SHORT ABSTRACT

"SHORT-TERM EFFECTS OF CIGARETTE SMOKING"

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1) In spite of Health Education campaigns the majority of smokers continue to smoke. This thesis presents some evidence concerning the factors underlying the maintenance of cigarette smoking, in terms of the short term effects of cigarette smoking on a variety of physiological measures of arousal.

2) Both stimulant, depressant and mixed effects of cigarette smoking were demonstrated on a number of physiological variables (EEG, electrodermal and EMG). No consistent effect was found on respiration rate or irregularity. Heart rate was invariably increased by cigarette smoking.

3) Sham smoking accounted for approximately 50% of all effects in both directions (stimulant or depressant), with the exception of cigarette induced tachycardia which appeared to be entirely accounted for by tobacco smoke inhalation and by implication nicotine.

4) The pre-smoking 'starting-state' of the subject had important consequences as regards the magnitude and direction of smoking effect, stimulant versus depressant. Cigarette smoking tended to produce stimulant effects in subjects with low levels of pre-smoking physiological arousal (EEG, electrodermal) and depressant effects in subjects exhibiting high levels of pre-smoking arousal.

5) The vigour of smoking style (puffing rate, puff duration and pressure, inhalation) increased during stress and also increased with low nicotine delivery cigarettes.

6) These results are interpreted as supporting an 'Arousal Modulation' model of cigarette smoking, i.e. smokers can use cigarette smoking as a device for controlling their level of arousal towards an 'optimum' by virtue of the biphasic stimulant-depressant dose response of nicotine and to some extent, by virtue of the effects of smoking behaviour in the absence of nicotine.

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LONG ABSTRACT

Two of the most commonly made observations about cigarette smoking are that smokers find extreme difficulty in giving up the habit and that when questioned as to the subjective nature of the enjoyment they obtain from smoking, a multitude of replies are given, some of them appearing contradictory at first sight, e.g. 'smoking relaxes me' and 'smoking perks me up when bored or sleepy'. These two basic observations are the starting points of the two main models of smoking behaviour: 'Addiction' models (cf. difficulty in giving up) and 'Arousal Modulation' models (cf. subjective reports of mood changes). Both 'Addiction' and "Arousal Modulation' models of cigarette smoking postulate that the primary reinforcer for the habit is nicotine, although the activity associated with smoking, i.e. taste, smell, physical manipulation of the cigarette, may acquire secondary reinforcing properties by virtue of the association of the smoking behaviour with the primary reinforcer, nicotine. Although nicotine has never been definitely proven to be the primary reinforcer (perhaps because of the obfuscating nature of smoking behaviour itself), there is much circumstantial evidence that nicotine is essential for maintenance of smoking behaviour.

Thus, nicotine is an extremely potent psychoactive drug and is absorbed from smoking in sufficient quantities to produce obvious physiological effects, e.g. tachycardia. Similarly, smoking behaviour is seldom observed unless the individual obtains some pharmacological reinforcement, e.g. THC from cannabis smoking, opiates from opium smoking. We might also observe that nicotine absorption represents a common denominator for snuffing, chewing and pipe smoking of tobacco. The effects of associated tar cannot be entirely excluded on this basis (as can carbon

monoxide) but it would appear likely that tar merely signals the arrival of nicotine to the smoker, since nicotine-free herbal cigarettes which also produce tar, are relatively unpopular. The relative popularity of inhalation-style cigarette smoking compared with snuffing, chewing, cigar or pipe smoking of tobacco is easily explained. None of these latter methods produce as rapid and as efficient absorption of nicotine as does inhalation-style cigarette smoking.

'Arousal Modulation' and 'Nicotine Addiction' models differ in the view taken of nicotine action. The former, 'Arousal Modulation' model postulates that nicotine, by virtue of its biphasic stimulant-depressant dose-response, (stimulant at low dosages versus depressant at high dosages) can effect changes in CNS arousal levels which can be stimulating or tranquillising to the smoker, depending upon the exact dosage absorbed. Since the cigarette smoker can easily control nicotine intake by altering smoking behaviour (i.e. puffing rate, puff intensity, inhalation), the smoker has at his disposal a 'tool' which combines to some extent the virtues of coffee (stimulant) and alcohol (depressant). This 'tool' can be used to control arousal towards a hypothetical optimum, i.e. to relax the anxious smoker and stimulate the bored or drowsy smoker. There is indeed some evidence (EEG, CNV and EMG) that these sorts of effects are possible. There is also evidence to show that smoking can improve various measures of performance (learning, memory, vigilance, etc.) perhaps as a consequence of this dual stimulant/tranquilliser property of nicotine.

'Nicotine Addiction' models of smoking postulate that certain CNS receptors become addicted to nicotine, i.e. they signal punishment when nicotine level at these sites falls below a critical level. From this point of view, we might regard the desire to smoke as a consequence of

nicotine 'hunger' in the classical drive sense, the purpose of smoking being to maintain nicotine homeostasis, just as regular heroin injections maintain opiate homeostasis at the CNS opiate receptors. There is a certain amount of evidence to support this contention. Thus, direct pharmacological manipulation (±) of nicotine at CNS receptors using, (-) nicotinic blockers (mecamylamine) or (+) intravenous nicotine shots/ infusion, produces alterations of smoking behaviour in the predicted directions (+ or - respectively). Similarly, smokers appear to be able to compensate, to some extent, for variations in cigarette nicotine delivery and so obtain fairly constant plasma nicotine levels.

Both types of smoking theory can muster supporting evidence and present mutual criticisms. Thus, the 'Nicotine Addiction' theorist can regard the postulated beneficial effects of smoking - relaxation or stimulation - as a subjective rationalisation for the feeling of relief produced by the arrival of nicotine at depleted CNS sites. However, the 'Arousal Modulation' theorist can reply that nicotine withdrawal symptoms comparable to going 'cold turkey' in heroin addiction have never been demonstrated and that, in any case, CNS as opposed to plasma nicotine levels fluctuate much more rapidly than can be explained by the smoker attempting to achieve nicotine homeostasis.

The truth probably lies somewhere between these two models, but since there is evidence, from genetic and longitudinal studies, that smokers are to some extent innately different from non-smokers, only longitudinal studies can ultimately resolve this question.

The work presented in this thesis investigates the objective physiological evidence for the claim that smokers can obtain these postulated stimulant and depressant effects from cigarette smoking, as appropriate to situation-induced and/or 'starting state' levels of arousal.

Smoking behaviour was observed in order to determine whether or not the smoker attempted to obtain small (stimulant) or large (depressant) dosages of nicotine as appropriate.

The results reduce to four major findings.

(i) Both stimulant, depressant and mixed effects of cigarette smoking were demonstrated on a number of physiological variables (EEG, electrodermal and EMG). No consistent effect was found on respiration rate or irregularity. Heart rate was invariably increased by cigarette-smoking.

(ii) The 'starting state' of the subject had important consequences as regards the magnitude and/or direction of smoking effect, stimulant versus depressant. Thus, for subjects in high arousal, i.e. stress conditions, cigarette smoking produced either definitely depressant or mixed effects on EEG 'α' and SCL, while during low arousal, i.e. sensory isolation conditions, cigarette smoking produced strong stimulant effects on these measures. Similarly, analysis of individual differences in levels of activity in various arousal systems, particularly EEG 'α' and SFs, demonstrated that individuals with low baseline levels of arousal tended to show stimulant effects from cigarette smoking, whereas individuals with high baseline levels of arousal tended to show depressant effects from cigarette smoking. Personality, as a starting state mediator of smoking effect, appeared to be of relatively minor importance. High cigarette consumption was a strong predictor of reduced cigarette induced tachy-cardia, perhaps as a consequence of tachyphylaxis or elevated 'tonic' plasma nicotine levels.

(iii) Sham smoking accounted for around 50% of all effects, in both directions (stimulant or depressant), with the exception of cigarette induced tachycardia, which appeared to be entirely accounted for by

tobacco smoke inhalation, and thus by implication was entirely due to pharmacological actions of nicotine. In consequence, nicotine probably accounted for less than 50% of any smoking effect, with the exception of tachycardia, since sham smoking an unlit cigarette is only a poor approximation of a true nicotine-free smoking placebo.

(iv) Smoking style varied in the predicted directions. Increased vigour of cigarette smoking occurred during stress to obtain larger (depressant) dosages of nicotine. Increased vigour of cigarette smoking occurred in response to smoke dilution by ventilated holders. The latter 'self titration' for nicotine appeared to be extremely rapid, being 80% successful within the period of two successive cigarettes, from analyses of burnt tobacco weight, and approaching 100% successful as regards comparisons of smoking effect on physiological measures, including heart rate, between high and low delivery cigarettes. The crucial regulatory variable appeared to be puff pressure in both cases. Striking and stable idiosyncracies of the vigour of smoking style were evidenced which perhaps resulted from individual differences in nicotine sensitivity.

The implication of these results is that cigarette smoking represents an activity which could be used by a smoker to regulate his or her arousal level in the direction appropriate to the situation, i.e. to relax the anxious smoker and to stimulate the drowsy or bored smoker. The question of major interest is to what extent can the laboratory results be extended to the 'real world'? It is probable that the laboratory results give a fair indication of what range of effects may be achieved from smoking a cigarette by the solitary smoker when anxious, bored or drowsy. These effects would probably be reinforcing.

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ACKNOWLEDGEMENTS

I wish to thank friends and colleagues for their help and advice, and specifically my mother and father for help in typing, Mrs. Valerie Mitchell for typing, Ms. Ros Ferner for proof reading and comments, Dr. G.L. Mangan, Dr. H. Ashton, Professor J.W. Thompson, Mr. R. Stepney, Dr. T. Paisey and Dr. R.E. Thornton for advice, Mr. Ricardo Marsh for much help with the CNV and Mr. P. Ward and other technicians at the Psychology Department for technical help.

Experimental work was carried out with the technical support and services of the Department of Experimental Psychology, Oxford, and the Clinical Psychopharmacology Unit, Newcastle upon Tyne.

The experimental work was funded by an S.S.R.C. studentship.

CHAPTER 1

I N T R O D U C T I O N

Historical

Over 65 million years ago the ancestors of today's tobacco plant were undergoing evolution of their plant chemistry to produce alkaloids such as nicotine. Alkaloids have no known function in plant metabolism and it has been suggested that they are evolutionarily justified as a chemical deterrent against herbivores (Bever, 1970). Indeed, some authors (Swain, 1974; Gritz and Siegel, 1979) have noted that this evolutionary advance of plant chemistry coincided with the sudden extinction of the dominant animal life-form of that era - the dinosaurs. These giant reptiles, unlike the birds and mammals that followed them, perhaps failed to evolve effective mechanisms with which to detect and/or detoxify alkaloids (N.B. there are many other theories concerning the extinction of dinosaurs).

The effectiveness of alkaloids, and nicotine in particular, as a chemical defence against modern animals, may be judged from a contemporary account of a wild tobacco, Nicotiana glauca (African Tree tobacco with high nicotine content).

