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EFFECTS OF TOBACCO SMOKING ON THE TOPOGRAPHIC EEG I

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Abstract

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1. The EEG and cardiovascular effects of smoking tobacco cigarettes of varying nicotine content were studied in Japanese chronic tobacco smokers.
2. Thirteen female and fifteen male adult normal volunteers were recruited for this study.
3. Each subject was asked to stop smoking the evening before coming to the laboratory the next morning, so they were approximately 10-12 hr deprived of cigarettes.
4. The objectives of this study were: a) To compare the mean differences in total activity in the *alpha*$_1$, *alpha*$_2$, *beta*, *delta*, and *theta* frequency bands before and after smoking a cigarette with 0, 0.27, 2.0, and 2.16 mg nicotine content in these 10-12 hr deprived tobacco smokers. b) To compare the topographic EEG patterns in such volunteers before and after smoking each of the above cigarettes. c) To compare the cardiovascular effects of smoking each of the above cigarettes in the same volunteers.
5. Smoking any of the four different types of cigarettes increased the total *alpha* EEG activity, although there were marked individual differences. Only after smoking nicotine containing cigarettes was there a mean decrease in *alpha*$_1$ (8.0-9.8 Hz) and an increase in *alpha*$_2$ (10-11.8 Hz) activity in the EEG, not only in the occipital areas but also more diffusely throughout the cerebral cortex. There were no consistent mean changes in EEG *delta*, *theta*, or *beta* activity. Individual differences were marked, irrespective of the nicotine content of the cigarette smoked. Baseline state, individual subject variation, and nicotine content of the cigarette smoked determine the EEG effects observed. Zero nicotine cigarette smoking also caused EEG changes, including an increase in *alpha*$_1$ and *alpha*$_2$ activity.
6. In contrast to smoking a zero nicotine cigarette, the cardiovascular effects of tobacco smoking include a slight increase in heart rate, systolic, and diastolic blood pressure.

Keywords: acute cardiovascular effects of tobacco smoking, Japanese tobacco smokers, nicotine, plasma nicotine and cotinine, tobacco smoking abstinence (10-12 hr), topographic EEG.

Abbreviations: electrocardiogram (EKG), electroencephalogram (EEG)

Introduction

There have been many reports on the EEG effects of tobacco smoking involving subjects with variable periods of abstinence. Differences in experimental design, varying content of nicotine, etc. have contributed to a confusing number of conclusions, some of which are the exact opposite of others. In addition, a large variety of EEG techniques have been used.

Motivation for the maintenance of the tobacco smoking habit still has not been elucidated. In 1988, the U.S. Surgeon General reported that nicotine is a highly addictive substance and is the basis for the tobacco smoking habit. Such a statement does not suggest any mechanism to explain why nicotine is reinforcing to some individuals. Edwards and Warburton (1982) expressed a concern for the lack of research using the topographic EEG. They stated that such research is necessary in order to understand the effects of tobacco smoking on different brain systems. The present investigation was designed to study the topographic EEG of adult Japanese tobacco smoking volunteers inasmuch as it is generally recognized that Japanese frequently smoke a large number of tobacco cigarettes. A preliminary abstract of this research was first presented by Domino and Matsuoka (1990) and is now being reported in detail.

Methods

Subjects

This study involving experiments on human subjects was conducted under the guidelines of the Helsinki Declaration of 1975. Healthy adult male and female volunteers 21 to 61 years of age with a history of chronic (over one year) daily tobacco smoking and who inhaled were recruited for this study. Informed consent was obtained from all of the volunteers. Each subject was asked to stop smoking the evening before coming to the laboratory the next morning. Therefore, the subjects were deprived of smoking about 10-12 hr prior to being given a cigarette to smoke. Four different types of nonfiltered cigarettes were used. The subjects were unaware of which kind of cigarette they smoked.

