Available online at www.sciencedirect.com
SCIENCE DIRECT®
Pharmacology, Biochemistry and Behavior 77 (2004) 103–109
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

EEG power spectra and auditory P300 during free smoking and enforced smoking abstinence

Vincenzo Teneggi[a,*], Lisa Squassante[a], Stefano Milleri[a], Alberto Polo[b], Paola Lanteri[c], Luigi Ziviani[a], Alan Bye[a]

[a]*Discovery Medicine, GlaxoSmithKline SpA, Via Fleming 4, 37135 Verona, Italy*
[b]*Neurologia, Ospedale Pieve di Sacco, Padua, Italy*
[c]*Neurologia, Università di Verona, Verona, Italy*

Received 6 April 2003; received in revised form 7 October 2003; accepted 7 October 2003

Abstract

We investigated resting EEG and auditory P300 during free smoking and 36 h of enforced smoking abstinence in 12 healthy volunteers. Resting EEG was recorded on 19 scalp leads and auditory P300 was obtained by an oddball paradigm task. Spectral analysis of EEG (absolute and relative power, mean frequency), latency and amplitude of auditory P300 were considered for statistical analysis. EEG changes were not significant during free smoking but were significant during smoking abstinence. Theta absolute power increased by +57% ($P<.001$), whereas alpha and delta absolute power increased by +26% ($P<.01$) and +19% ($P<.01$), respectively; theta absolute power change was delayed and prolonged. Alpha mean frequency reduced by −0.31 Hz ($P<.001$), whereas delta, theta and beta1 mean frequency increased by +0.13 Hz ($P<.05$), +0.09 Hz ($P<.05$) and +0.23 Hz ($P<.01$), respectively. Auditory P300 amplitude and latency were unaffected by smoking abstinence. Resting EEG, but not auditory P300, was sufficiently sensitive to detect changes during enforced smoking abstinence, and EEG bands had different temporal changes.

Keywords: EEG; Spectral analysis; Auditory P300

1. Introduction

Quantitative EEG techniques have been largely used to study pharmacological effects on human brain activity. Recording of healthy subjects in eye-closed, resting (but alert) conditions show alpha (8–13 Hz) waves dominating the parietooccipital cortex. Most investigators analysed the dominant alpha frequency (mean and peak frequency) as a reliable brain measure, whereas less attention has been paid to theta absolute power or beta activity variations.

Cigarette smoking has been associated with subjective mood changes and increased alertness and arousal (Knott, 1998; Knott et al., 1998). The recognition of these effects, however, remained somewhat more elusive in laboratory assessments. The EEG is a noninvasive technique to assess central nervous system arousal and regional changes in brain activity. Earlier studies (Ulet and Itil, 1969; Knott and Venables, 1977; Herning et al., 1983) indicated that statistically significant EEG power spectra changes accompanied short-term nicotine abstinence. Different studies have recognised that short-term (1–10 days) nicotine abstinence is associated with the slowing of EEG, as given by an increase in theta power and a decrease in alpha frequency (Pickworth et al., 1989; Knott, 1990). These EEG changes have been reported more recently (Gilbert et al., 1999a) also with prolonged (31 days) nicotine abstinence. EEG information on electrocortical effects of nicotine administration suggested that nicotine could have direct effects, rather than simply reversing the abstinence-induced EEG slowing (Foulds et al., 1994). It has been outlined that while improving arousal, nicotine can enhance attention, learning, and memory (Warburton et al., 1992). Behavioural assessments have rarely found such performance improvements; thus, additional electrophysiological tests were introduced to validate cognitive tasks. Event-related potentials (ERPs) are a time-differentiated waveform recorded on the scalp

* Corresponding author. Tel.: +39-045-92-18520; fax: +39-045-92-18191.
E-mail address: vincenzo.2.teneggi@gsk.com (V. Teneggi).

0091-3057/$ – see front matter © 2003 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2003.10.002

that correlate with information processing. In particular the P300, a positive wave occurring between 250 and 500 ms following the onset of a meaningful event has been assumed to be a measure of mnemonic, attentional, and decision-making activity (Donchin and Johnson, 1978; Picton, 1992).

Most of the studies mentioned above investigated EEG and P300 changes with a single or daily interval measurement. We explored the resting EEG and the auditory P300 during free smoking and smoking abstinence by means of measurements repeated two to three times a day. The main hypothesis was that repeated EEG assessments could better recognise time onset of EEG band changes and their time course. No specific hypothesis was made for auditory P300 other than it could detect task changes if sufficiently sensitive.

