Hz centred on the photic driving frequency. Examination of the intercorrelations between these three PD analysis widths (minimum intercorrelation r=0.99) and re-examination of the hard-copy spectral analyses indicated that the ±0.5 Hz analysis width for photic driving was most reliable. This decision was based on the observation that the ±1 Hz analysis width appeared to be too wide for the extremely sharp driving response—picking up extraneous background beta activitiy, whereas the choice of exact 'point' photic driving frequency under-represented the amplitude of the driving response in a few cases where the observed peak was just off the 'point' frequency. Individual variation in raw photic driving power was considerable, and to avoid problems of non-normality a log transformation was utilised [60]; other authors have advocated a slight variant, the square root transformation [48] but this appeared to have no additional advantage. VEP components were identified as a sequence of positive and negative deflections as described by Ashton *et al.* [7] and Cooper *et al.* [12]. Peak latencies were measured from stimulus onset to peak maximum or minimum (trough) and were labelled as follows (with attached means±SD): N65 (62.9±10.8), P100 (101.7±11.9), N130 (132.0±16.9), P200 (193.1±18.1) (msec). This sequence corresponds to components III, IV, V and VI described by Creutzfeldt and Kuhnt [14]. Amplitudes of components were scored in μV from peak or trough to successive trough or peak. The amplitude of N65 was taken from the zero μV baseline.

Heart rate was scored in beats per minute (bpm) for 5 minute periods preceding and immediately following cigarette smoking or sham smoking. A one minute (maximum HR) period following smoking was also analysed but provided no further insights.

RESULTS

Results were analysed using ANOVA for repeated measures (BMDP2V method), where 'Group' refers to the real and sham smoking groups of subjects and 'Time' refers to pre- versus post-smoking. Significant mean effects of smoking were revealed by time × group interactions. SDs are attached to mean values where given in text. In addition, Table 1 details change (POST-PRE) real and sham smoking groups, with 95% confidence intervals and *t*-tests of 2-tailed significance of differences between groups.

Smoking Measures

Mean baseline CO (9.2±8.9 ppm), time since last cigarette (3.3±2.9 hr), number of cigarettes smoked prior to experiment since waking (3.3±3.1 cigs) and average daily cigarette consumption (16.8±6.9 cigs/day) were not significantly different between real versus sham groups. The time since last cigarette represented ad lib smoking until one hour prior to experimentation. Systematic intercorrelations between these measures in the range r=.49 to r=.77 were consistent with previous reports [62]. The correlations indicated that baseline CO level was monitoring smoking prior to experimentation; and that extent and recency of prior smoking was strongly related to the subjects' habitual cigarette consumption rate. The magnitude of these correlations was similar for real and sham groups.

Real smoking produced a mean rise in exhaled CO of 9.3±5.0 ppm whereas sham smoking produced virtually no change, a small decrease of −0.2±0.9 ppm which was within the measurement accuracy of the equipment. This CO rise following real smoking was highly significant by ANOVA, as revealed by the time × group interaction, F(1,28)=45.5,