> " ... the ostrich is particularly susceptible, the symptoms being staggering gait, spasmodic jerkings of the head, dullness and stupor. Death occurs within a few hours ... One seed is said to be certain death to a chick ostrich up to one month old." (Watt and Breyer-Brandwijk, 1962)

Although such experiences undoubtedly act as a deterrent for the would-be herbivore, the consumption of smaller quantities of (the

less toxic) tobacco leaf is not lethal for many animals, and may even be reinforcing (Watt and Breyer-Brandwijk, 1962). Indeed, it has been suggested that humans learned much about plant produced drugs through observing the effects of accidental self-administration by animals. Folklore abounds with such legendary discoveries of various alkaloid actions of coffee (caffeine), qat leaves (cathine, cathedine, cathenine), coca (cocaine), Datura (hyoscyamine, scopolamine, atropine), etc.

One typical story, told by an informant from the Huichol community of Bance de Calitice (Nayarit, Mexico), claims that tobacco was first used by birds which favoured the yellow flowers of the wild varieties (e.g. Nicotiana rustica). The tobacco enabled the birds to fly high and strong and see great visions. Accordingly, early man copied the behaviours in his quest to communicate with gods and see visions (while high, verging on toxic, doses of nicotine may be hallucinogenic in their own right, it is possible that 'communication' with gods requires the addition of other alkaloids to a smoking mixture (cf. Gritz and Siegel [1979] for review).

'Nicotiana tabacum' and 'Nicotiana rustica' are plants indigenous to the Americas. Natives of the Americas had smoked and chewed these herbs for a variety of narcotic, stimulant, medicinal, social and religious reasons for a long time prior to the arrival of European explorers. 'Tupa' or 'devil's tobacco' is the name by which the Mapuche Indians of Chile know the tall herb 'Lobelia tupa'. The Mapuche smoked the leaves for their narcotic effect. In addition, the expressed juice was used to relieve toothache and in North America 'Lobelia inflata' was also chewed for its narcotic effects. The active principle 'Lobeline' is similar to nicotine in action.

Just as the natives of the Americas are postulated to have modelled on animal drug-taking behaviour, so too did the first Spaniards

to set foot in the New World model the natives predilictiom to tobacco smoke.

> "I know of Spaniards who imitate this custom, and when I reprimanded the savage practice, they answered that it was not in their power to refrain from indulging in the habit". - De las Casas, the Bishop of Chiapas, who published the letters of Columbus, describing the initial encounter with tobacco smoke. (Lewin, 1931, p. 288)

Tobacco was first brought to Europe in the 16th Century by explorers such as Sir Walter Raleigh, M. Jean Nicot (hence 'nicotine') and André Thevet. Such was the rapidity of the growth of demand for this herb that by 1640 the annual export from Virginia and Maryland to England was over one million pounds to service almost 7,500 tobacco shops in London alone (Emboden, 1972). This spreading usage can be seen continuing today in the underdeveloped countries of the world.

To this extent, it is interesting to note that tobacco may replace an indigenous herb in popularity. After the arrival of white men in Australia tobacco became popular among the natives. Formerly, leaves of the Duboisia species were a popular narcotic going under the name of 'pituri' but it was not long before these people became interested in 'white fellow pituri'. This led to the use of some native tobaccos, N. suaveolana, N. excelsia and N. gossei, taken in a quid (chewing) form. The active principle of 'pituri' is scopolamine - primarily a depressant, secondarily a hallucinogen.

This rapid spread of tobacco usage was subjected to some opposition from the outset and anti-smoking measures have been taken from the earliest times. Thus, in 1590 the Pope outlawed all smoking in the Vatican under the threat of excommunication. In 1604 King James'

'Counterblasts to Tobacco' describes the habit thus:

> " ... in the black stinking fumes thereof nearest resembling the horrible Stygian smoke of the pit that is bottomless."

The trend of increasing smoking prevalence and tobacco consumption has continued up to the present day (cf. Figure A,B). However, there is recent evidence that consumption and prevalence has levelled off. This development probably reflects the results of Health Campaigns and perhaps, in addition, the fact that only a part of the population is 'at risk', as will be argued later.

What general conclusions can be drawn from these observations? They would appear to be the following:

(1) Since nicotine is the constituent common to snuff, chewing, cigar, pipe and cigarette tobacco, rather than any other constituent such as tar or carbon monoxide, nicotine would appear to be the most likely reinforcer for tobacco usage. Moreover, smoking as a habit, has never been widely practised in the absence of a pharmacologically active alkaloid such as cannabis or opium or nicotine.

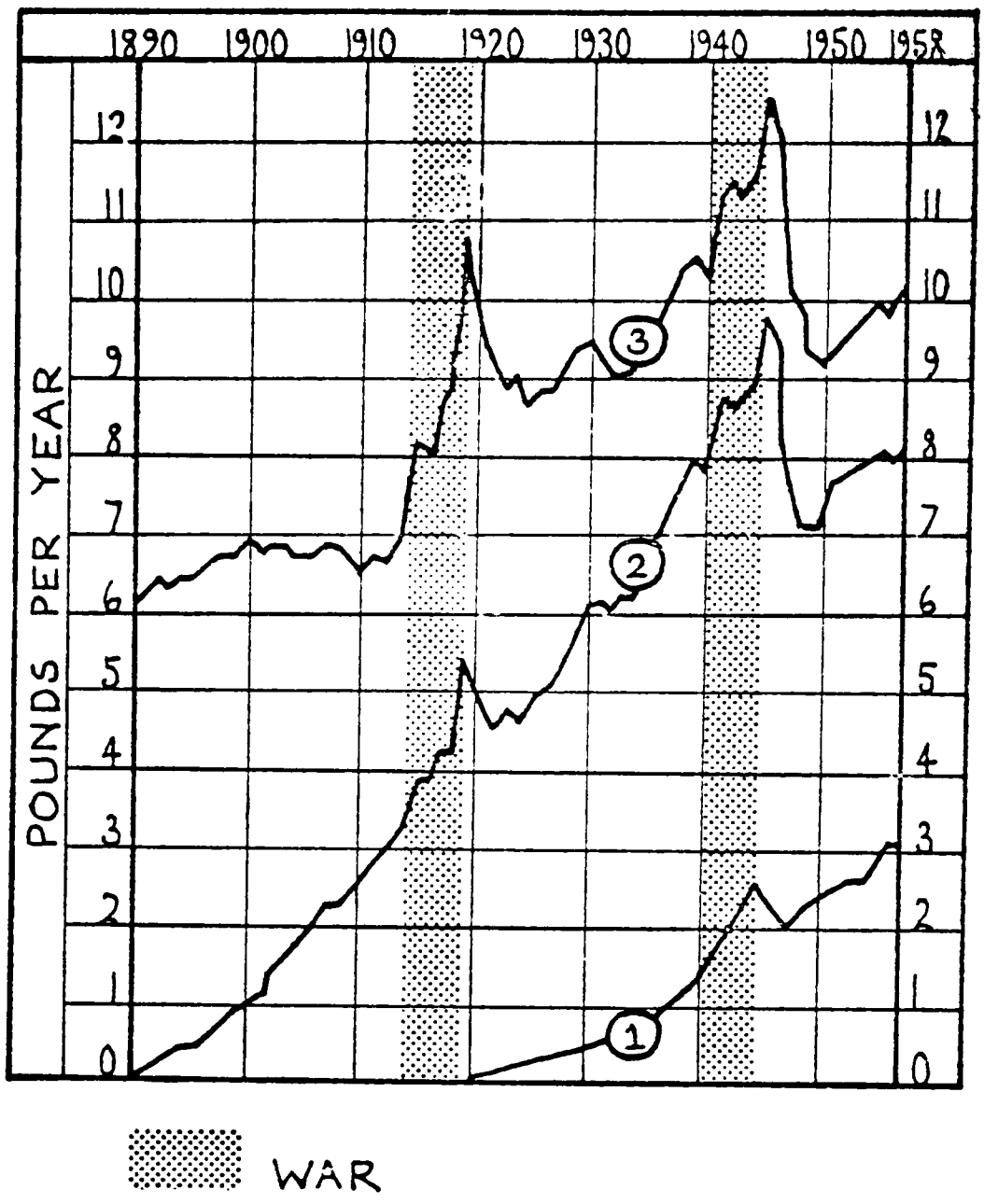
(2) Smoking, as opposed to snuff/chewing, appears to have been the preferred route of administration of tobacco and presumably nicotine, although this varied with fashion, e.g. snuff was popular in the 18th Century.
All these routes of administration, lung, buccal, nasal (mucosa) as opposed to ingestion will avoid degradation by the liver (absorption via the gut causes most of the nicotine to be degraded to cotinine in passing through the liver e.g. Russell [1976] or Goodman and Gilman [1971]).

ANNUAL TOBACCO CONSUMPTION PER ADULT
UNITED KINGDOM 1890-1958

① WOMEN (CIGARETTES)

② MEN (CIGARETTES)

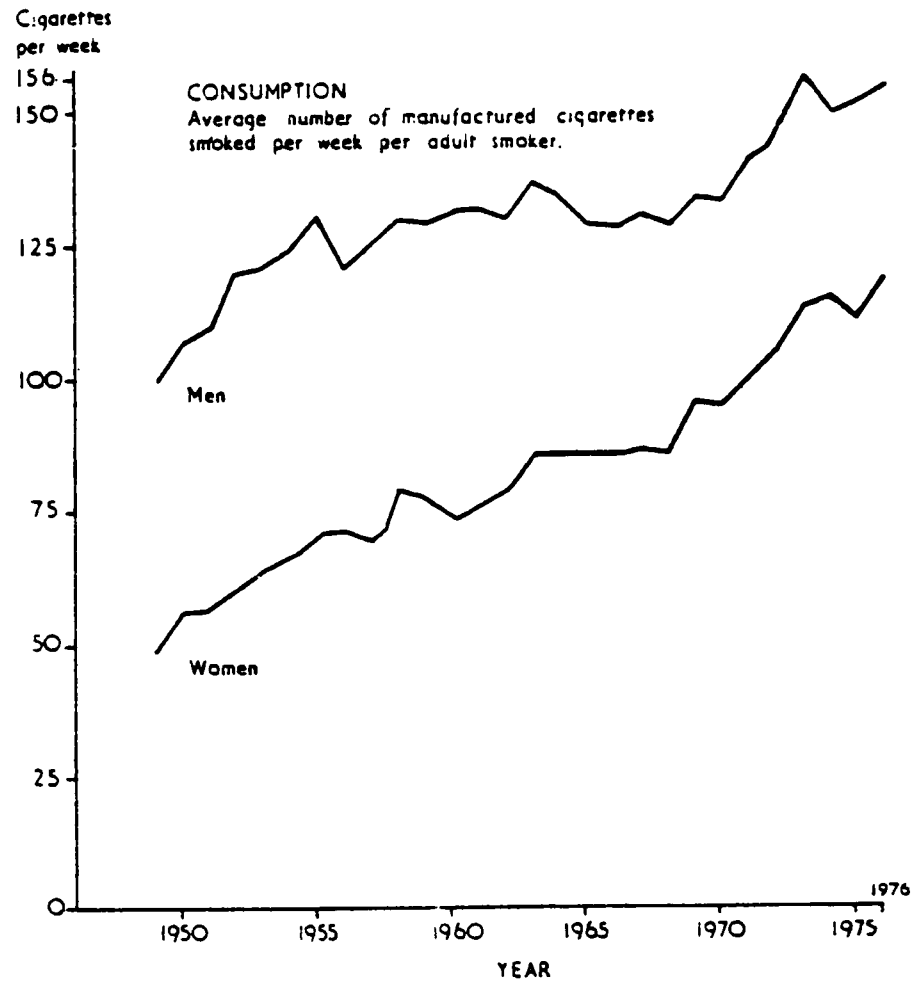
③ MEN (ALL TOBACCO)



By permission, after Royal College of Physicians Report (1962). Following this the number of cigarettes smoked by men dropped sharply, but has since risen to about its previous level. Women appear to have ignored the Report altogether.

