Short communications

Stimulant and depressant effects of cigarette smoking on brain activity in man

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Cigarette smoking was found to alter the E.E.G. negativity associated with attention: the 'contingent negative variation' was increased in some smokers and decreased in others. This finding is consistent with the known dual action of nicotine to stimulate or depress neural activity and suggests a means of investigating the effects of other centrally-acting drugs on the human brain.

Smokers commonly state that they feel either 'relaxed' or 'stimulated' by a cigarette, but there is little direct evidence of both depressant and stimulant effects of smoking on brain activity in man. Changes in electroencephalographic patterns associated with smoking (Murphree, Pfeiffer & Price, 1967; Lambiase & Serra, 1957) have usually been of a type associated with stimulation. In animals, however, Armitage, Hall & Sellers (1969) have reported stimulant and depressant effects of nicotine and cigarette smoke on both electrocortical activity and cortical acetylcholine output. Evidence is presented here that cigarette smoking in man can either increase or decrease the magnitude of one type of brain activity: the electroencephalographic response known as the 'contingent negative variation' (CNV).

The CNV, first described by Walter, Cooper, Aldridge, McCallum & Winter (1964), is a negative deflection seen on the E.E.G. trace in attentive subjects between a warning signal and an imperative signal, requiring a response. Its measurement depends on signal averaging techniques which allow the summation of E.E.G. responses to time-locked signals and their separation from variable background E.E.G. activity. The CNV is thought to reflect activity in the reticular activating system and is affected by the degree of alertness of the subject (McAdam, 1969). Although the full significance of the CNV has yet to be assessed, there is no doubt that its discovery constitutes an important advance in electroencephalography. So far there appear to be no published reports of the effects of drugs on the CNV.

On the hypothesis that stimulating effects of nicotine on the brain might increase the magnitude of the CNV and depressing effects might decrease it, we measured the CNV before, during and after smoking in 22 habitual smokers.

Methods.—CNVs were obtained by a modification of the method of Walter *et al.* (1964). The warning signal was a weak, momentary flash of light (0·3 joules; <100 ms); the imperative signal was a weak tone (frequency 500 Hz) presented 1·25 s later. The subject was required to press a button as soon as possible after the onset of the tone, which provided a reaction time recorded on a digital counter. The paired warning and imperative signals were presented to the subject at random intervals (4–8 s) in series of 10, each series lasting 1 min 10 seconds. The E.E.G. was derived between the left mastoid and vertex positions from two silver/silver chloride stick-on electrodes and was amplified by a Beckman Type S Dynograph with a long time constant (9 seconds). The output was fed into a CAT (Computer for the Averaging of Transients) and the averaged response to each series of 10 paired signals was traced out by an X–Y recorder. The magnitude of CNV thus obtained for a series of 10 paired signals was determined in terms of area and expressed in μV seconds.

After a practice run, a total of nine series of 10 paired signals were presented to the subject, with a rest period of 4 min between each series. After the first three (pre-smoking) series, the subject smoked approximately half a cigarette (down to a mark) and the fourth series of signals was presented immediately afterwards. Smoking was then resumed and when the cigarette was finished the fifth series of signals was presented. The fourth and fifth series of signals thus constituted the smoking series. These were followed by four post-smoking series, which ended 20 min after the subject had finished smoking.

Results.—The results showed that smoking significantly changed the magnitude of

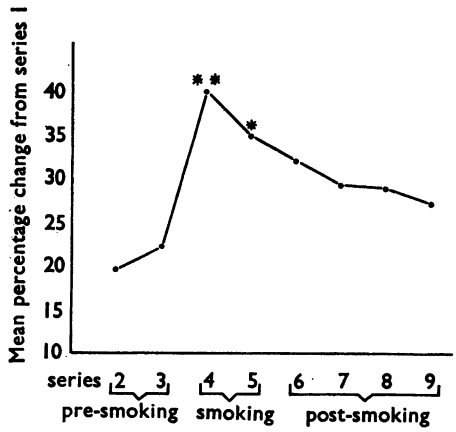

FIG. 1a. Graph showing the mean change in magnitude of the CNV associated with smoking in 22 subjects. The points represent the mean % change in CNV size between the first pre-smoking series (Series 1) and each subsequent series (see text). When compared with Series 1, the % change in CNV size was significantly greater in Series 4 (**$P<0{\cdot}001$) and Series 5 (*$P<0{\cdot}02$) than in either of the pre-smoking series (Series 2 and 3). After smoking, the % change ratios declined towards the pre-smoking levels. Mean changes in magnitude are based on changes in either direction, positive or negative.