2. Method

2.1. Study design

This was a randomised, double-blind, placebo-controlled, two-period crossover study with a 10 days washout in healthy volunteers. The study was set up to explore the effects of both a placebo and an investigational smoking cessation compound during free smoking and abstinence conditions (Fig. 1). The research was performed at the Clinical Pharmacology Unit of GlaxoSmithKline in Verona, Italy. Here we are reporting the study design and procedures related to the whole study, whereas results refer only to the placebo treatment during free smoking and abstinence conditions. The aim of this paper is to compare the resting EEG and auditory P300 during free smoking (Days 1 and 14) with abstinence (Days 15 and 16) conditions (Fig. 1). The comparison between the placebo and the smoking cessation compound will be the subject matter of a separate paper.

Subjects were in the Unit (in-patients) from the evening of Day −1 to the morning of Day 2 and from the evening of Day 13 to the morning of Day 17, whereas they were out of the Unit (out-patients), from the afternoon of Day 2 to the afternoon of Day 13, during each of the two study periods. From the morning of Day 15 they started the abstinence condition lasting 36 h. Subjects were randomly allocated to receive, in a crossover design, the investigational smoking cessation compound or matched placebo once a day (8 a.m.), from Day 1 to Day 16.

Twelve male smokers were enrolled. This sample size was expected to provide the study a power of 80% to detect a difference of 16 ms on Cz latency if the residual variability was around 12 ms, as observed in a previous in-house study. The subjects′ main characteristics were as follows: healthy condition, age 20–41 (mean ± S.D.: 28.9 ± 6.7), smoking ≥ 15 cigarettes/day in the last year, Fagerström nicotine Tolerance Questionnaire (FTQ) ≥ 7 and ≤ 9, regular sleep/wake-up schedule, right-handed and negative urine test for drugs of abuse.

Subjects had to be not motivated to quit smoking; drink on average less than 14 units of alcohol per week (1 unit = half pint of beer/1 glass of wine/1 measure of spirit); refrain from alcohol for 24 h before each inpatient study phase; refrain from smoking for 36 h during smoking abstinence condition; follow a predefined standard diet and refrain from coffee consumption (with the exception of morning and lunch coffee) during each inpatient phase; be free from any psychoactive drug administration during the previous 3 months and from prescription or over the counter current drug administration; read and comprehend Italian and give signed informed consent before study participation. Ethics Committee approval was obtained

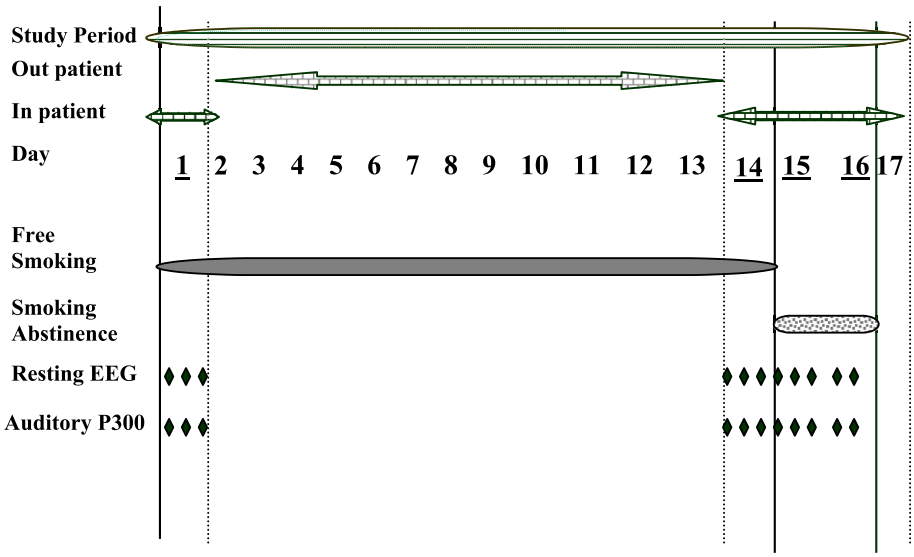

Fig. 1. Study diagram.