FIGURE A : Historical trends in tobacco consumption for the U.K. Note the increase in consumption during war. From Laurence (1973)

Trends in cigarette smoking in the UK among adult males and females since 1949: Consumption (Source. TRC)



Trends in cigarette smoking in the UK among adult males and females since 1948: Prevalence (Source: TRC)

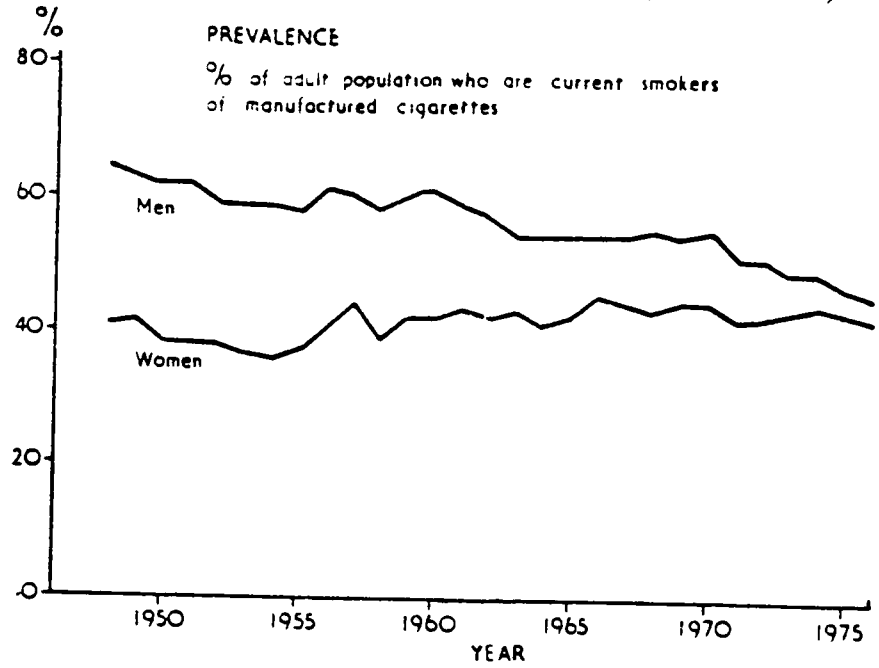


FIGURE B : Trends in cigarette smoking in the U.K. for adult males and females. Consumption (top) Prevalence (bottom), from Capell (1978).

(3) From the earliest times, the effects ascribed to tobacco and the reasons for usage have varied widely - religious, medicinal, aphrodisiac, social/political (peace pipe), anti-fatigue, and tranquillising. One might broadly describe these as being stimulant and depressant:

stimulant : anti-fatigue, aphrodisiac

depressant : medicinal, social, tranquillising

It is difficult to say whether the religious usage was primarily stimulant /depressant or both. The stimulant and depressant properties of nicotine are, as will be argued later, the ultimate reinforcer for cigarette smoking.

Areas of smoking research

Since the publication of the Surgeon General's Report in 1964, and subsequent Health Department reports in various countries, which firmly established the health hazards of cigarette smoking, there has been a steady expansion of research into all areas concerned with smoking and, in particular, behavioural, i.e. non-disease related: Public Health education studies, cessation programmes, etc. (the 1978 Directory of on-going research in Smoking and Health lists 973 research projects across the world). However, the effects on the consumption of cigarettes has been relatively slight in comparison to the effort expended. The explanation put forward in this thesis is that much of the behavioural research into smoking has overtly or tacitly assumed a Nicotine Addiction Model and that this underlying assumption is unsound.

GENERAL

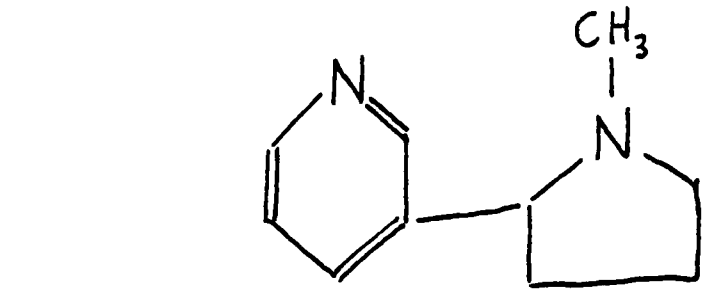
Nicotine, first isolated from the leaves of tobacco by Posselt and Reiman in 1828, is one of the alkaloids. It is colourless, volatile and strongly alkaline in reaction. On exposure to air it turns brown and acquires the odour of tobacco. The alkaloid is readily soluble in water, alcohol and ether and forms water-soluble salts. Under atmospheric pressure, it boils at 246° C and is consequently volatilized in the cone of burning tobacco at 800° C. The free base is present in the smoke suspended on minute droplets of tar (0.3 - 1.0 μ) which are small enough to reach the small airways and lung alveoli. The structure of nicotine shows it to be a combination of a pyridine and a pyrrolidine ring (Goodman and Gilman, 1971; Russell, 1976).

Lobeline is the closest plant-derived (from Lobelia inflata) analogue of nicotine and shares many of its pharmacological properties to the extent of cross-tolerance. However, it is less potent than nicotine which may account for the fact that, apart from limited usage in some South American tribes, it has not enjoyed the international popularity of Nicotiana tabacum (Emboden, 1972).

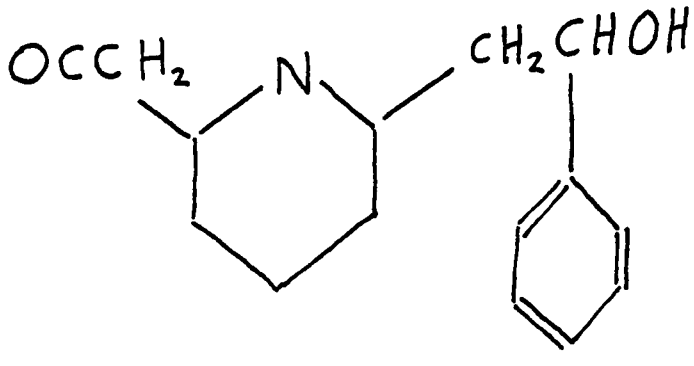
Nicotine exists in both ionized and neutral forms - depending on the ambient pH. At body pH (7.36-7.44) it is mainly ionized with a positive charge on the quaternary nitrogen and this, the Nicotinium ion, is the pharmacologically active form (cf. Figure 1).

The structural basis for the pharmacological activity of the nicotinium ion would appear to be resemblance to acetylcholine in terms of the spacing of positive and negative charges (cf. Figure 2 ; after Kier (1968) and Cynoweth, Ternas, Simeral and Maciel (1973)).

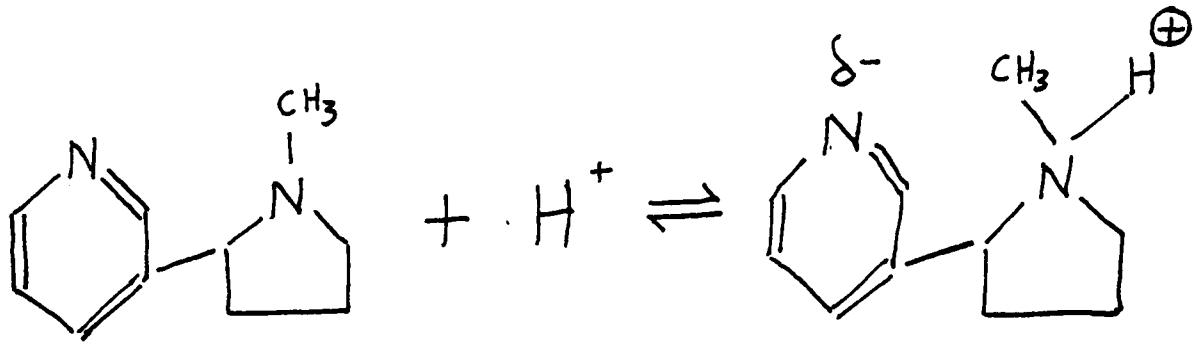
Acetylcholine is a flexible molecule and can thus take up another



NICOTINE BASE



LOBELINE



NICOTINE BASE NICOTINIUM ION

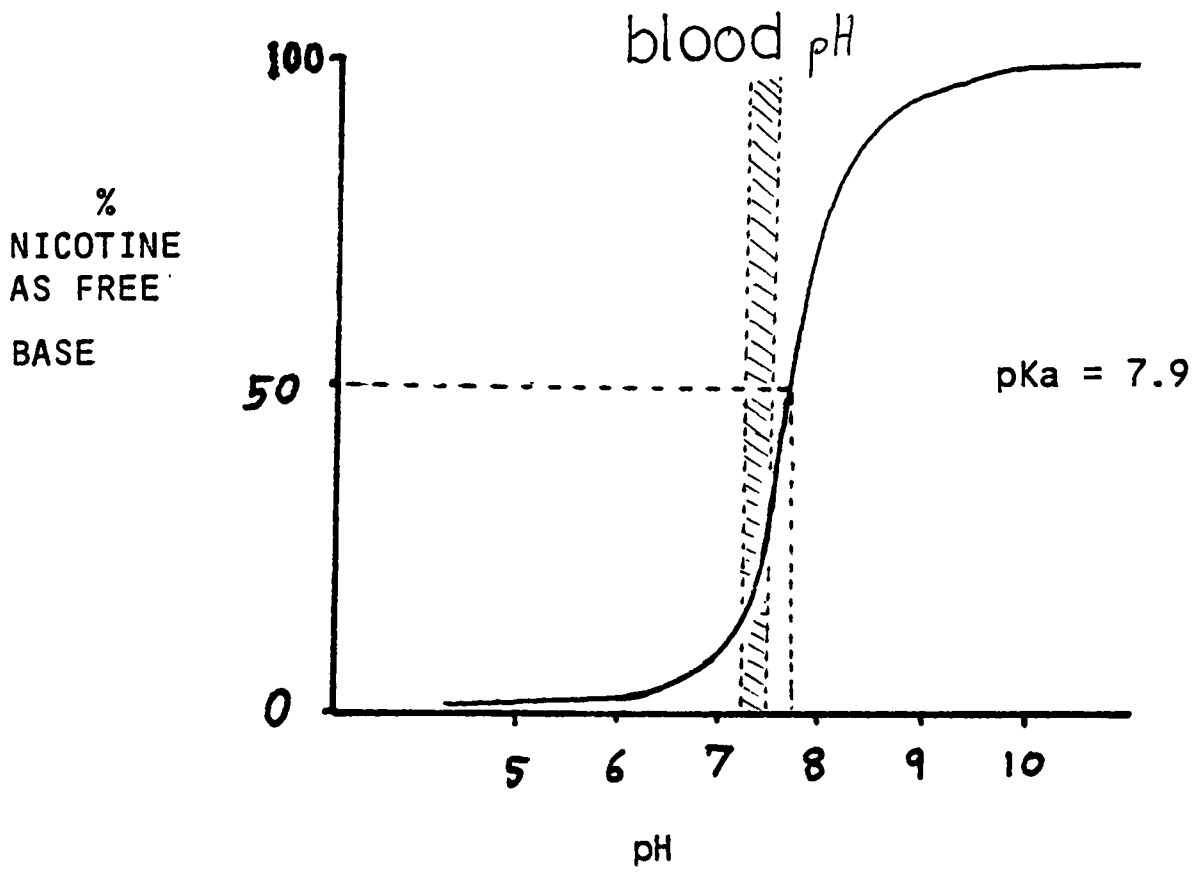
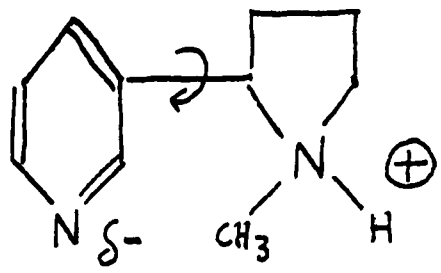
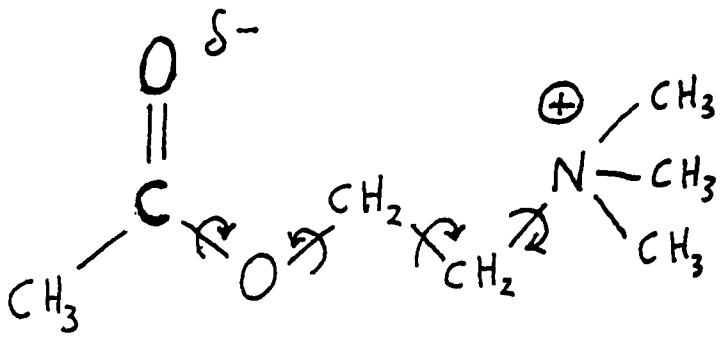