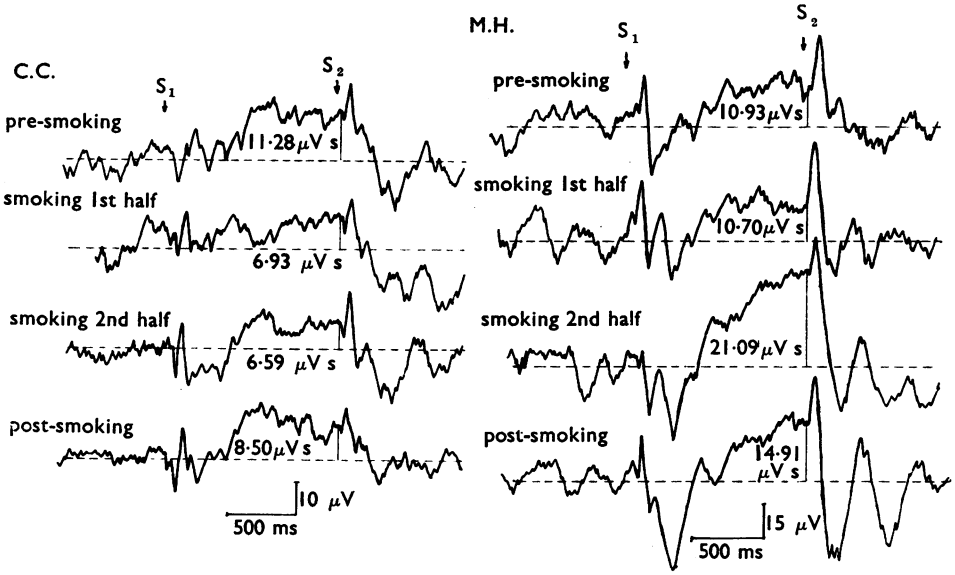

FIG. 1b. CNVs obtained from two subjects showing changes in magnitude in different directions. Subject C.C. (left) shows a decrease and subject M.H. (right) shows an increase after smoking. CNV represents the averaged response to 10 pairs of signals. S_1 and S_2=light and tone signals.

the CNV which was decreased in some subjects and increased in others. The percentage change (increase or decrease) in CNV magnitude between the first pre-smoking series and each of the smoking series was significantly greater than the percentage change between the first and second pre-smoking series ($P<0{\cdot}001$ for the series following the first half of the cigarette; $P<0{\cdot}02$ for that following the second; t tests following analysis of variance). The percentage changes between the CNVs of the three pre-smoking series were not significantly different. After smoking, the size of the CNV gradually returned towards the pre-smoking levels (see Figure 1).

Smoking a cigarette was thus associated

with changes in CNV magnitude statistically greater than those due to chance variations such as occurred between pre-smoking series, and these changes in magnitude occurred in both positive and negative directions. The predominant effect of smoking under the conditions of the experiment was a decrease in CNV magnitude. This occurred in 11 of the 22 subjects after the first or second half of the cigarette or both. Seven subjects showed an increase in the size of the CNV, while in four subjects there was a biphasic effect.

The experiment was repeated in 11 of the 22 subjects (one week to 3 months later) and all showed a response in the same direction as previously observed. Thus the effect of smoking a cigarette under these conditions appeared to be relatively constant for a particular subject.

No consistent overall relationship between nicotine intake or reaction time and CNV magnitude was found.

Discussion.—These results show that CNV magnitude was significantly affected by smoking which was associated with both increases and decreases in CNV size. It seems likely that these effects were due to nicotine rather than to other factors in cigarette smoking. Puffing on an unlit cigarette had no effect on the CNV. Simultaneously monitored blood pressure and CNV changes associated with smoking in a subsequent series showed no correlation. Nor did observed changes in carboxyhaemoglobin levels appear to be related to changes in CNV magnitude.

It is likely that rises in CNV magnitude represent stimulant effects and falls in CNV magnitude depressant effects at some level in the brain (Rebert, 1972). Preliminary experiments with caffeine (300 mg) and nitrazepam (2·5 mg) have shown very similar rises and falls in CNV magnitude to those observed with nicotine. These studies are still in progress.

These results in man agree with the findings in animals (Armitage *et al.*, 1969) that nicotine can both stimulate and depress brain activity, and with behavioural studies in man showing that smoking can both decrease and increase reaction times in a car simulator (Ashton, Savage, Telford, Thompson & Watson, 1972). The finding that centrally acting drugs can affect the CNV also suggests a new way of measuring the effects of other psychotropic drugs on brain activity in man.

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