Table 1
Summary statistics (mean ± S.D.) of EEG parameters at 4–10 h on Day 1 (free smoke, $n=12$), Day 14 (free smoke, $n=9$), and Day 16 (abstinence, $n=9$)

	Log absolute power			Mean frequency (Hz)		
	Day 1 (free smoke)	Day 14 (free smoke)	Day 16 (abstinence)	Day 1 (free smoke)	Day 14 (free smoke)	Day 16 (abstinence)
Delta	1.156 ± 0.285	1.055 ± 0.312	1.231 ± 0.260	1.90 ± 1.13	1.89 ± 0.13	2.02 ± 0.09
Theta	1.045 ± 0.604	0.859 ± 0.565	1.309 ± 0.618	5.85 ± 0.30	5.83 ± 0.20	5.92 ± 0.22
Alpha	2.164 ± 0.814	1.979 ± 0.654	2.211 ± 0.712	9.72 ± 0.39	9.80 ± 0.47	9.50 ± 0.38
Beta1	0.410 ± 0.693	0.233 ± 0.769	0.310 ± 0.633	14.32 ± 0.50	14.19 ± 0.51	14.41 ± 0.29

before the start of the study, which was conducted in accordance with the Declaration of Helsinki.

2.2. Study procedures

Pharmacodynamic measurements, resting EEG, and auditory P300 parameters were registered at predefined times—during free smoking: before, 4 and 10 h after dosing on Days 1 and 14; during smoking abstinence: 4 and 10 h after dosing on Day 15, before, 4 and 10 h after dosing on Day 16. Measurements of Day 16 corresponded to 24, 28 and 34 h of smoking abstinence.

Electrophysiological measurements were performed in accordance with the rules of the International Pharmaco-EEG Group. A Sirius WR (E.B. Neuro) was used for all EEG and auditory P300 recording and measurements. Electrode impedance was kept below 5 KΩ, but values up to 10 KΩ were considered acceptable. Filter settings were 0.5 and 70 Hz and sampling frequency was 512 points. During data acquisition the subjects sat on an armchair in a soundproof room with their eyes closed.

The EEG signal from 19 scalp leads within a cap (10–20 system) was recorded using linked-ears reference, with one additional channel for EOG monitoring. After visual examination, at least 150 EEG epochs of 2 s free from contamination were analysed for a total of 5 min per recording. Absolute and relative power spectrum and mean frequency of delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), and beta1 (12–18 Hz) activities for all 19 derivations were calculated.

The auditory P300 recording was made before the resting EEG registration. At the screening, a check with the acoustic signal set to 0 (normal value for a standard population) was performed to assess if the subject had a normal acoustic function. Between auditory P300 trials, there was a resting period of at least 1 min.

A standard auditory oddball paradigm was used for P300 generation. Two electrodes of the cap (Cz and Pz according to the international 10–20 system) with binaural ear link were used for the P300 evaluation. Filter settings were 0.5 and 30 Hz, according to the IFNC recommended standard for long-latency auditory ERP (Ebmeier et al.,

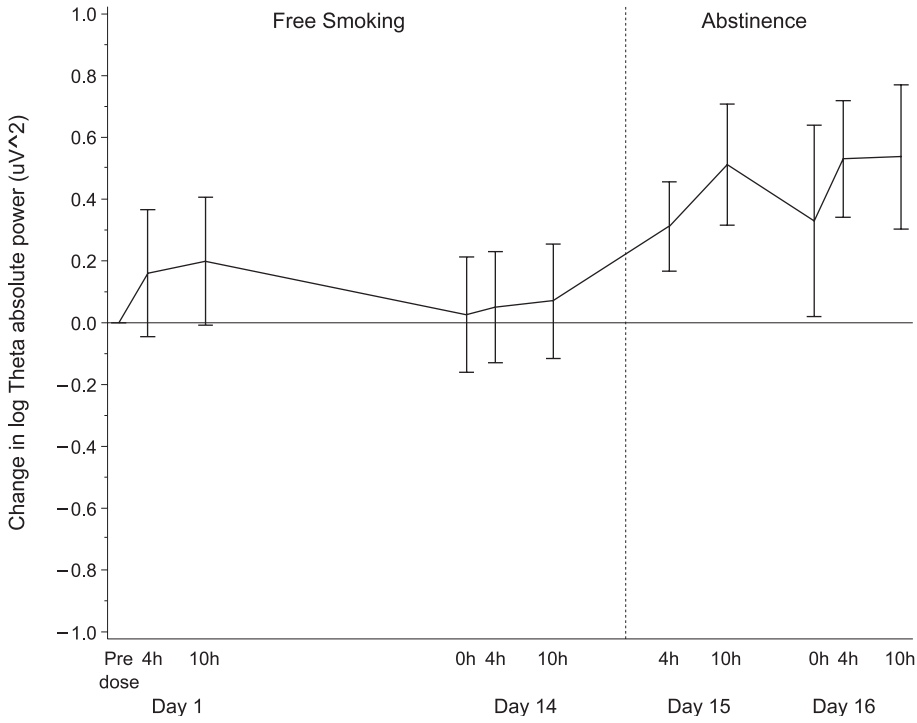

Fig. 2. Mean ± S.D. of changes from predose Day 1 of log-transformed theta absolute power during free smoking and abstinence.