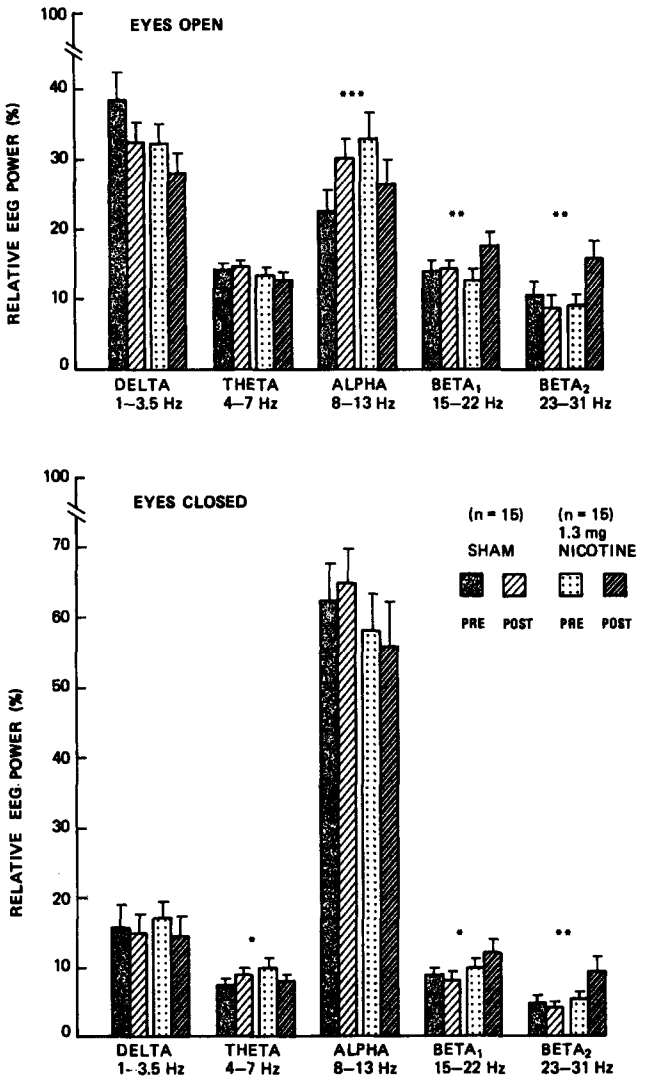

FIG. 2. Relative EEG power [(band power/total power) × 100%] with (top) eyes open and (bottom) eyes closed. pre- and post-smoking a real (1.3 mg nicotine) or sham (0 mg nicotine) cigarette. S.E. bars are shown and significant effects of real versus sham smoking marked with asterisks (significant time × group ANOVA interactions). *$p<0.05$; **$p<0.01$; ***$p<0.001$ ($df=1,28$).

$p<0.0001$, significant effects also occurred for group, $F(1,28)=6.9$, $p<0.05$, time, $F(1,28)=41.7$, $p<0.0001$.

For the real smoking group, mean whole butt length was 29.3±4.6 mm. Mean butt filter nicotine was 0.81±0.24 mg, equivalent to a (mouth) delivery of 1.38±0.41 mg. This value was very similar to that predicted by standard machine smoking (1.3 mg) and indicated that subjects were not over- or under-smoking cigarettes away from the general population 'norm' in any systematic fashion. The SDs indicated that individual differences in smoking vigour occurred, as has been generally observed inside and outside the laboratory [55]. Butt filter nicotine, length of tobacco rod burnt and rise in exhaled CO level positively intercorrelated (in the range r=.39 to r=.64), suggesting that these measures were monitoring some common variance in the vigour of smoking the experimental cigarette.

Heart Rate

Real but not sham smoking significantly elevated heart rate from baseline (76.2±10.87 bpm) by a mean of 11.4±9.1 bpm, a small mean drop (−1.3±2.3 bpm) occurring after sham smoking. ANOVA revealed highly significant effects for time × group, $F(1,28)=27.3$, $p<0.0001$, for time, $F(1,28)=17.4$, $p<0.0001$, and group, $F(1,28)=5.34$, $p<0.05$. Smoking-induced heart rate elevation has been reported before [46], is almost exclusively due to nicotine [31] and is initially due to nicotine action directly on heart and on CNS, although later circulating hormone changes may sustain the effect [15].

EEG

Mean dominant alpha frequency (10.08±0.90 Hz) with eyes closed was increased by real smoking (0.60±0.48 Hz) but was virtually unchanged by sham smoking (−0.03±0.39 Hz). Due to the high reliability of alpha frequency as an EEG measure, this small frequency shift was highly significant as revealed by the time × group interaction for ANOVA, $F(1,28)=15.79$, $p<0.001$; significant effects also occurred for time, $F(1,28)=12.64$, $p<0.001$, but not for group. Alpha frequency with eyes open was not analysed because of alpha-blocking (see Data Analysis).

Relative powers in the EEG bands are illustrated in Fig. 2, together with time × group interactions indicating smoking effects.

Relative power in the delta band revealed no significant effects of smoking. All time × group, time and group effects were non-significant with the exception of a time-related decrease in delta with eyes open which occurred in both real and sham smoking groups, $F(1,28)=5.28$, $p<0.05$.

Real but not sham smoking produced a small decrease in theta with eyes closed as revealed by time × group interaction, $F(1,28)=4.65$, $p<0.05$. All other effects and interactions were non-significant.

Mean activity in the alpha band revealed only one significant result, a decrease in alpha following real smoking versus an increase following sham smoking with eyes open [time × group interaction, $F(1,28)=13.7$, $p<0.001$]. A similar effect occurred with eyes closed but failed significance.