FIGURE 1 : Structure of Nicotine and Lobeline. Formation of the nicotinium ion and dissociation curve.

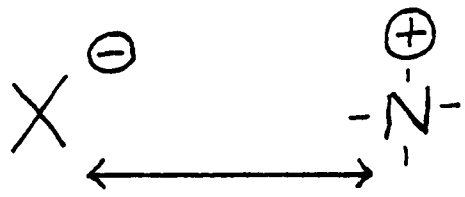
After: Travell (1960)



NICOTINIUM ION



ACETYLCHOLINE

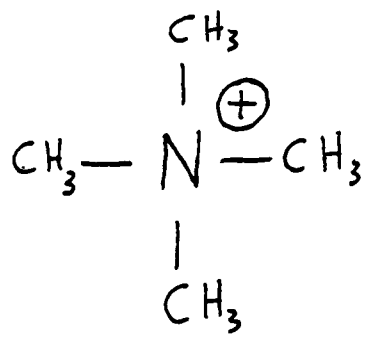


CRITICAL CHARGE SPACING FOR NICOTINE AGONISTS

4.85 ± 0.1A

(Rotational Axes:

Methyl group rotations ignored)



N.B. the negative charge may not be absolutely essential for activity since TMA does not possess it.

TMA, a synthetic nicotinic agonist

FIGURE 2 : Similarity of charge structure between the nicotinium ion and acetycholine.

After: Kier (1968) and Cynoweth, Ternas, Simeral and Maciel (1973).

conformation which allows it to bind to another type of cholinergic receptor - muscarinic - which nicotine cannot do, presumably because it has only one bond to rotate around thus achieving a much more limited range of configurations than acetylcholine, which has four bonds to act as major axes of rotation (see Kier, 1968 and Cynoweth et al., 1973, for a more detailed discussion) (cf. Figure 2).

Muscarine, pilocarpine and arecoline are closely related mushroom and plant-derived cholinomimetic alkaloids containing a positively charged nitrogen atom. The crucial difference between them and nicotine is that they are agonists for muscarinic receptors whereas nicotine is selective for nicotinic receptors and hence the names. Stimulation of these two types of cholinergic receptors can lead to totally different effects (see later "Pharmacology of Nicotine"; thus nicotine in the range of doses absorbed from smoking has relatively minor stimulant and depressant effects whereas the various muscarinic agonists can produce hallucinogenic effects in addition to straight stimulant effects (muscarine from amanita muscaria - fly agaric). Arecoline, from Betel nut chewing, is a mild stimulant and internal parasiticide, these benefits offsetting the unpleasant concomitants of the habit, which are the large amounts of red saliva regularly spat out (Emboden, 1972).

PHARMACOKINETICS

(i) Absorption

(ii) Blood levels

(iii) Distribution

(iv) Metabolism and Excretion

(i) Absorption

As mentioned earlier, the pKa of nicotine is 7.9 and over the pH range 9 to 7 the sigmoid dissociation curve accounts for over 80% of

the ionisation of nicotine base to nicotinium ion (cf. Figure 1). This has important consequences for both absorption and excretion of nicotine since the nicotinium ion is far less permeable to membranes than the base, presumably because the presence of strong charges on the molecule makes it difficult to pass through the lipid phase of the membrane - ions being more stable in high (aqueous) rather than low (lipid) dielectric constant environments. Thus alkaline conditions will favour the uncharged nicotine base and so lead to greater ease of absorption than do acidic conditions.

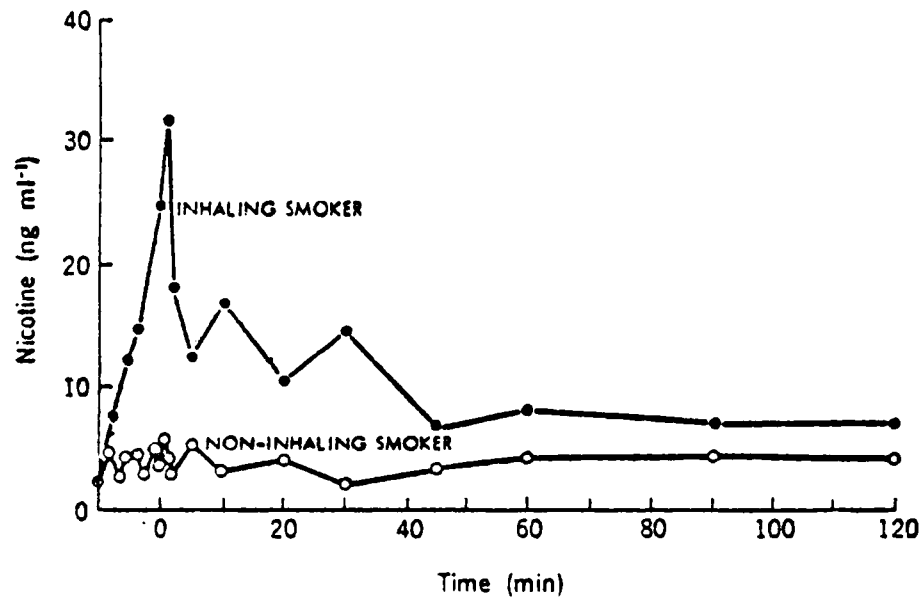
Such high pH conditions are found in air-cured pipe and cigar smoke (pH = 8.5) and the intestinal juices, whereas low pH conditions are found in flue-cured cigarette smoke (pH = 5.5) and even lower pH in the stomach acids. Neutral conditions are found in the lung alveolar fluids (pH = 7.4). The saliva and urine can vary typically over pH ranges 5.6 - 7.6 and 5.2 - 6.5 respectively (pH data from Russell, 1976; Russell and Feyerabend, 1978; and Schachter, 1977). These variations in pH have important consequences for absorption and re-absorption of nicotine.

Thus an effective dose of nicotine (as indicated by such measures as rise in heart rate, femoral arterial pressure or directly from plasma nicotine levels (Armitage, Hall and Morrison, 1968; Armitage and Turner, 1970; Armitage, 1978) may be absorbed from the small area of the buccal mucosa in the case of alkaline cigar and pipe smoke (nicotine base), whereas absorption of nicotine from acidic cigarette smoke (nicotinium ion) in the buccal mucosa is virtually zero. This is one of the factors favouring inhalation-style smoking of cigarettes - the much greater surface area of the lungs (of the order of the area of a tennis court) overcomes the absorption difficulty with acidic cigarette smoke. Absorption through the lungs is very nearly as efficient as intravenous injection (cf. Figure 3,

4) and far faster and more efficient than buccal absorption (Armitage, Hall and Morrison, 1968) although the crucial variable is probably the rate of absorption; in particular, whether the dose is absorbed slowly as in the case of buccal absorption of cigar/pipe smoke, chewing tobacco and intravenous nicotine infusion or in rapid discrete doses - bolus form, as in the case of cigarette smoke inhalation and intravenous nicotine bolus injection. This is crucial not only in terms of the final biphasic pharmacological effects and behavioural consequences of nicotine (as discussed later) but also in terms of blood levels. It appears from work on cats that higher blood nicotine may be obtained after multiple bolus injections than after slow intravenous injections of the same amount of nicotine given over the same period of time (Turner, 1971) and that this will cause much higher brain nicotine concentrations (see Distribution of nicotine).

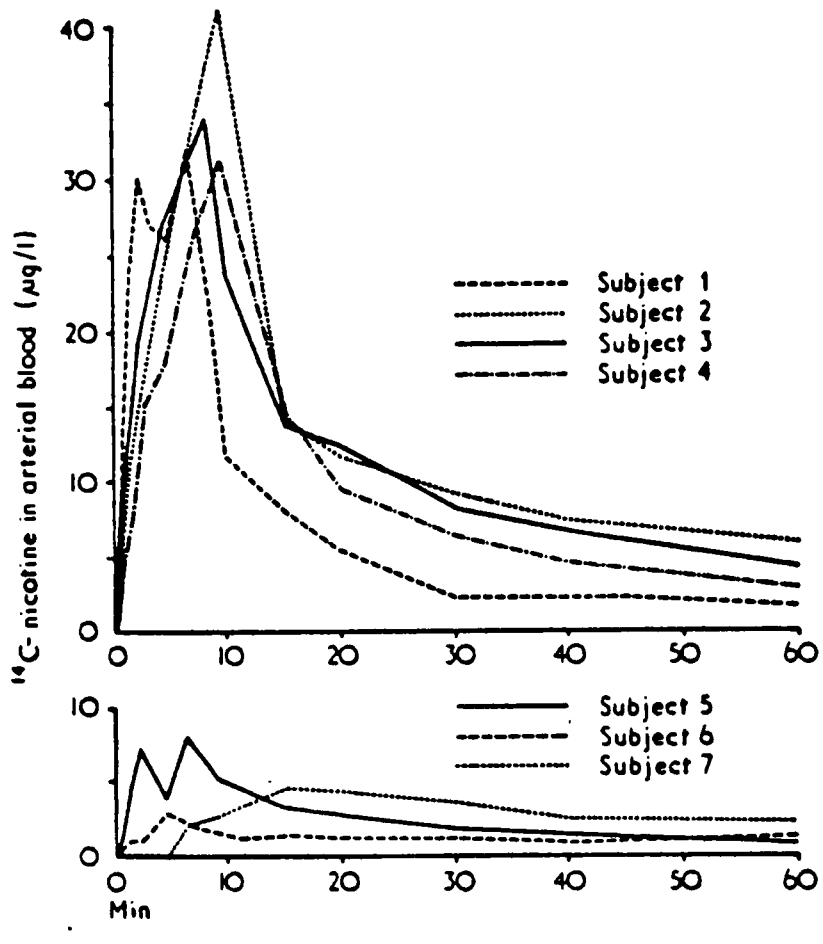
Studies have alsoshown that the buccal absorption of nicotine is dependent on the pH of the buccal saliva which can be experimentally varied by the use of buffered solutions (Beckett and Triggs, 1967). Since the pH of saliva shows diurnal variations (5.6 - 7.6; Brawley, 1935) and also changes before, during and just after a meal (Travell, 1960) it has been suggested by Russell (1976) that such pH fluctuations may affect buccal absorption of nicotine during smoking as well as salivary excretion and re-absorption of nicotine after smoking.