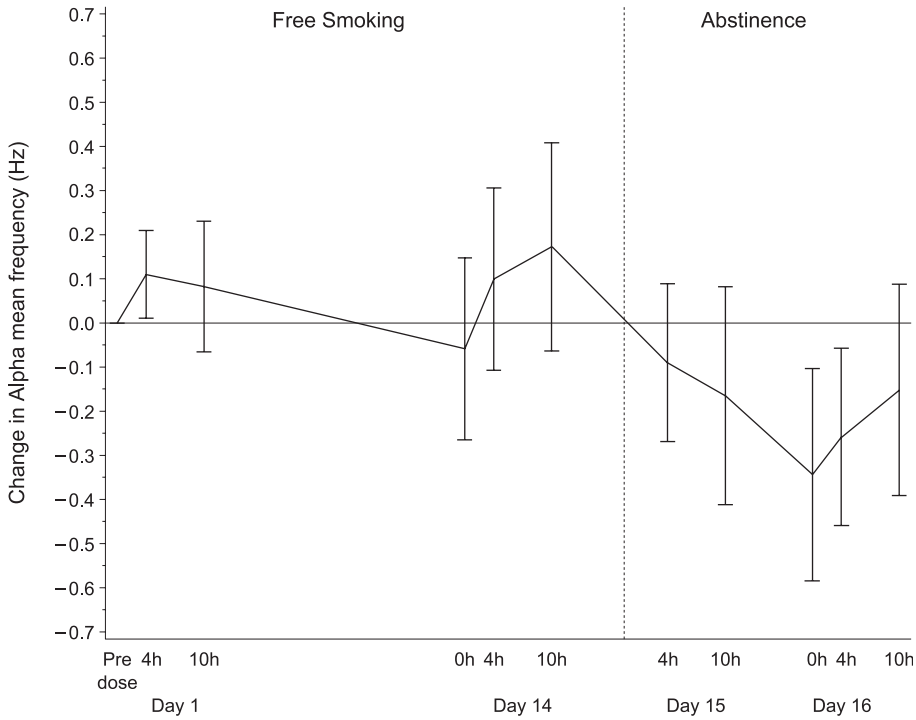

Fig. 3. Mean ± S.D. of changes from predose Day 1 of alpha mean frequency during free smoking and abstinence.

1992; Goodin et al., 1992, 1994). Subjects listened to a series of two tones, with a frequency of 1000 Hz for frequent and 2000 Hz for infrequent tones. Subjects were asked to count the infrequent tones. The tones were presented binaurally through earphones with duration of 50 ms (10-ms rise and 10-ms fall time) and the intensity was 60 dB over the normal threshold. The intertone interval was randomised between 1.2 and 2 s, with frequent tones comprising 85% and infrequent comprising 15% of all tones. The total number of tones the subject was asked to count was about 20.

Response to rare tone was recorded three times. Two tracks with the shorter value for the P300 latency in Cz and two tracks with the shorter value for the P300 latency in Pz were chosen and then averaged to calculate mean curves for Cz and Pz. The recording began 100 ms before the stimulus and continued 1000 ms after. The amplitude of P300 was calculated between prestimulus averaged EEG baseline and the major positive peak occurring between 250 and 500 ms poststimulus onset. The latency of P300 wave was slightly different between parietal and central leads and was therefore individually measured in the point of major positivity.

To check for smoking abstinence compliance, exhaled carbon monoxide (CO) was measured at 0, 4, 10, 24, 28 and 34 h starting on Day 15. Alcohol breath test, for alcohol abstinence compliance, was performed at the Unit admission on Days −1 and 13.