The beta bands produced a series of significant results. Significant time × group interactions occurred with eyes closed for beta1, $F(1,28)=6.8$, $p<0.05$, and beta2, $F(1,28)=7.6$, $p<0.01$, and with eyes open for beta1, $F(1,28)=9.0$, $p<0.01$, and beta2, $F(1,28)=10.4$, $p<0.01$. Effects of time were significant only with eyes open, for beta1, $F(1,28)=9.3$, $p<0.01$, all other effects were non-significant.

Visual Evoked Potentials (VEP)

Mean VEP amplitudes were as follows: N65 (from zero) 8.4±6.9 μV; N65P100 22.8±11.3 μV; P100N130 15.1±10.9 μV; N130P200 29.8±15.1 μV. Mean latencies have been detailed earlier (cf. Data Analysis). Anova revealed no significant effects of smoking on VEP amplitudes or latencies.

Photic Driving (PD)

Photic driving at 16 Hz (1.28±0.39 log 10 μV × μV/Hz) was more efficient than at 26 Hz (0.80±0.47 log 10 μV × μV/Hz) [paired $t(29)=5.97$, 2-tailed $p<0.0001$]. Photic driving has commonly been observed to be less efficient at higher frequencies [48]. Effects of smoking on mean photic driving response were non-significant for both 16 Hz and 26 Hz.

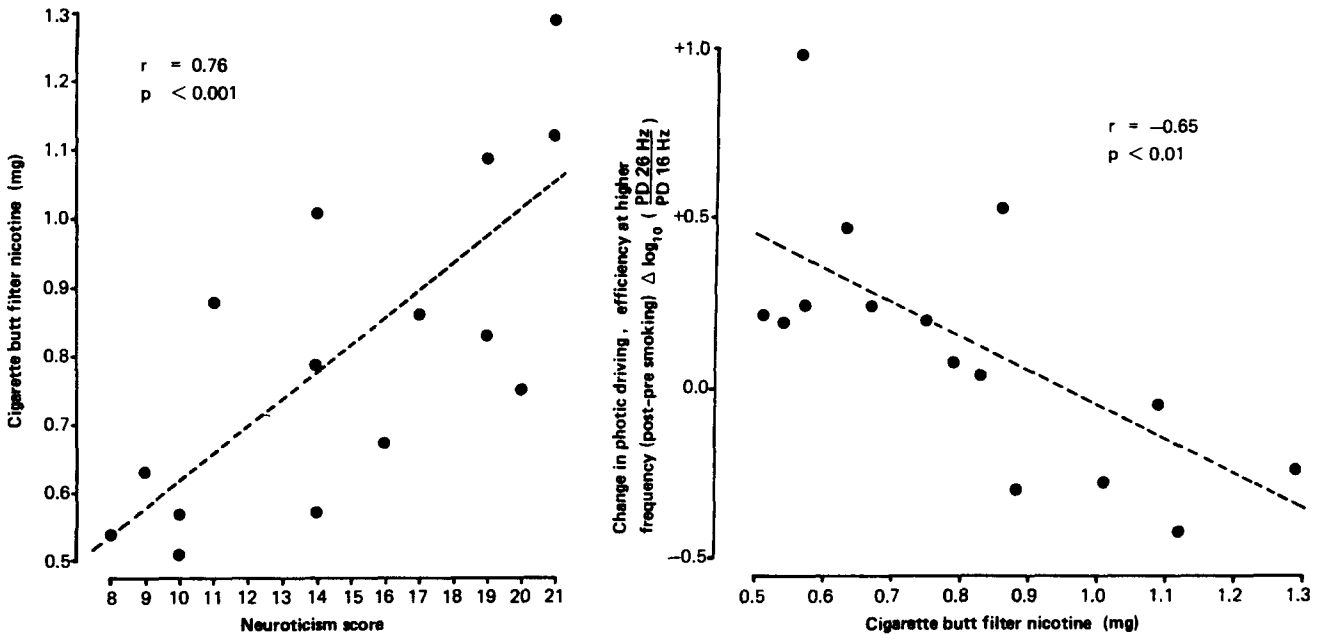

FIG. 3. (Left) Relationship between neuroticism personality score (Eysenck Personality Questionnaire) and cigarette butt filter nicotine. Note that the more neurotic individuals extracted greater nicotine deliveries from the cigarette (nicotine delivered = butt filter nicotine × 1.703 mg). (Right) Relationship between butt filter nicotine and post-pre-smoking change in photic driving (PD) balance, where positive change indicates relatively greater PD at higher frequency (increased 'lability' following smoking) and negative change indicates relatively greater PD at lower frequency (increased 'stability' following smoking). Note that changes in the direction of increased 'stability' are associated with greater nicotine delivery and vice versa (nicotine delivered = butt filter nicotine × 1.703 mg). Dotted lines represent fitted linear regression lines.