Four separate groups of subjects were studied. The first group of six (four females, two males) smoked a nicotine free cigarette which contained a blend of orange, cocoa, and wheat leaves. The second group of seven (four females and three males) smoked a University of Kentucky low nicotine (0.27 mg) research cigarette (Lo3A1). The third group of ten (five females, five males) smoked a University of Kentucky high nicotine (2.16 mg) research cigarette (Hi2R1). The fourth group of five males smoked a commercial tobacco (2.0 mg nicotine) cigarette. Inasmuch as the research cigarettes were relatively old and stale, their content of nicotine was reanalyzed with the low nicotine cigarette = 0.3, 25 mg tar, and the high nicotine cigarette = 2.0 mg and 32 mg tar consistent with their original analyses. The reanalysis of the nicotine and tar content was kindly provided by Dr. Tsutomu Ikeda, Manager, Scientific Information, Japan Tobacco Co., Tokyo, Japan. It should be noted that the (Hi2R1) cigarette had

an extremely high tar level that is not commercially available. In order to obtain resting EEG recordings, the subjects were asked to close their eyelids and relax before and after tobacco smoking.

Equipment

A Nihon Kohden 17 channel EEG, Model No. 4317, was used for recording the EEG data on line as well as on magnetic tape. A Sony data tape recording system, NFR-3000 series, Model No. DFR-3915, was used for recording 16 channels of EEG data. An interface was provided by a Magatani Unit which allowed 16 channel recording on the 8 channel Sony tape recorder. Subsequently, the data were replayed from the tape recorder back through the EEG amplifiers to a Nihon Kohden ATAC 4540 frequency spectral analyzer. The topographic system used a total of 16 scalp electrodes to each ear as reference. EEG recordings were taken from F_{p1}, F_{p2}, F_3, F_7, F_z, F_4, F_8, T_3, C_3, C_z, C_4, T_4, P_1, P_2, O_1, O_2. The placement of the scalp electrodes is shown in Fig 1. Heart rate (Lead II, EKG) was recorded on the 17th channel of the polygraph. Systemic arterial blood pressure was measured by auscultation. After baseline recordings, each subject volunteered to smoke one randomly assigned cigarette.

Topographic EEG Analysis

The topographic EEG data are based upon the voltages of a 6 x 6 grid of the top of the head. This technique has been developed by Ueno et al. (1975) and Matsuoka et al. (1979). In Fig 1 the black circles represent actual electrode sites and the open circles estimated sites.

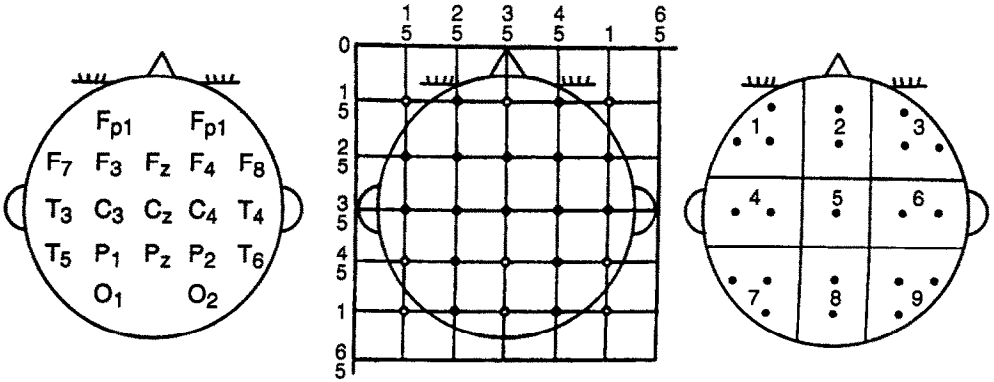

Fig 1. Scalp electrode placements and derived grid used as the basis of the topographic EEG recordings.

A matrix printout of EEG data included a series of five vertical columns of which there are five values in each column of the derived EEG data in μV/10 sec intervals. The matrix data expressed in μV/10 sec represents the square root of the power (amplitude) for a given frequency band, either *delta* (δ), *theta* (θ), *alpha*$_1$ (α_1), *alpha*$_2$ (α_2), or *beta* (β). The entire matrix for a given frequency is also averaged to provide