2.3. Statistical methods

EEG power spectral analysis parameters and amplitude and latency from auditory P300 were at first summarised for each subject across the scalp electrodes by mean values. Absolute and relative power were preliminarily transformed by means of log and logit transformation, respectively. Measurements taken after 4–10 h on Days 1 and 14, during free smoking, and on Day 16, during abstinence, were then averaged and adjusted for baseline, calculating the change from predose Day 1 value. These changes from baseline were compared between Day 14 and Day 1 and between Day 16 and Day 14 by analysis of variance (ANOVA), allowing for the factors subject and day. Topographic maps were produced for each EEG band. These descriptive significance probability maps are based on the results of tests from

Table 2
Summary statistics (mean ± S.D.) of P300 parameters at 4–10 h on Day 1 (free smoke, $n=12$), Day 14 (free smoke, $n=9$), and Day 16 (abstinence, $n=9$)

	Latency (ms)			Amplitude (μV)		
	Day 1 (free smoke)	Day 14 (free smoke)	Day 16 (abstinence)	Day 1 (free smoke)	Day 14 (free smoke)	Day 16 (abstinence)
Cz	306.8 ± 21.2	303.2 ± 22.2	306.2 ± 20.7	9.39 ± 3.27	9.66 ± 3.35	10.00 ± 2.87
Pz	300.0 ± 21.8	301.6 ± 23.1	302.8 ± 18.8	9.21 ± 2.60	8.56 ± 2.67	8.46 ± 2.98

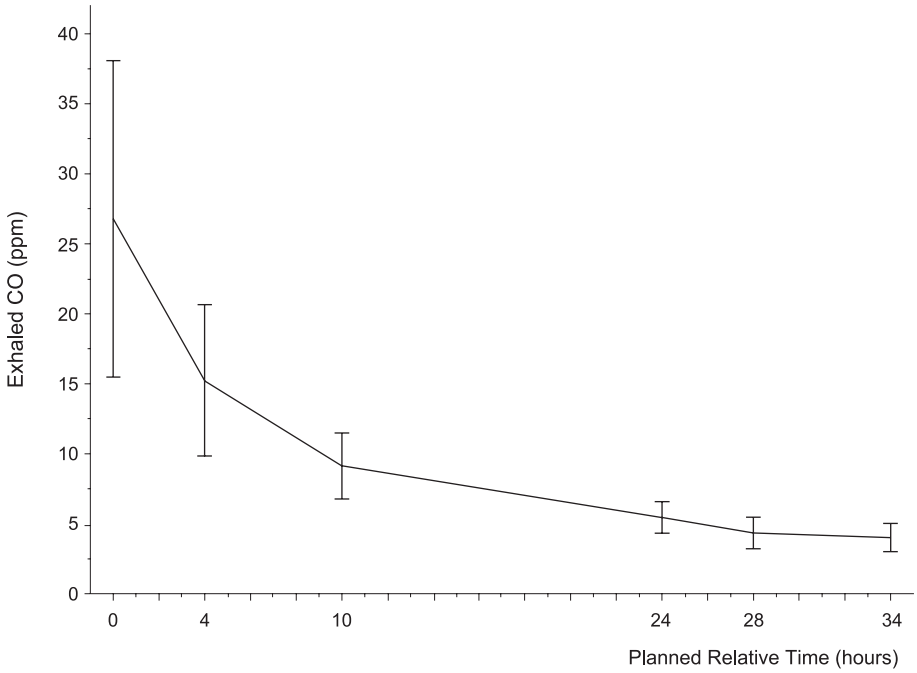

Fig. 4. Mean ± S.D. of exhaled CO on Days 15–16 (abstinence).

ANOVA for independent electrodes. All the statistical analyses were produced using SAS Version 8 for Windows.

3. Results

Spectral analysis of the resting EEG in different experimental conditions and summary statistics are illustrated in Table 1.

Changes occurring between EEG recordings of Days 1 and 14 during free smoking were not significant for any band, with the exception of a mild decrease in alpha absolute power ($P<.05$).

EEG scores were significantly changed by enforced smoking abstinence. The absolute theta power greatly increased (+57%, $P<.001$), corresponding to an increased relative power (+32% $P<.001$). The delta and alpha absolute powers increased to a lesser extent (+19%, $P<.01$ and +26%, $P<.01$, respectively), without any corresponding increase of their relative power. The mean alpha frequency was reduced by abstinence (−0.31 Hz, $P<.001$); minor changes involved delta and theta mean frequencies with a shift to higher values (+0.13 Hz, $P<.05$ and +0.09 Hz, $P<.05$), as did beta1 mean frequency (+0.23, $P<.01$).

Analysis of individual scalp leads was also performed, attempting to evaluate differences in topographical changes between free smoking and abstinence. The entire scalp showed a highly significant increase ($P<.001$) in theta absolute power, with the highest F values found along the right frontocentral and central electrodes: F4, F2, Fz and C4, Pz, respectively. The entire scalp showed a highly significant decrease ($P<.001$) in alpha mean frequency, with the highest F values found over the central and parietocentral electrodes: C4, C3 and Pz, respectively.