The reason that ingestion of tobacco as opposed to smoking, chewing and snuffing tobacco has never become a popular habit probably resides in the fact that absorption of nicotine by this route is very slow and inefficient. Thus, nicotine will not be absorbed easily from the stomach because of the extremely acidic environment. Travell (1960) found that nicotine injected into the ligated cat stomach at pH 8.6 in a dose of

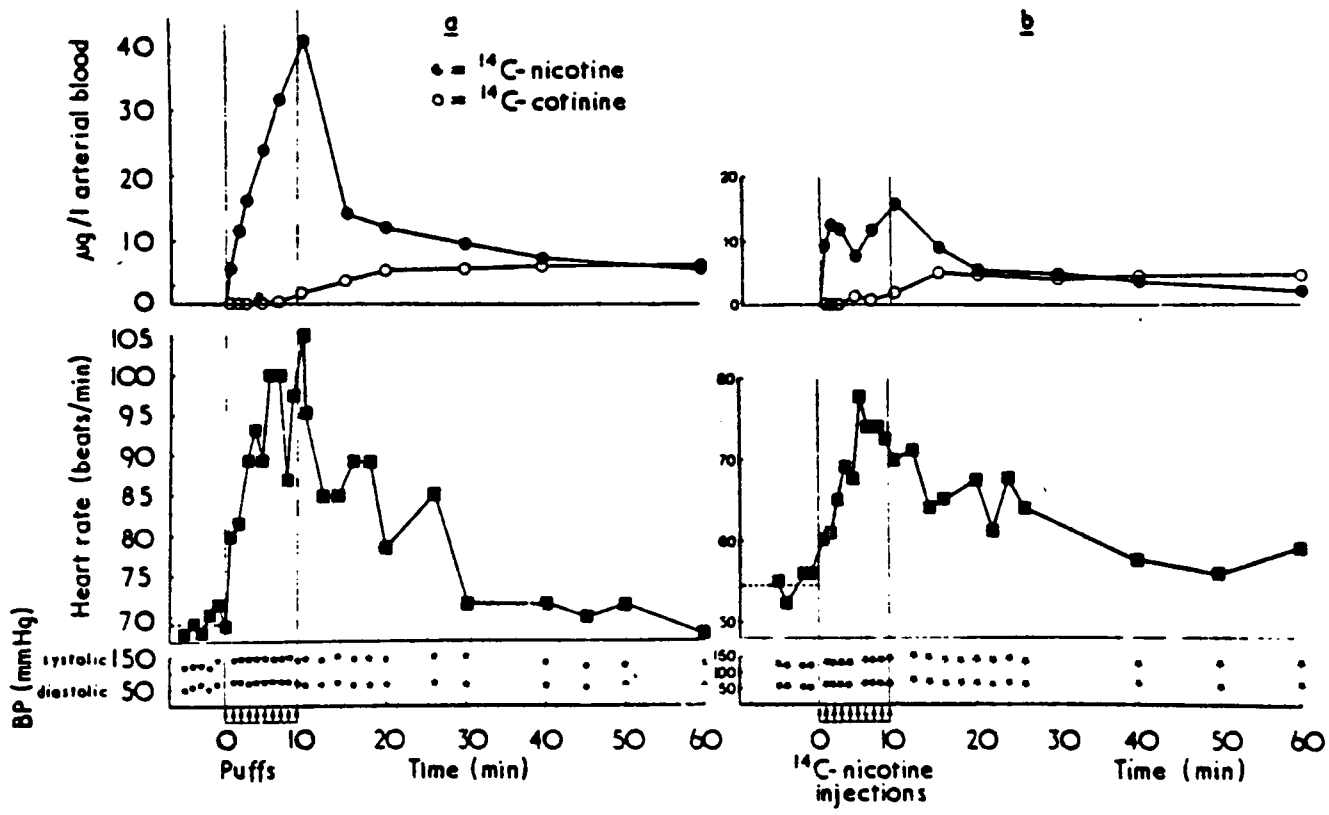


Plasma nicotine concentrations in an inhaling smoker and a non-inhaling smoker during and after smoking one cigarette which was discarded at time = 0 min.

FIGURE 3 : Plasma nicotine concentrations in an inhaling and non-inhaling smoker. From Russell (1976).



Arterial blood levels of ^{14}C-nicotine in habitual smokers, presumed to inhale (subjects 1 - 4), in an inhabitual smoker presumed to inhale less deeply (subject 5) and in non-smokers (subjects 6 & 7) after smoking one cigarette labelled with ^{14}C-nicotine.



Arterial blood levels of ^{14}C-nicotine (●) and ^{14}C-cotinine (○) heart rate (■), and blood pressure (*) during and after smoking a cigarette labelled with ^{14}C-nicotine (a) and during and after intravenous administration of 1 mg ^{14}C-nicotine given in ten divided doses, each of 0.1 mg (b).

FIGURE 4 : Arterial blood levels of ^{14}C nicotine in smokers. From Armitage (1978)

20 µg/Kg (at least twice the buffered fatal dose for cats) was fatal in 41 minutes whereas 50 µg/Kg injected into the stomach at pH 1.2 caused no effects. Absorption of effective doses of nicotine will thus have to wait until the stomach contents pass into the intestines and are neutralised. Data from Russell and Feyerbend (1978) suggested that ingested nicotine in humans takes 3.5 hours to appear in the plasma, although drinking water (two 270 ml drinks) improves absorption markedly, presumably by causing gastric emptying and dilution of the acidic gastric juices. However, consideration of the huge doses[1] of ingested nicotine, required to mimic the plasma nicotine levels achieved by smoking, demonstrates that the aspiring tobacco eater would regularly swallow mouthfuls of tobacco leaf unless he took the precaution of consuming bicarbonate to neutralise his gastric acids. However, this could have serious consequences since nicotine overdose can be fatal.

Even after the ingested nicotine is absorbed a large proportion will be subject to degradation by the liver since, unlike nicotine absorbed by the mouth or lungs, all the nicotine absorbed from the gut will pass through the liver via the Hepatic-Portal system before reaching the major target organ - the brain. Re-absorption of previously excreted nicotine from the bladder and renal tubules will occur at high pH and this may be of some consequence as regards 'bumps' in blood nicotine levels and in determining smoking rates (cf. later under 'Metabolism and Excretion').

(ii) Blood Levels

With the recent advances in assay procedures such as gas chromatography, which distinguishes nicotine from its metabolites, it has

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1 44mg nicotine ingested produced a plasma nicotine level of 40ng/ml. Under identical conditions - 12 hour abstention from smoking, acidic control of urine pH, ad libitum fluids - 40Ng/ml plasma nicotine was achieved after the second 1.2mg cigarette.

been possible to construct fairly accurate time-based plasma nicotine profiles for smokers. It would appear that plasma nicotine, for smokers who inhale, peaks about the time of finishing smoking a cigarette. The decay side of the curve has a half-life of less than 30 minutes and probably separates into two stages, (a) an initial rapid drop caused by re-distributions within the body, e.g. uptake by the brain and venous mixing - this 'alpha' half-life is 2-3 minutes (Russell and Feyerabend, 1978) and (b) subsequently a slower 'bumpy'[2] decline caused by degradation of nicotine by the liver, kidney and lungs and nicotine excretion by the kidneys and to a lesser extent through the gut, salivary glands and sweat glands.

Considerable variations in plasma 'beta' half-lives have been reported which may represent both true individual differences in rates of nicotine metabolism and excretion and also variations in smoking style which will determine how rapidly the peak plasma nicotine levels are achieved and subsequently drop through the 'alpha' (re-distribution) and 'beta' (metabolism and excretion) phases. Typical 'beta' half-lives are 20-30 minutes for venous blood-nicotine (Russell, 1976), and 10-15 minutes for arterial, brachial, blood-nicotine (Armitage, 1978).

The major point of interest in the time-based plasma nicotine profiles is the extreme rapidity of the peak rise and initial drop (cf. Figure 3,4). This is a feature of absorption of nicotine by inhalation. If the non-inhaling cigarette smoker shown had been puffing a cigar or

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[2] The 'bumps' are suggested by Russell (1976) not to be errors but to be due probably to re-distributions, e.g. release from the brain, urinary bladder re-absorption (especially under conditions where the urinary pH is shifting from high to low - see later), salivary re-absorption and perhaps even metabolic re-cycling: reduction of nicotine-1-N-oxide back to nicotine by the N-oxidereductase system in the colon (Russell, 1976), although this latter effect must be small since the re-cycled nicotine will be subject to degradation in the liver before entering general circulation.

pipe of air-cured tobacco instead (which would have allowed buccal absorption of nicotine, cf. earlier) one would have observed a much slower rise in plasma nicotine than with inhaled smoke. This has been demonstrated on cats (Armitage et al., 1968) and more recently in humans using ^{14}C nicotine labelled cigarettes and cigars with measurements of arterial nicotine (cf. Armitage, 1978). In fact, the peak venous blood nicotine concentrations probably represent a serious under-estimate of the peak arterial bolus concentrations, which actually arrive at the brain, of the order x4 to x5 (Russell, 1976) and more refined continuously repeated sampling of blood in the carotid would probably reveal a 'saw-toothed' curve, the 'teeth' corresponding to nicotine blood boli after inhalation of each smoke puff.

This pattern of arrival of nicotine at the brain has the important consequence that the equilibration of the brain with the bolus peaks achieves higher brain-cell nicotine levels than would be possible with the blood levels shown after nicotine bolus dispersion or with those blood levels obtained by slower absorption of far larger quantities of nicotine, e.g. by slow intravenous infusion or buccal absorption. This in turn has implications concerning control by the inhaling smoker of nicotine intake: the 'puff-by-puff finger-tip control' as described by Armitage (1978). This method allows the smoker to titrate himself with nicotine very accurately, whether to obtain a stimulant or depressant dose, or maintain some 'set' nicotine level for a while. Furthermore, the great number of nicotine boli reinforcements available for inhalation style versus non-inhalation style smoking probably accounts for the greater popularity of inhalation-style cigarette smoking as opposed to the cigar, pipe-smoking or chewing or snuffing - the so-called "dependence on high-nicotine boli " described by Russell and Feyerabend (1978). These

implications and their bearing on the nature of reinforcement(s) involved in tobacco smoking are discussed more fully later.