a mean ± standard deviation. A single epoch of 10 sec provides data for a total of 16 actual and 4 estimated recording sites in the topographic matrix for a given frequency band. The color distribution using the matrix data for topographic analysis is based upon a calibration voltage of 20 or 30 μV for 10 different colors. The actual printout of a topographic map based upon numbers for a given frequency varies from 0-10, of which 10 represents a total of 20 or 30 μV depending upon the scale used. Topographic maps were developed in two different modes, the first of which represents the actual numerical value for different frequencies and the second a color display of the frequency bands. Each of the subject's topographic analysis was available as a printout for the various frequencies as well as a color coded topographic map. In this study the following band widths were used: *delta* - 1 to 3.9 Hz, *theta* - 4.0 to 7.8 Hz, *alpha*$_1$ - 8.0 to 9.8 Hz, *alpha*$_2$ - 10 to 11.8 Hz, *beta* - 12 to 28 Hz. These band widths and the square root of the power (amplitude) differ slightly from those originally reported in the abstract of this research (Domino and Matsuoka, 1990).

Plasma Nicotine and Cotinine Analysis

Plasma nicotine and cotinine were determined using the methods described by Hariharan *et al.* (1988) and Domino *et al.* (1992). Approximately 5 ml of venous blood were withdrawn into heparinized tubes immediately before and after tobacco smoking. The plasma was separated and frozen at -20 °C until a convenient time for batch analysis.

Data Analysis

All of the data were organized in a spread sheet format for subsequent statistical analysis. Correlated and non-correlated two-tailed Student "t" tests were used to determine statistical probabilities with $p < .05$.

Results

EEG Effects

In most of the volunteers before smoking there was a relative decrease in *alpha* activity which increased after smoking. This EEG pattern frequently changed after smoking any of the four different cigarettes. There were marked individual differences. Smoking high nicotine cigarettes tended to increase total EEG *alpha* activity, as illustrated in the ink tracing in Fig 2. From this raw EEG tracing, it is impossible to determine discrete and subtle EEG changes as might be expected in an awake subject after inhaling tobacco smoke of varying nicotine content.

A complete analysis of the effects of tobacco smoking on mean ± S.E. total cortical EEG activity (separated into discrete frequency bands) is summarized in Fig 3. Interestingly, only after smoking nicotine containing cigarettes was there a mean decrease in *alpha*$_1$ (8.0-9.8 Hz) and an increase in *alpha*$_2$ (10.0-11.8 Hz) amplitude in the EEG. In these subjects there were no consistent mean changes in *delta*, *theta*, or *beta* activity, although some trends were noted, as seen in Fig 3. Individual differences were marked, irrespective of the nicotine content of the cigarette smoked.

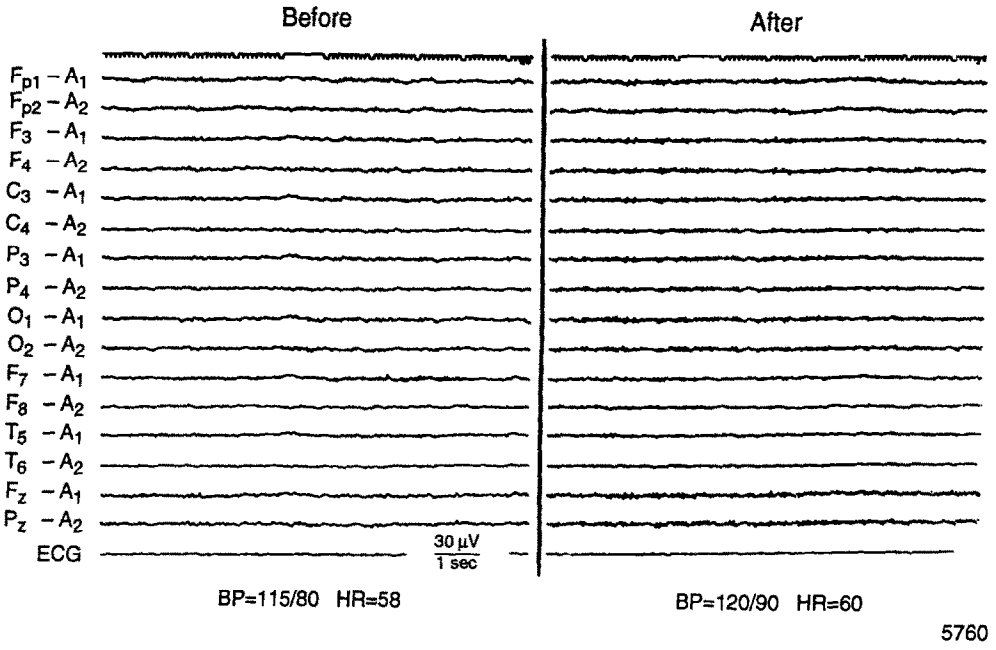

Fig 2. EEG effects of smoking a University of Kentucky high nicotine research cigarette (2.16 mg nicotine) in a normal smoker.