Finally, we have studied the temporal profile of the EEG modifications. During the free smoking condition, the EEG power spectra was not different between Day 1 and Day 14 and between each recording session (0 h, 4 h, 10 h). During the abstinence condition, an increase in the absolute power of theta activity was observed in the first recording (4 h) but was greater in the successive recording (10 h), without any modification thereafter (34 h of smoking abstinence), as shown in Fig. 2. The shift to lower mean frequency of the alpha activity, however, as shown in Fig. 3, occurred in a short time after smoking cessation (4 and 10 h), became greater in the 24-h recording with a trend of recovery thereafter (34 h of smoking abstinence).

Summary statistics (mean and S.D.) of auditory P300 parameters in the different experimental conditions are illustrated in Table 2. We have not found significant modifications of latency and amplitude of auditory P300, either from central or parietal scalp leads.

Exhaled CO, measured at 0, 4, 10, 24, 28, and 34 h starting on Day 15 to monitor for smoking abstinence compliance, is reported in Fig. 4. As expected, CO concentration decreased below 10 ppm after 10 h of abstinence with a further decrease to around 5 ppm after 34 h.

4. Discussion

An increasing body of data is supporting specific changes with resting EEG during smoking abstinence in

cigarette smokers. These changes seem to be indicative of worsened cigarette craving, arousal and mood.

We have observed EEG changes during the first days of smoking abstinence: the alpha mean frequency shifted to a lower value and the theta absolute power increased. In agreement with previous reports, they are considered overall effects of tobacco abstinence. Most studies suggest that the nicotine component of tobacco smoke is responsible for the EEG changes (Edwards and Warburton, 1988). Smoke-inhaled nicotine produces a shift in scalp recorded activity from low (delta, theta, alpha1) to high (alpha2, beta) frequencies, a response profile not dissimilar to that seen with other central stimulants such as amphetamine (Knott, 1990; Pickworth et al., 1997; Houlihan et al., 2001). On the other hand, during tobacco abstinence the spectral analysis showed a slowing of the EEG characterized by decreasing alpha frequency and increasing theta power (Pickworth et al., 1989; Gilbert, 1987; Domino, 1998). Statistically significant changes of the EEG power spectra accompanied short-time nicotine deprivation (Houlihan et al., 2001).

The follow-up of the EEG changes has been evaluated by a few authors (Herning et al., 1983; Pickworth et al., 1989; Gilbert et al., 1997; Knott and Venables, 1977). They showed that in the first days of smoking cessation, EEG and subjective and behavioural effects are at maximum: alpha frequency decreased rapidly (5–29 h) and theta power increased significantly within 29 h after deprivation, with both these changes persisting for the duration of deprivation. In agreement with the above authors, we have also found that alpha frequency variations occurred rapidly (within 24 h of smoking abstinence) and reversing the day after (34 h of smoking abstinence). A different trend was noted for the modification of the theta absolute power: its enhancement (4–10 h of smoking abstinence) persisted at the end of EEG monitoring (34 h of smoking abstinence). The detection of this finding can be attributed to the relatively short time interval between repeated EEG assessments.

We have found topographical asymmetric EEG changes not dissimilar to those seen by other authors. Topographical specific EEG effects to nicotine deprivation can be due to either lateralization of the alpha band power (Gilbert et al., 1989, 2000) and to a larger amount of theta power in frontal than in posterior cortex (Pickworth et al., 1989; Gilbert, 1987; Gilbert et al., 1999b).

During smoking abstinence, affective and cognitive changes similar to subclinical depression and related stress response have been described (Covey et al., 1990; Gilbert et al., 1999a). In depressive conditions EEG asymmetry, with greater activation on right than left hemisphere, has also been reported (Davidson et al., 1990; Tomarken and Davidson, 1990). These findings have led to the suggestion that as in depressed people, in abstinent smokers the EEG asymmetry could be due to a heterogeneous distribution or activation of nicotine receptors (London et al., 1985; Gilbert, 1987; Knott et al., 1999).

More recently, brain investigations by means of functional imaging have effectively shown that nicotine is involved in regulating regional blood flow and regional cerebral metabolism (Ghatan et al., 1998; Domino et al., 2000). All these findings give very strong support for the interpretation of power spectra EEG changes. Some authors have supported the importance of nicotine/cholinergic mechanisms mediating arousal and attention in healthy subjects and a reversal effect of a nicotine-induced abstinence deficit (Foulds et al., 1996; Pineda et al., 1998; Mancuso et al., 1999).