(iii) Distribution of nicotine in the body

Our knowledge of the distribution of nicotine in man following smoking is as yet largely inferential since the techniques employed in animal research, i.e. nicotine assay of organs at various times post-smoking or post-injection together with whole body auto-radiographs with ^{14}C-labelled nicotine are inapplicable. However, with sensitive counters placed over the body and brain and low proportions of ^{14}C-labelled to unlabelled nicotine, investigators might reasonably attenpt similar whole-body autoradiographs in man since, analogously, radioactive xenon or krypton has been used (safely) to measure variations in distribution of blood flow to different parts of the human brain (cf. Sveinsdottir, Torloff, Risberg, Ingvar and Lassen [1970]).

The distribution of nicotine in the body depends very much on the route and rate of administration. Thus, any mode of nicotine administration which involves an initial route through the portal venous system, i.e. ingested nicotine or intraperitoneal injections, will result largely in nicotine being concentrated in the liver and degraded, whereas intravenous injections or absorption through the lungs will avoid this and initially lead to a preferential concentration of nicotine in the brain. In addition, fast rates of nicotine administration - rapid injections of nicotine intravenously or absorption through the lungs to produce nicotine boli - will favour initial concentration of nicotine in the brain,'bolus uptake', both for the reasons given earlier, and also because the high concentration of arterial blood nicotine achieved by these methods, and subsequent blood nicotine equilibration with brain tissue, leads to high nicotine levels in the brain (Stahlhandshake, 1970).

Whole body autoradiograph of mice injected intravenously with ^{14}C-labelled cigarette nicotine clearly shows the rapid uptake of nicotine by the brain, liver, kidneys, salivary glands and cells in the fundus of the stomach (Schmiterlöw et al., 1967). Five minutes after injection most of the nicotine is in these organs and tissues. Thirty minutes after injection, most of the nicotine taken up by the brain has left and has been taken up by the liver, kidneys, salivary glands and stomach. The rapid clearance from the brain is not due to metabolism since the brain does not metabolise nicotine. In contrast, by 30 minutes, most of the radioactivity in the liver and kidneys is due to metabolites rather than unchanged nicotine. The nicotine in the brain is concentrated in the grey rather than the white matter and particularly high levels occur in the cellular layer of the hippocampus (which has implications regarding the effect of smoking on the orienting response and memory - cf. later discussion). These findings have since been confirmed by later studies in cats (Turner, 1969 and 1971).

The study of Stahlhandshake (1970) using radioactively-labelled nicotine injections in mice supports and extends the above work. By injection of ^{14}C-nicotine by different routes - intravenously (i.v.) and intraperitoneally (i.p.) - it was possible to demonstrate that the major part of the ^{14}C-nicotine was concentrated in the first few minutes in the brain (i.v.) and liver (i.p.) respectively, according to the route taken, and that with i.p. injections the blood level of nicotine was much less. This is presumably due to nicotine degradation by the liver in the case of the i.p. injections, since all the injected nicotine enters the venous portal system.

This interpretation was supported by the fact that phenobarbitone

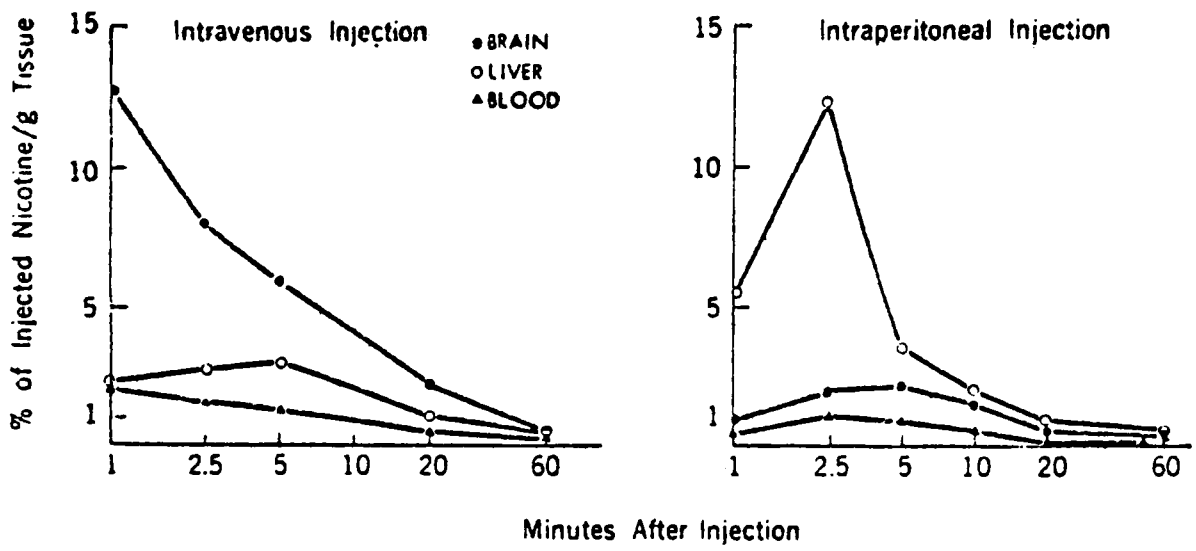
pre-treatment, known to increase the rate of metabolism of many drugs, lowered brain nicotine levels obtained after intraperitoneal injection but not the levels produced by intravenous nicotine. The phenobarbitone pre-treatment enhances the liver metabolism of nicotine and so differentially reduces the brain nicotine with the intraperitoneal route of administration.

The relatively higher brain-blood nicotine gradient seen in the first few minutes post-intravenous nicotine injection as opposed to post-intraperitoneal injection is most likely to be the effect of 'bolus-uptake' (cf. Figure 5). This is reflected in the fact that, during the first few minutes, the brain-blood ratio of the i.v. nicotine injection route is falling, whereas with the i.p. nicotine injection it is rising. This point would be clearer if blood-nicotine levels were available immediately post-nicotine injection since the nicotine bolus has already passed the brain by the time the first reading (at 1 minute) has been taken. In addition, closer consideration of the data from this experiment would seem to indicate that there is an active uptake of nicotine by the brain against a concentration gradient (cf. brain versus blood levels in the i.p. injection case above).[3] Active uptake of nicotine is known to occur in the superior cervical ganglion and to be further enhanced ('activation uptake') on nicotine-induced depolarisation of the cells (Brown et al., 1969 and 1971).

In general, these results would seem extendable to the in vivo effects of human smoking, since there is little reason to suppose that such basic mechanisms of nicotine uptake by the brain or liver metabolism should be different across mammalian species. The time course of such

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[3] The maintenance of a brain-blood difference in the case of the i.p. nicotine injection cannot be explained in terms of the 'bolus uptake' since there is no initial high nicotine concentration in the blood as there is immediately after rapid i.v. injection of nicotine.



Nicotine concentrations in the brain, liver and blood of mice at various times after an intravenous or an intraperitoneal injection of ^{14}C-nicotine. Each value represents the average of at least three animals.

FIGURE 5 : Nicotine concentrations in brain, liver and blood of mice after i.v. (left) and i.p. (right) injections.

From Stalhandshake (1970)

events is a different matter since the metabolic rate and circulation are much faster in the smaller mammals. In particular, one might note that the blood nicotine - by decapitation, therefore, arterial rather than venous - has half-life of about 5 minutes post i.v. injection in the mouse as compared with values of venous half-lives of 20-30 minutes (Russell, 1976), or brachial arterial half-lives of about 10-15 minutes in man (Armitage, 1978)

If one attempts some crude time scaling between man and mouse (an arguable procedure) then one arrives at a figure of about 10 minutes, or less, for the brain-nicotine half-life in man, post-inhalation style smoking. This half-life would be increased, of course, in the case of slow buccal absorption of nicotine by pipe or cigar. Thus, assuming the time of cigarette smoking averages 5 minutes (it is often more), one may tentatively suggest that 5-10 minutes post-smoking, the brain nicotine in man has halved. If this figure is accurate it has serious implications for any theory suggesting that, in man, the purpose of cigarette smoking is simply to maintain nicotine at brain receptors at some steady state concentration. Such a theory would be more closely approximated in the case of slow buccal absorption by cigar and pipe smoking or by chewing tobacco. This point has been noted by such researchers as Russell (1976) and Armitage (1978) who suggest that different styles of smoking may reflect underlying different reasons for smoking. This aspect is discussed more fully later (cf. under 'Reinforcing Nature of Smoking').

METABOLISM AND EXCRETION OF NICOTINE

Nicotine is an extremely poisonous substance. The nicotine content of one cigar, about 60 mg. would be fatal to a human if injected intravenously. Whilst the brain of the smoker actively takes up nicotine, the body attempts the task of ridding it from the smoker in two ways (a)

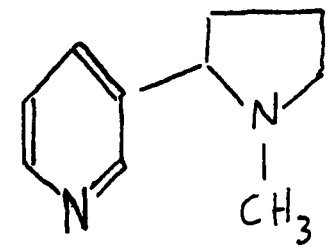
metabolism to inactive forms and (b) excretion of the active molecule.

Metabolism. Nicotine is converted into two main metabolites, cotinine and nicotine -1'-N-oxide. These are formed by two alternative pathways of oxidative metabolism involving N-oxidation or alpha-carbon oxidation of the pyrrolidine ring (cf. Figure 6).

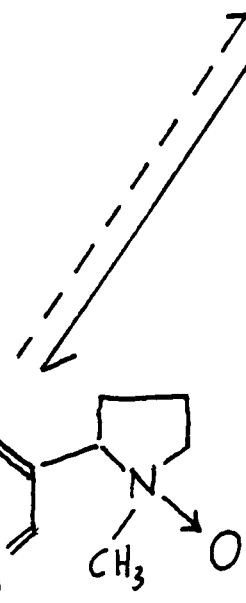
Conversion of nicotine to cotinine occurs in the liver, kidneys, and lung but not in the brain (Turner et al., 1975) and is the major pathway of nicotine inactivation. Under normal conditions of fluctuating urinary pH the amount of nicotine -1'-N-oxide excreted in the urine of smokers is about half that of cotinine excretion (Beckett et al., 1971). The reduction of nicotine -1'-N-oxide to nicotine in the lower gastro-intestinal tract is unlikely to be very important since the re-metabolised nicotine will be largely degraded again by the liver during its first pass into general circulation as referred to earlier.

There is now evidence that nicotine metabolism is increased by repeated exposure - comparison of smokers and non-smokers reveals that the proportion of nicotine metabolites to unchanged nicotine excreted in the urine is much higher in smokers than in non-smokers (Beckett et al., 1971). This is not surprising since metabolic tolerance due to induction of enzymes is well known in other drugs such as amphetamine, alcohol, cannabis, etc. It is not known, however, how strong an effect this would have on the plasma or brain half-life of a heavy smoker as opposed to a light smoker.