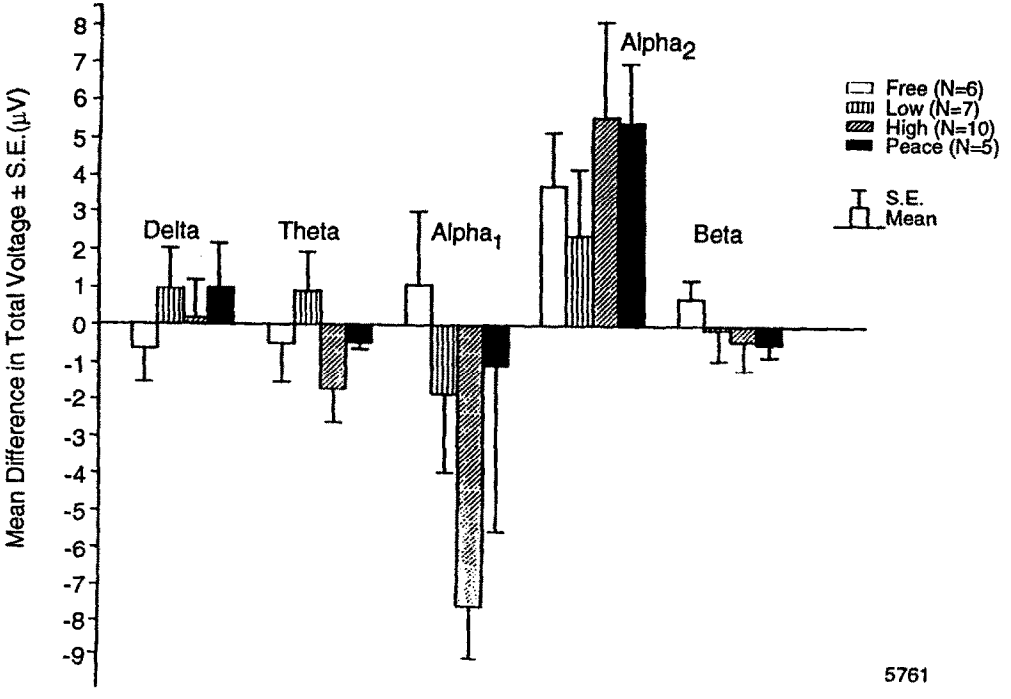

Fig 3. Effects of smoking on total cortical EEG activity.

Topographic EEG Patterns

Individual differences also were marked in the topographic EEG patterns irrespective of the nicotine content of the cigarettes smoked. This was especially evident after smoking the zero and low nicotine containing cigarettes. In contrast, after smoking the high nicotine containing cigarettes, more consistent EEG changes were noted.

Two major trends were observed following tobacco smoking. There was a tendency to increase the total distribution of *alpha* activity in the cerebral cortex, but individual differences were marked. In some subjects, a diffuse increase in $alpha_2$ EEG activity was seen after tobacco smoking. In other subjects, only an increase in $alpha_2$ EEG activity in the occipital areas was observed after smoking similar tobacco cigarettes. These two patterns are shown in Fig 4 and 5 from two different subjects who smoked the 2.0 mg nicotine commercial cigarettes.