Inter-Subject Variation in Effects of Cigarette Smoking

The effects of smoking were analysed from two perspectives: first, prediction of the magnitude of effect where significant effects occurred for real versus sham smoking as revealed by ANOVA; second, elucidation of predictions of direction and magnitude of change where no significant mean smoking effect was revealed by ANOVA. The latter analysis was most important as regards VEP and PD and was justified by the observation that nicotine can produce mixed stimulant and depressant effects as a function of dosage, personality, situation, and task or stimulus variation (see Introduction). For brevity, only a selection of the major results are presented. Degrees of freedom are $df=13$ (n=15) associated with (r) correlation coefficient, probabilities are 2-tailed in all cases.

Heart Rate (HR) Rise Predictors

Greater smoking-induced HR elevation was associated with lower basal CO levels ($r=-0.50$, $p<0.10$) and lower basal HR ($r=-0.59$, $p<0.05$). This result implied that prior exposure to cigarettes (e.g., as monitored by basal CO level), reduced HR elevation from smoking; an interpretation consistent with nicotine tachyphylaxis [54]. The limiting role of higher basal HR might be viewed as a 'ceiling-effect.' However, such an effect may have been secondary to the fact that basal HR correlated significantly with basal CO level ($r=0.51$, $p<0.10$) and so indirectly monitored smoking prior to experimentation. Neither rise in CO following smoking or butt nicotine predicted magnitude of smoking-induced HR elevation. Thus nicotine tachyphylaxis rather than particular nicotine dosage over the range reported here would appear to have been the (limiting) variable of major importance as regards smoking-induced HR elevation.

EEG Band Change Predictors

The major finding was that greater degree of prior exposure to cigarettes limited smoking-induced increases in beta band activity. The correlations between basal CO level and smoking-induced rise in beta activity varied between $r=-0.44$ ($p<0.10$) for beta1 with eyes closed to $r=-0.69$ ($p<0.01$) for beta2 with eyes open. Rise in CO following smoking and butt nicotine were not predictive. There was an indication that high psychoticism (P) scores (Eysenck Personality Questionnaire) predicted less smoking-induced increases in the beta bands, the correlation achieving $r=-0.62$ ($p<0.05$) for beta2 with eyes open. This correlation was independent of basal CO levels. It may be relevant that individuals with high P scores are postulated to be cortically less arousable [21].

An important negative finding emerged: the small smoking-induced mean reductions in the alpha and theta bands were not convincingly predictable from nicotine delivered (or CO rise) or from such variables as prior smoking and average daily cigarette consumption.

Visual Evoked Potentials (VEP) and Photic Driving (PD) Change Predictors

By contrast with the predictors of smoking-induced changes in tonic EEG, the amount of nicotine delivered rather than degree of smoking prior to the experiment (monitored by basal CO levels) predicted changes in VEP and PD following smoking. For VEP, greater nicotine delivery was associated with increases in amplitude following smoking, e.g., for P100N130 post-pre-smoking change ($r=0.47$, $p<0.10$) and for N130P200 post-pre-smoking change ($r=0.48$, $p<0.10$). The situation was more complicated for PD. At the lower PD frequency of 16 Hz, the correlation between (post-pre-smoking) change in PD and nicotine de-