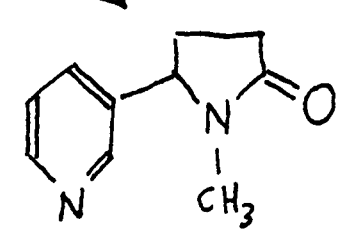
Excretion of nicotine. Nicotine and its metabolites are largely eliminated from the body via urine although it is also present in sweat, saliva and the milk of lactating women (Perlman and Dannenberg, 1942). In the cat 90 per cent of the radioactivity of a given dose of labelled nicotine is excreted in the urine in three days and 77 per cent in the



NICOTINE



NICOTINE-N-OXIDE



COTININE

FIGURE 6 : Alternative metabolic pathways of nicotine to inactive metabolites: nicotine-N-oxide and cotinine. After Russell (1976)

first twenty-four hours (Turner, 1969, 1971).

As is the case with its absorption, the excretion of unchanged nicotine is pH dependent. When the pH is low (5.5 or less) the nicotine is almost totally ionised and cannot be re-absorbed through the kidney tubules. Under these conditions 30 to 40 per cent of an intravenous dose and, by inference, nicotine absorbed from smoking is excreted in the urine as unchanged nicotine (Beckett et al. 1971; Goodman and Gilman, 1971). On the other hand, if the pH of urine exceeds 8.0 most of the nicotine is re-absorbed from the urine not only through the renal tubules but from the bladder too (Travell, 1960). Under normal conditions of fluctuating urinary pH, smokers excrete similar amounts of nicotine and cotinine in their urine and about half as much nicotine -1'-N-oxide (Gorrod and Jenner, 1975). Earlier, pH had been implicated as a mediating variable in smoking style and for the input of nicotine to the system. Interestingly enough, pH crops up again regarding nicotine output from the system as a possible mediator in accounting for observed increases of smoking rate during stress. Schachter (1978) has proposed that the observed decreases of urinary pH during stress, leading to increased nicotine excretion, accounts for the increases in smoking rate in stressed smokers. This aspect is discussed in greater detail later.

SUMMARY OF AND CONCLUSIONS FROM NICOTINE PHARMACOKINETICS

1. The dissociation curve of nicotine base to the ionic form takes places over pH ranges encountered in the media from which nicotine is absorbed or re-absorbed - the tobacco smoke itself, saliva, gastric juices and urine.

2. Since the free base is much more easily absorbed than the nicotinium ion, this has important consequences for both the chosen route of nicotine absorption, i.e. inhalation style versus buccal absorption and,

through re-absorption of nicotine from urine, for the half-lives of blood nicotine levels and thus perhaps for smoking rates.

3. One other factor is perhaps equally important in determining the preferred method of absorption of nicotine in Man, i.e. tobacco smoking. Nicotine absorbed via the buccal mucosa (pipe and cigar) or lungs (cigarettes) is less susceptible to inactivation in the liver than is ingested nicotine.

4. The relative popularity of inhalation style smoking, as opposed to buccal absorption by puffing, chewing or snuffing, cannot be totally explained in terms of pH of tobacco smoke, since cigar and pipe smokers are frequently observed to inhale in some measure. A more convincing explanation is that inhalation style smoking enables nicotine in the form of a concentrated blood bolus to reach the presumed major target area - the brain - very rapidly (around 10 seconds) and initially higher and more controllable brain nicotine levels to be achieved than via buccal absorption. This may imply that different styles of tobacco smoking are based on different nicotine 'needs'.

5. The extremely short brain nicotine half-lifes (5-10 minutes post smoking) estimated for Man have serious implications regarding any model explaining cigarette smoking simply in terms of achieving nicotine homeostasis at brain receptors.

PHYSIOLOGICAL EFFECTS OF NICOTINE AND CIGARETTE SMOKING

PHARMACOLOGY OF NICOTINE - GENERAL

SPECIFIC EFFECTS - MECHANISMS AND REINFORCING NATURE

1. EFFECTS ON THE CARDIOVASCULAR SYSTEM

   (i) Mechanisms

   (ii) Reinforcing nature

2. EFFECTS ON RELEASE OF CATECHOLAMINES

   (i) Mechanisms

   (ii) Reinforcing nature

3. EFFECTS ON THE RELEASE OF OTHER CIRCULATORY FACTORS

   (i) Mechanisms

   (ii) Reinforcing nature

4. EFFECTS ON SKELETAL MUSCLE

   (i) Mechanisms

   (ii) Reinforcing nature

5. EFFECTS ON THE ELECTRODERMAL SYSTEM

   (i) Mechanisms

   (ii) Reinforcing nature

6. EFFECTS OF NICOTINE AND CIGARETTE SMOKING ON THE BRAIN

   (i) Mechanisms:

   (a) Effects on tonic EEG

   (b) Ach release and EEG

   (c) Phasic EEG: Evoked Potentials,
   Photic Driving,
   CNV.

   (ii) Pharmacological basis of CNS effects and their reinforcing nature

7. EFFECTS OF NICOTINE AND CIGARETTE SMOKING ON PERFORMANCE

(i) Effects on learning

(ii) Effects consolidation

(iii) Effects on performance of established behaviour

8. EFFECTS OF NICOTINE AND TOBACCO SMOKING ON

(1) Appetite and (2) Aggressiveness

9. SUMMARY AND CONCLUSIONS OF PHYSIOLOGICAL EFFECTS OF NICOTINE AND CIGARETTE SMOKING, EFFECTS ON PERFORMANCE AND EFFECTS ON APPETITE AND AGGRESSIVENESS

PHARMACOLOGY OF NICOTINE - GENERAL

Nicotine has two main types of activity. Firstly, its classical action as a cholinergic agonist, mimicing the activity of acetylcholine on post-synaptic nicotine receptors (Goodman and Gilman, 1971). This in turn can cause the release of a variety of transmitters, including acetylcholine itself (Armitage et al., 1969), noradrenaline (Hall and Turner, 1972), serotinin (Essman, 1973), and, possibly, dopamine (Russell, 1976), and peptides (Lal et al., 1976). The two kinds of actions occur whenever these receptors and transmitters are found and nicotine, therefore, has effects throughout the nervous system. Indeed, about the only receptors to escape a nicotine effect are the muscarinic (cholinergic) receptors and even these may be affected indirectly via an action on preganglionic neurones.

The primary mode of action of nicotine in the brain is still uncertain although it would seem likely to be similar to that on the more easily accessible and hence more intensively studied systems: the peripheral ganglia and neuromuscular junction. When applied to peripheral ganglia or neuromuscular junction, nicotine first facilitates, then blocks, impulse transmission (Paton and Perry, 1953). Acetycholine shows similar dual actions at these sites in the presence of an anti-cholinesterase.

At least two types of cholinergic receptors exist, which have been defined in terms of their relative selectivity for nicotine (nicotinic receptors) as opposed to muscarine (muscarinic receptors) (Goodman and Gilman, 1971).

Differentiation of these two types of receptors is possible by

use of selective antagonists. Nicotinic receptors are blocked by tetraethylammonium (TEA), hexamethonium (C6), pentolinium, mecamylamine, etc., whereas muscarinic receptors are blocked by atropine and scopolamine.

Nicotine action on the brain would thus appear to mimic the nicotine action of ACh on many brain synapses, that is, an initial excitatory action followed by a possible later inhibitory one. This action has in fact been observed by Phillis and York (1968), who injected nicotine (20 µg) into the brains of rats by close arterial injection, and also by lung ventilation with cigarette smoke. After a brief stimulation (of cortical neuronal firing to pulsed injections of L-Glutamate, a cortical transmitter) a more prolonged depression was noted. However, the mechanism is probably not exactly the same as the in vivo action of ACh. Thus the in vivo action of ACh on nicotine receptors would typically end at the point of excitation since cholinesterase would destroy it and prevent any subsequent effects of prolonged excessive action on nicotine receptors, that is, inhibitory blockade through persistent depolarisation.

Much of the perplexity and paradox of nicotine effects result from the biphasic action at cholinoceptive sites. Confusion also exists from the fact that nicotine affects the balance of the activity in a number of opposing systems centrally within the brain, as well as the balance between the sympathetic and parasympathetic systems peripherally. Thus increase in the heart rate may arise from a blockade of parasympathetic activity or from an increase in sympathetic activity. Compounded with this are variations in nicotine distribution and regional differences

in dose-effectiveness and the time course of its actions on opposing systems (Russell, 1976). In addition, it has been shown in animals that the starting state of the organism can modify the uptake, metabolism and neurochemical effects of nicotine (Essman, 1973), as well as the subsequent behavioural effects (Domino, 1973). This is not surprising, however, since the starting state of the organism is know to modify the effects of other drugs. For example, amphetamine will produce depression of high baseline rates of operant response in the rat and elevation of low rates (Kelleher and Morse, 1968). Such effects are often subsumed under the concept of 'Inverted-U" curves relating performance to arousal.

Given the wide-ranging action of nicotine directly and indirectly throughout the nervous system,together with the efficiency and speed with which it is absorbed by cigarette smoking,it is not surprising that effects have been found on nearly every physiological or performance measure studied.

A brief review of the major findings follows, with an attempt to interpret the results in terms of their possible reinforcing nature for the maintenance of cigarette smoking.

SPECIFIC EFFECTS - MECHANISMS AND REINFORCING NATURE

1. EFFECTS ON THE CARDIOVASCULAR SYSTEM

(i) Mechanisms

The cardiovascular effects of doses of nicotine equivalent to those obtained by cigarette smoking are predominantly stimulant, whether administered by injection (Lucchesi, Schuster and Emley, 1967), aerosol (Herxheimer, Griffiths, Hamilton and Wakefield, 1967) or, indeed, by cigarette smoking (Payne, 1914). The heart rate elevation usually observed after cigarette smoking appears to be exclusively due to the pharmacological

action of nicotine in the smoke since the observed increases in pulse rate (and blood pressure) after nicotine has been absorbed do not occur to controls for the vehicle of administration such as aerosol propellant or to inhalation of nicotine-free cigarette smoke (Herxheimer et al., 1967) and not to sham smoking nor deep breathing (Elliott and Thysell, 1968).

The mechanism of nicotine action on the cardiovascular system is a good example of the complexity of its pharmacological effects. Thus nicotine can increase the heart rate by excitation of sympathetic or paralysis of parasympathetic cardiac ganglia and, of course, vice-versa because of nicotine's biphasic properties, although brachycardia is in fact seldom observed. In addition, the effects of the drug on the chemoreceptors of the carotid and aortic bodies and on medullary centres influence heart, as do also the cardiovascular compensatory reflexes resulting from changes in blood pressure caused by nicotine. In addition, it appears that nicotine can directly stimulate the postganglionic nerve endings in the heart with local release of catecholamines in cardiactissue. Finally, nicotine tends to produce a discharge of epinephrine from the adrenal medulla and this hormone accelerates cardiac rate and raises blood pressure (Goodman and Gilman, 1971), although this adrenal gland release of epinephrine is less likely to be of major importance in cigarette smoking induced cardiovascular changes since the rise in circulating catecholamines occurs after the observed cardiovascular effects (Cryer, Haymond, Santiago and Shah, 1976).