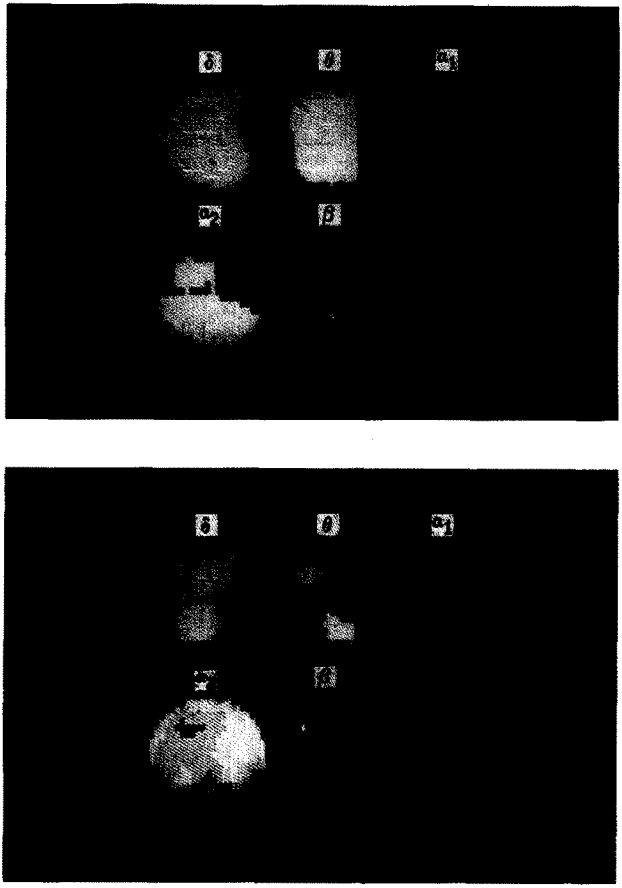

Fig 4 A. Control topographic EEG pattern before tobacco smoking. 4B. Topographic EEG pattern after smoking a high nicotine (2.0 mg) cigarette in this subject. The five different EEG bands, δ, θ, α_1, α_2, and β are shown color coded in this and the subsequent figure. The marked decrease in α_1 and the increase in α_2 activity after tobacco smoking as noted.

A

B

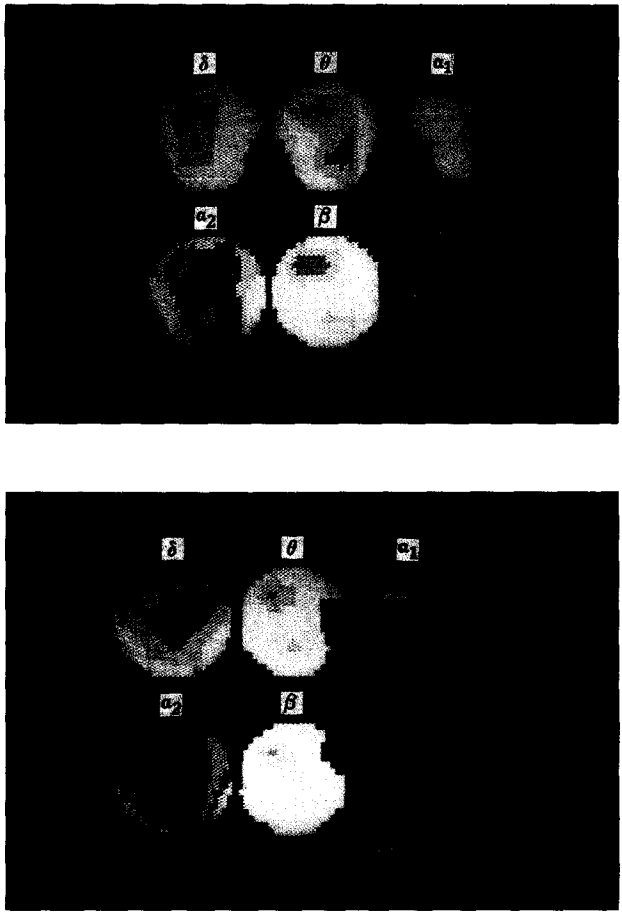

Fig 5 A. Control topographic EEG pattern before tobacco smoking. 5B. Topographic EEG pattern after smoking a high nicotine (2.0 mg) cigarette in a different subject. Note the marked diffuse and more anterior increase in α_2 activity, etc. in this subject after tobacco smoking.