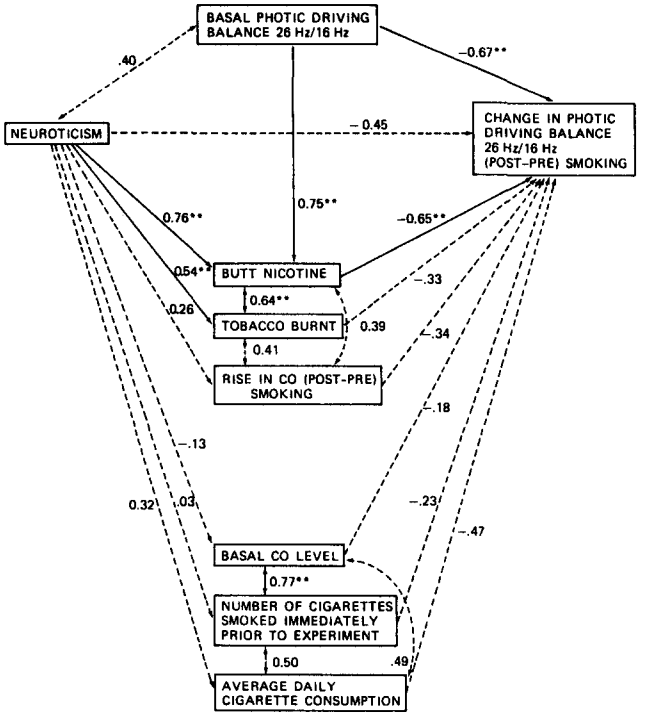

FIG. 4. Main relationships involved in predicting change in PD balance following smoking. Solid line indicates a significant relationship at 2-tailed $p<0.05$ (*) or $p<0.01$ (**), $df=13$.

livery was similar to that for VEP (r=0.45, $p<0.10$). However, this relationship reversed for PD at 26 Hz (r=−0.53, $p<0.05$). PD balance, a psychophysiological measure of 'lability-stability' of the central nervous system [43] illustrated this relationship most clearly [see Fig. 3; where linear fitted regression line slopes were: neuroticism (X) with butt nicotine (Y), slope=0.40, 95% confidence interval 0.20 to 0.61; butt nicotine (X) with (post-pre) smoking change in PD balance (Y), slope=−0.10, 95% confidence interval −0.17 to −0.03]. Basal PD balance and neuroticism (Eysenck Personality Questionnaire) were also important predictors, which probably exerted their influence indirectly through nicotine delivery rather than directly on their own account (see Figs. 3 and 4).

DISCUSSION

Cigarette smoking as compared with sham smoking significantly elevated heart rate, increased relative EEG power in beta1 and beta2 bands, decreased alpha and, to a lesser extent theta activity, but had no significant effect on delta activity. Dominant EEG alpha frequency was significantly increased following real as opposed to sham smoking. Smoking had no significant mean effect on visual evoked potential (VEP) amplitudes or latencies. The mean effect on photic driving (PD) at 16 Hz and 26 Hz was similarly non-significant. These results indicated a stimulant effect of cigarette smoking (and by inference of nicotine) on tonic EEG but not on those phasic aspects of EEG monitored by VEP and PD. Such a dissociation between tonic and phasic aspects of smoking on electrocortical activity is reminiscent of the observation of Pradhan and Guha [50] that nicotine produced tonic EEG activation in the cortex of the cat while depressing evoked responses.

The detailed pattern of effects of smoking on the tonic EEG bands differed from those reported by Herning *et al.* [28] who reported effects (reductions) for the theta and alpha but not (increases) in the beta bands. By contrast, significant increases in beta activity occurred here following smoking but the effects for alpha were smaller and for theta were minimal. One possible explanation is that the experiment of Herning *et al.* [28] appeared to be designed to maximise the observation of 'tobacco withdrawal' effects: all subjects habitually smoked a minimum of 30 cigarettes and often 'more than 2 packs' per day. Smoking-induced reductions of activity in the slow EEG bands, particularly theta, may represent the reversal of a 'tobacco withdrawal' syndrome including both drowsiness and irritability [56], analogous to withdrawal from chronic use of strong stimulants such as amphetamine or cocaine [28]. In addition, there was no significant evidence that variables such as average cigarette consumption, number of cigarettes smoked prior to testing and basal CO level (an indirect monitor of ad lib smoking prior to experimentation) predicted the magnitude of smoking-induced reductions of EEG theta or alpha.

The smoking-induced increases in beta activity and relatively small effects for the slow EEG bands observed here might have represented true 'above-baseline' as opposed to reversal of 'tobacco withdrawal' effects due to the fact that subjects were not heavy smokers and were subject to only minimal tobacco deprivation prior to experimentation. Nevertheless, the magnitude of smoking effect on beta (but not alpha or theta) bands was attenuated as a function of the extent 'ad lib' smoking antecedent to experimentation. This suggested that some short-acting nicotine tolerance occurred for beta band effects, analogous to the nicotine tachyphylaxis observed with smoking-induced heart rate elevation [54], and which also appeared to have occurred for heart rate in this experiment.