Because behavioural tasks provide limited information on processing stages, additional investigation by ERPs have recently been performed. In the present study, auditory P300 obtained by oddball acoustic paradigm did not show any change between free smoking and abstinence. Other authors who used auditory stimuli failed to report P300 latency variation (Norton et al., 1991). On the other hand, studies performed with a visual task showed that subjects who smoke before their tests exhibit faster visual P300 latencies than nonsmoking and smoking-deprived subjects (Pineda et al., 1998; Houlihan et al., 1996). These conflicting results could be due to differences in cortical arousal induced by the auditory and visual tasks.

The discrimination task performed during the auditory P300 recording is probably too easy and the underlying processing activity does not involve relevant behavioural changes. The specific changes, during different smoking conditions, with visual P300, but not auditory P300, may also be the result of the relatively greater concentration of nicotinic receptors in the visual than in the auditory system (Ghatan et al., 1998).

Desynchronization of the spontaneous activity of cells in the cortex may represent one such mechanism of arousal, probably correlated with a shift from lower to higher EEG frequencies.

Statistical significance of the findings obtained should be interpreted with care, in light of the consideration that the statistical analysis of drug-induced EEG alterations has proven problematic for several reasons including (1) the considerable high intra- and inter-subject variability intrinsic to EEG data, (2) the lack of independence and the collinearity between recording sites and EEG measures, (3) the nonnormal distribution of EEG variables, and (4) the high ratio of EEG variable to subject numbers and the implementation of numerous tests that will increase Type I errors and may lead to erroneous conclusions (Knott, 2000). Despite this caution, the evidence of the strong signals we observed and the consistency of these patterns with those reported in literature sustain our interpretation.

We conclude that the most relevant findings of this study were the reduction of mean alpha frequency, the increase of the absolute theta power, and the asymmetry of EEG during smoking abstinence. However, although alpha, theta and asymmetry changes of EEG were reported by previous researches, the temporal difference between alpha and theta

changes was not yet mentioned. These EEG results are consistent with effects opposed to those occurring during alertness. EEG asymmetries, in particular, can be associated with changes of mood reported by abstinent smokers.

References

Covey LS, Glassman AH, Steiner F. Depression and depressive symptoms in smoking cessation. Compr Psychiatry 1990;31:350–4.

Davidson RJ, Ekman P, Saron CD, Senulis JA, Friesen WV. Approach/Withdrawal and cerebral asymmetry: emotional expression and brain physiology. J Pers Soc Psychol 1990;58:330–41.

Domino EF. Tobacco smoking, nicotine and EEG brain topography. In: Koga Y, Nagata K, Hirata K, editors. Brain tomography today. Amsterdam (Netherlands): Elsevier; 1998. p. 793–8. International Congress Series 1147, Excerpta Medica.

Domino EF, Minoshima S, Guthrie SK, Ohl L, Ni L, Koeppe RA, et al. Effects of nicotine on regional cerebral glucose metabolism in awake resting tobacco smokers. Neuroscience 2000;101:277–82.

Donchin E, Johnson Jr R. On how P300 amplitude varies with the utility of the eliciting stimuli. Electroencephalogr Clin Neurophysiol 1978; 44(4):424–37.

Ebmeier KP, Glabus M, Potter DD, Salzen EA. The effect of different high pass filters settings on peak latencies in the event related potentials of schizophrenics, patients with Parkinson's disease and controls. Electroencephalogr Clin Neurophysiol 1992;84:280–7.

Edwards J, Warburton D. Smoking, nicotine and electrocortical activity. Pharmacol Ther 1983;19:147–64.

Foulds J, McSorley K, Sneddon J, Feyerabend C, Jarvis MJ, Russell MAH. Effect of subcutaneous nicotine injections on EEG alpha frequency in non-smokers: a placebo-controlled pilot study. Psychopharmacology 1994;163–6.

Foulds J, Stapleton J, Swettenham J, Bell N, McSorley K, Russel MAH. Cognitive performance effects of subcutaneous nicotine in smokers and never-smokers. Psychopharmacology 1996;127:31–8.

Ghatan PH, Ingvar M, Eriksson L, Stone-Elander S, Serrander M, Ekberg K, et al. Cerebral effects of nicotine during cognition in smokers and non-smokers. Psychopharmacology 1998;136:179–89.

Gilbert DG. Effects of smoking and nicotine on EEG lateralisation as a function of personality. Pers Individ Differ 1987;8:933–41.

Gilbert DG, Robinson J, Chamberlin C, Spielberger C. Effects of smoking/nicotine on anxiety, heart rate and lateralization of EEG during a stressful movie. Psychophysiology 1989;26:311–20.