Cardiovascular Effects

Heart rate and mean systemic arterial blood pressure were measured as a control for the efficiency of tobacco smoking and the absorption of nicotine. The mean data obtained are illustrated in the bar graphs in Fig 6. Smoking the nicotine free cigarette produced no increase in mean blood pressure or heart rate. In contrast, smoking any of the nicotine containing cigarettes increased mean blood pressure and heart rate by a small degree.

Plasma Nicotine and Cotinine Levels

During the course of this study it was noted that the Japanese volunteers who smoked

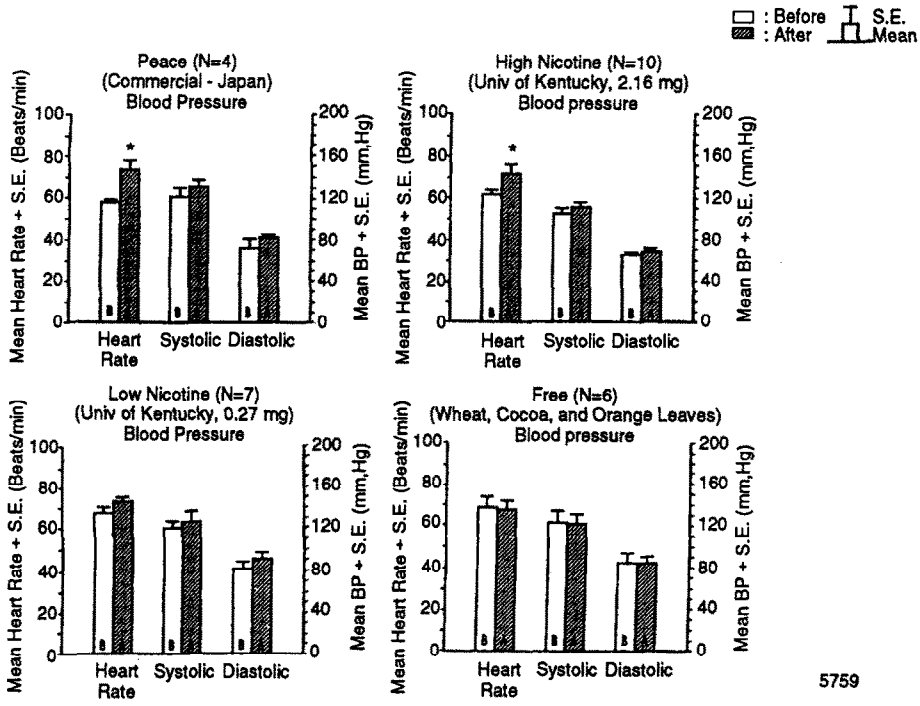

Fig 6. Cardiovascular effects of smoking different nicotine containing cigarettes.

the low as well as the high nicotine cigarettes had relatively small increases in systemic arterial blood pressure and heart rate. Therefore, it was decided to obtain pre- and post-blood samples on the remaining five of seven low and three of ten high nicotine cigarette smokers. The mean ± S.E. change in plasma nicotine after smoking low nicotine cigarettes was 0.5 ± 0.1 ng/ml and only 5.4 ± 1.2 ng/ml after smoking the high nicotine cigarettes. The mean ± S.E. pretobacco smoking cotinine levels for all eight volunteers was 212.1 ± 48.8 and 214.1 ± 51.1 ng/ml post-tobacco smoking. There was no difference in cotinine levels pre-post smoking for either the low or high nicotine containing cigarettes. Presmoking plasma cotinine levels ranged from 46.8 to 461.8 ng/ml, indicating that there was a ten fold variation in the presmoking state. Although the tobacco smokers were asked to stop smoking overnight for an approximate 10-12 hr period of abstinence, there was no independent confirmation that they actually complied. Evidence of noncompliance to this request for abstinence from smoking was noted in the marked range of presmoking plasma levels of nicotine in these eight tobacco smokers from 0 to 25.0 ng/ml with a mean ± S.E. of 9.2 ± 3.4 ng/ml.