The failure of smoking to induce any significant change in mean VEP amplitude was perhaps unsurprising given contradictory reports concerning the direction of effect of smoking on evoked potential amplitude. Thus both increases [18, 19, 26, 64] and decreases [37, 59, 61] in evoked potential amplitudes have been observed following smoking. Friedman and Meares [18] have suggested that the direction of smoking effect may be modality dependent; with amplitude reductions in auditory EP [18,19] but increases in visual EP [18, 19, 26, 64]. Although attractive, this hypothesis cannot explain a number of studies in which either 'mixed' or opposite to prediction effects were observed in the auditory modality [39,40] and visual modality [37, 59, 61]. A hypothesis with greater explanatory power is that smoking may produce both increases and decreases in evoked potential amplitude and other responses such as electrodermal [1, 10, 22, 24], EEG alpha blocking [23] or contingent negative variation (CNV) [8, 9, 57] depending on a number of factors, including nicotine dose, nature of the task and personality. These diverse findings have been incorporated into models of smoking such as arousal modulation [41], 'psychological tool' [5,42] and stimulus filter [20] which propose a functional explanation for smoking behaviour in terms of modulation of mood and arousal, enhanced selective attention under conditions of monotony or distraction, as well as amelioration of nicotine withdrawal symptoms particularly in heavy smokers. A similar hypothesis has been proposed by Pomerleau and Pomerleau [49].

Such models may account for the effects of smoking on photic driving (PD) in the present experiment. Smoking

produced no significant overall mean change in PD. However, examination of individual differences in the direction of PD change following smoking demonstrated systematic relationships with neuroticism personality scores and (mouth) nicotine delivery. Change in photic driving balance, a monitor of 'lability-stability' of the CNS [43], depended on (mouth) nicotine which in turn was (positively) related to neuroticism personality score. Higher nicotine delivery predicted increases in PD response at the lower frequency (16 Hz) but decreases at the higher frequency (26 Hz). In terms of PD balance, this can be viewed as a stabilising effect, i.e., a shift towards CNS 'stability' for those individuals who were more neurotic, more electrocortically 'labile' and smoked their cigarette harder; and vice-versa (Figs. 3 and 4). While correlation does not necessarily imply causation, this result was consistent with the view [8] that nicotine tends towards stimulant actions at low doses and depressant actions at higher doses. Such a stabilising or homeostatic role of smoking has been predicted as one aspect of the arousal modulation model of smoking [42].

The variation in prediction efficiency between butt nicotine and rise in exhaled CO (as opposed to basal CO level) was probably accounted for by the fact that they are both indirect measures of blood nicotine level, which itself probably underestimates peak as opposed to trough CNS nicotine levels (because of the arterial nicotine bolus effect with inhalation-style cigarette smoking [54]). Basal CO levels correlate well with (venous) trough blood nicotine levels, in the range $r=0.89$ to 0.96 within cigarettes of the same brand; by contrast rise in blood nicotine following smoking a single cigarette correlates poorly with rise in CO [6]. Quite apart from possible differential lung distribution and absorption factors for gas (CO) versus particles (nicotine-tar), the CO and nicotine delivery of a cigarette are only loosely linked. The ratio of CO to nicotine delivered in given volume of smoke is determined to some extent by the exact puff pressure profiles produced by individual smokers [13]. In the experiment reported here, butt nicotine was the better predictor. Peak plasma nicotine levels, although an indirect indicator of peak CNS nicotine levels, would be useful in further elucidating this point.

In conclusion, the present results indicated that smoking (and by inference nicotine) produced stimulant effects on tonic EEG. The fact that these changes occurred with a short period of cigarette deprivation suggested that reversal of a nicotine 'withdrawal syndrome' [28] could not entirely account for effects of smoking on EEG, although this may be important in chronic heavy smokers. By contrast, the direction of effect on phasic responses (VEP, PD) varied as a linked function of personality and dose of nicotine delivered from the cigarette. It would be of interest to use other nicotine formulations, e.g., nicotine chewing gum, to examine the effect on electrocortical measures of nicotine as delivered by slow buccal absorption, as opposed to the rapid CNS delivery achieved with inhalation-style smoking. Moreover, this could be of potential clinical significance in understanding which smokers obtain most relief from craving when using nicotine chewing gum [63].

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