Gilbert DG, McCleron FJ, Rabinovich NE, Dibb WD, Plath LC, Hiyane S, Jensen RA. EEG, physiology and task-related mood fail to resolve across 31 days of smoking abstinence: relation to depressive traits, nicotine exposure and dependence. Exp Clin Psychopharmacol 1999a;7(4): 427–43.

Gilbert DG, Crauthers DM, Mooney DK, McClernon FJ, Jensen RA, et al. Effects of monetary contingencies on smoking relapse: influence of trait depression, personality and habitual nicotine intake. Exp Clin Psychopharmacol 1999b;7:174–81.

Gilbert DG, Dibb WD, Plath LC, Hiyane SG. Effects of nicotine and caffeine, separately and in combination, on EEG topography, mood, heart rate, cortisol and vigilance. Psychophysiology 2000;37(5):583–95.

Goodin DS, Aminoff MJ, Chequer RS. Effect of different high-pass filters on the long-latency event related auditory evoked potentials in normal human subjects and individuals infected with the immunodeficiency virus. J Clin Neurophysiol 1992;9:97–104.

Goodin D, Desmedt J, Maurer K, Nuwer MR. IFCN recommended standards for long-latency auditory event related potentials. Electroencephalogr Clin Neurophysiol 1994;91:18–20.

Herning R, Jones R, Bachman J. EEG change during tobacco withdrawal. Psychophysiology 1983;20:507–12.

Houlihan ME, Pritchard WS, Robinson JH. Faster P300 latency after smoking in visual but not auditory oddball tasks. Psychopharmacology 1996;123:231–8.

Houlihan M, Pritchard W, Robinson J. EEG effects of smoking: is there tachyphylaxis? Neuropsychobiology 2001;44:54–8.

Knott V. Dynamic EEG changes during cigarette smoking. Neuropsychobiology 1988;19:54–60.

Knott V. Neuroelectric correlates of smoking behaviour. In: Adlkofer F, editor. Advances in pharmacological sciences: effects of nicotine on biological systems I. Hamburg: Birkhauser Verlag; 1990. p. 491–500.

Knott VJ. Quantitative EEG methods and measures in human psychopharmacological research. Hum Psychopharmacol Clin Exp 2000;15: 479–98.

Knott V, Venables P. EEG alpha correlates of nonsmokers, smoking and smoking deprivation. Psychophysiology 1977;14:150–6.

Knott VJ, Harr A, Ilivitsky V, Mahoney C. The cholinergic basis of the smoking-induced EEG activation profile. Neuropsychobiology 1998; 38:97–100

Knott V, Bosman, Mahoney C, Ilivistry V, Quirit K. Transdermal nicotine: single dose effects on mood, EEG, performance and event related potentials. Pharmacol Biochem Behav 1999;63:253–61.

London ED, Connolly RJ, Szikszay M, Wamsley JK. Distribution of cerebral metabolic effects of nicotine in the rat. Eur J Pharmacol 1985;110(3):391–2.

Mancuso G, Warburton DM, Mélen M, Sherwood N, Tirelli E. Selective effects of nicotine on attentional processes. Psychopharmacology 1999; 146:199–204.

Norton R, Howard R, Brown K. Nicotine dose dependent effects of smoking on P300 and mood. Med Sci Res 1991;19:355–6.

Picton T. The P300 wave of the human event-related potential. J Clin Neurophysiol 1992;9:456–79.

Pickworth WB, Herning RI, Henningfield JE. Spontaneous EEG changes during tobacco abstinence and nicotine substitution in human volunteers. J Pharmacol Exp Ther 1989;251(3):976–82.

Pickworth WB, Fant RV, Butschky MF, Henningfield JE. Effects of mecamylamine on spontaneous EEG and performance in smokers and nonsmokers. Pharmacol Biochem Behav 1997;56(2):181–7.

Pineda JA, Herrera C, Kang C, Sandler A. Effects of cigarette smoking and 12-h abstention on working memory during a serial-probe recognition task. Psychopharmacology 1998;139:311–21.

Tomarken DM, Davidson RJ, Henriques JB. Resting frontal brain asymmetry predicts affective responses to films. J Pers Soc Psychol 1990;59: 791–801.

Ulet JA, Itil TM. Quantitative electroencephalogram in smoking and smoking deprivation. Science 1969;164:969–70.

Warburton DM, Rusted JM, Fowler J. A comparison of the attentional and consolidation hypotheses for the facilitation of memory by nicotine. Psychopharmacology 1992;108(4):443–7.