Discussion

EEG Changes

This study involving adult male and female Japanese tobacco smokers provides some data which confirms the literature and other data which is unexpected. The expected findings are that tobacco smoking in a nicotine concentration dependent manner alters scalp EEG patterns. The unexpected finding is that even though individual variation is marked, smoking a zero nicotine content cigarette had EEG effects including a slight decrease in total *delta* and *theta*, a slight increase in *beta*, and a definite increase in total *alpha* (*alpha*$_1$ + *alpha*$_2$ activity; Fig 3). In contrast, smoking a high nicotine research or commercial cigarette decreased *alpha*$_1$ and increased *alpha*$_2$ activity. Surprisingly, in this study there was no increase in EEG *beta* activity after tobacco smoking irrespective of the nicotine content of the cigarette. Smoking any of the four different types of cigarettes which contained 0, 0.27, 2.0, and 2.16 mg of nicotine increased total *alpha* EEG activity. Especially important was the finding that the effects of increasing concentrations of nicotine cannot be distinguished by measuring the total *alpha* activity. Only by separating the *alpha* frequency band into *alpha*$_1$ and *alpha*$_2$ subgroups were clear cut differences observed. An even greater subdivision of *alpha* frequencies may lead to even greater differences. Ulett and Itil (1969) showed that after being deprived of tobacco smoking for 24 hr eight heavy smokers had a shift to the left in their power frequency spectrum to a mean peak *alpha* frequency of 9.5 Hz, whereas their mean peak *alpha* frequency was 10.5 Hz while smoking. Subsequently, Itil et al. (1971) did a more detailed study of 32 male tobacco smokers also using EEG analog power spectral analysis during 24 hr of smoking deprivation and after cigarette smoking. During deprivation there was an increase in EEG power in the 5.5, 6.0, 6.5, 7.0, 8.0 and 9.0 Hz bands and a decrease in EEG power in the 11-18 Hz bands. These EEG changes which occurred during deprivation were reversed after smoking three tobacco cigarettes within 10 min. Similarly, Knott and Venables (1977) reported that nonsmokers had a mean dominant *alpha* frequency of 10 Hz, while 13-15 hr deprived smokers had a mean dominant *alpha* frequency of 9.3-9.4 Hz. The dominant *alpha* frequency of the deprived smokers increased to 9.8 Hz three to five min and to 10.0 Hz 13 to 15 min after smoking two 1.6 mg nicotine tobacco cigarettes. Subsequently, Knott and Venables (1979) and Knott (1988, 1989, 1991) elaborated on these findings using a variety of EEG techniques including topographic analyses.

Topographic Mapping

Topographic mapping provides additional information regarding the effects of tobacco smoking that is nicotine concentration dependent. After smoking nicotine containing cigarettes there was a mean increase in *alpha*$_2$ (10.0-11.8 Hz) activity in the EEG, not only in the occipital areas but also more diffusely throughout the cerebral cortex. Two major trends were observed following tobacco smoking. There was a tendency to increase *alpha* activity in the cortex, but individual differences were marked. In some subjects, a diffuse increase in *alpha*$_2$ EEG activity was seen after tobacco smoking.

In other subjects, only an increase in $alpha_2$ EEG activity in the occipital areas was observed after smoking similar tobacco cigarettes. Individual differences were marked, irrespective of the nicotine content of the cigarettes smoked. Baseline state, the nicotine content of the cigarettes smoked, and individual subject variation, including different smoking patterns, all determine the EEG effects observed. Zero nicotine cigarette smoking also caused EEG changes, including an increase in $alpha_1$ and $alpha_2$ activity. No decrease in $alpha_1$ activity was noted. The findings in the present study are generally similar to those described by Domino *et al.* (1992) using Caucasian tobacco smokers.

Cardiovascular Effects

In contrast to smoking a zero nicotine cigarette, the cardiovascular effects of tobacco smoking include a slight increase in heart rate, systolic, and diastolic blood pressure.

Conclusions

Baseline state, individual subject variation, and the nicotine content of the cigarettes smoked determine the EEG effects observed. After tobacco smoking, the topographic distribution of EEG frequencies reveals a diffuse increase in $alpha_2$ activity which is greatest in those smoking a high nicotine cigarette. Zero nicotine cigarette smoking also causes EEG changes but not a decrease in $alpha_1$ and an increase in $alpha_2$ activity.

The cardiovascular changes of tobacco smoking result in an increase in heart rate, systolic and diastolic blood pressure in contrast to smoking a zero nicotine cigarette.

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