In summary, nicotine or cigarette smoking - but not sham smoking - usually has an acute dose-related sympathomimetic effect on the cardiovascular system, increasing pulse rate (major effects lasting 10-15 minutes post-smoking), increase blood pressure (returns to normal in about 20

minutes), increasing muscle blood flow and decreasing peripheral blood flow as measured by decreased finger-tip temperature, toe temperature and foot blood flow (these latter effects lasting longer than heart rate change). This occur together with a rise in blood levels of free fatty acids, catecholamines, vasopressin, adrenal hormones, growth hormones and blood lactate/pyruvate ratio (Ashton et al., 1976; Cryer et al., 1976).

Conversely, these sympathomimetic effects can be prevented by adrenergic blockade of the cigarette smoker by using, for example, an α-blocker-phentolamine and a β-blocker-propranolol (Cryer et al., 1976). Growth hormone and cortisol release are not blockaded by α and β blockers and are presumably released by nicotine in a non-adrenergic mediated fashion.

Although this nicotine induced tachycardia following cigarette smoking is one of the most reliable correlates of cigarette smoking, a rapid receptor tolerance - tachiphylaxis - quickly ensues. This is often observed by the early morning smoker - the first cigarette of the day having subjectively the strongest effects. This has been demonstrated in studies with rapidly injected nicotine designed to mimic the in vivo nicotine concentrations encountered by cigarette smokers (Russell and Feyerabend, 1978) and earlier observed in successive decrements in tachycardia produced by smoking successive cigarettes after elapse of a short period of abstinence due to experimental demand or to sleep (Frankenhaeuser, Myrsten, Waszak, Neri and Post, 1968; Elliott and Thysell, 1968; Armitage, 1970). In these studies the typical elevations of 10-20 b.p.m. in heart rate observed after the first cigarette are, after only a few cigarettes, reduced to about 5 b.p.m. Such large reductions in heart rate are unlikely to be caused by subjects successively taking

less nicotine out of each cigarette since successive rises in nicotine plasma levels due to cigarette smoking remain fairly constant (Russell and Feyerabend, 1978) provided the smokers are not forced to smoke cigarettes at unnaturally high frequencies. Further, neither the observed puffing rates nor the butt nicotines decrease throughout the day (Armitage. 1970). It is also interesting to note that one of the few radio-telemetry studies of subjects ad lib smoking in a more 'free' situation as compared with that of the laboratory found little or no evidence for cigarettes to increase heart rate (Erwin, 1971). It would seem reasonable, therefore, to suppose that apart from the first few cigarettes of the day the smoker will tend to experience cigarette induced tachycardia not substantially different from the variations in heart rate resulting from normal day-to-day activities.

In contrast, the smoker will experience a gradual rise in tonic heart rate throughout the course of the day's smoking of the order of ten beats per minute morning versus evening (Armitage, 1970), compared with a small drop towards evening in non-smokers. This is probably due to the observed gradual accumulation of nicotine in the blood throughout the day (Russell and Feyerabend, 1978).

(ii) Reinforcing nature.

It is possible that tachycardia and associated cardiovascular effects of nicotine represent one of the reinforcers of the smoking habit. The most obvious mechanism for reinforcement would be to postulate that smokers have chronically low heart rates which they wish to elevate to cope with their day-to-day activities. However, the evidence does not bear this out. Thus, Larson and Silvette (1971, p.75) reviewing the available data conclude that smokers, on average, have neither a higher or lower pulse rate than non-smokers. However, no longitudinal data on

heart rate of smokers before commencement of the habit is available as far as this author is aware, so that the non-significance of any differences could possibly be ascribed to chronic effects of nicotine on the smoker's heart rate.

Schachter (1973) makes the interesting suggestion that the 'calming' effects ascribed to cigarette smoking may be paradoxically due to the general sympathetic arousal caused by cigarette smoking of which heart rate is one measure. This essentially 'attribution' theory of the calming properties of smoking suggests that in a 'fearful' situation the smoker will light up in order to ascribe the feedback of sympathetic responses he is experiencing, as a result of his fears or anxieties, to the sympathomimetic effects of the cigarette. Thus the smoker relabels the visceral sensations he is experiencing as pleasurable.

Apart from Schachter's cognitive hypothesis an explanation of the calming effects of smoking can be based on the Law of Initial Values: 'high autonomic excitation preceding stimulation is correlated with low autonomic reactivity upon stimulation' (Lacey, 1956). According to this explanation, smoking will exert its calming influences by increasing autonomic excitation and thus reducing autonomic reactivity to further aversive stimulation. Similar explanations might be couched in terms of Lacey's (1967) hypothesis that 'sensory-rejection is associated with heart rate acceleration', together with the subsequent work by Hare, see review (Hare, 1975), which supports the notion that anticipatory heart rate elevations to shock may form part of a defensive response (Sokolov, 1963), which is indicative of a coping response to a stressor.

However, there are two major difficulties with any model of smoking behaviour in which tachycardia is a primary reinforcer for the habit. Firstly, tachyphylaxis occurs to smoking and so will attenuate

any major cardiovascular effects after the first few cigarettes of the day, although it is true that 'tonic' heart rate will rise through the course of a day's smoking. [This can be seen in Schachter's own experiment - the second cigarette produces relatively little tachycardia (cf. Figure 7).] Secondly, adrenergic blockade with β adrenergic blockers such as oxprenolol largely prevent the sympathomimetic effects of smoking but do not prevent the subjective pleasurable effects (Carruthers, 1976). In fact, it is well established that β blockers themselves have anxiolytic properties (Turner, Granville-Grossman and Smart, 1965; Taggart and Carruthers, 1972), probably because they damp down sympathetic over-activity associated with stress.

Such considerations reinforce the view that the pleasures associated with smoking are mainly due to direct stimulation of the central nervous system which is relatively unaffected by the β-blockade, rather than the easily suppressible peripheral consequences of increased sympathetic activity.

2. EFFECTS ON RELEASE OF CATECHOLAMINES

(i) Mechanisms

As stated above, nicotine or cigarette smoking generally has a sympathomimetic effect on the cardiovascular system (CVS).

The associated release of catecholamines from the adrenal medulla is sufficient but not necessary for these CVS effects, as Cryer et al. (1976) point out, since the time course of adrenal stimulation is slower than that of tachycardia. The question thus arises whether or not nicotine induced elevation of catecholamines are important for the smoking habit.

The Cryer et al. (1976) study is interesting since although there is general agreement that smoking produces release of adrenaline as

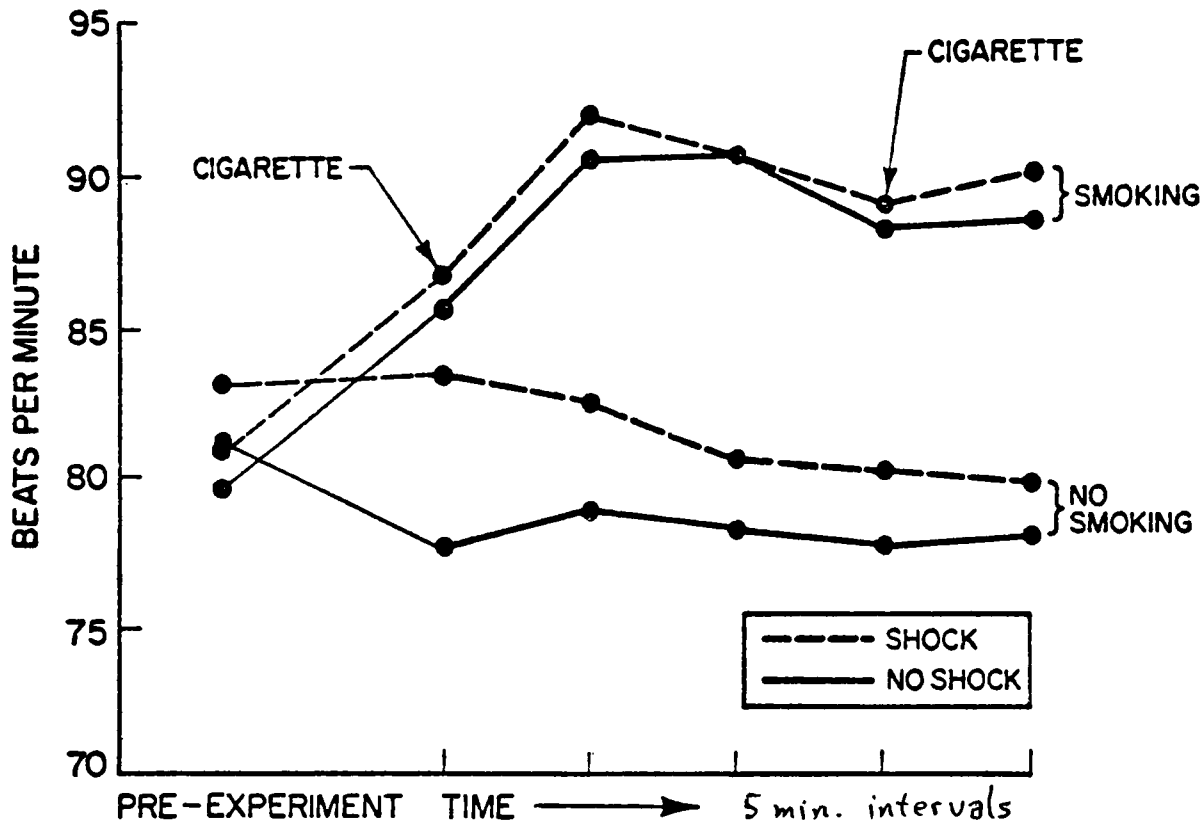


FIGURE 7 : The effects of electric shock and smoking on heart rate. From Schachter (1973)

measured in the blood (e.g. Hill and Wynder, 1974) or urine, (e.g., Agué, 1974), very few human studies apart from Cryer et al. (1976) have found smoking associated increments of circulatory as opposed to synaptic noradrenaline (the sympathetic neuro-transmitter) either in the blood (Hill and Wynder, 1974), or urine (Frankenhaeuser et al., 1970; Frankenhaeuser et al., 1971).

The latter studies demonstrate that the rate of excretion of adrenaline in urine increased by an average of 38 per cent during a 90-minutes period following the smoking of two 1.3 mg nicotine cigarettes; with cigarettes of higher nicotine yield (2.3 mg nicotine/cigarette) urinary adrenaline was increased by 83 per cent. There were corresponding dose-related decreases in noradrenaline excretion of 12 per cent and 17 per cent respectively.

The usual finding that smoking reduces circulatory noradrenaline levels may be related to the reduction of aggression by nicotine (see later under 'Nicotine and Aggressiveness'), since the noradrenaline to adrenaline ratio has been suggested as an indicator of the 'fight-flight' dimension of arousal (Ax, 1953; Funkenstein, 1955; or Gray, 1971). It is possible that starting state is important; so that individuals with high NA levels could show smoking-related reductions of NA and vice-versa for individuals with low NA levels. One study (Myrsten and Andersson, 1978) suggests that the starting state of the smoker is important in determining the final outcome of cigarette smoking. This investigation found that when a reaction time task was performed under stressful conditions, which itself produced an increase in adrenaline release rate, smoking produced no further adrenaline increases.

One could regard this as a 'ceiling effect' or as a consequence of the smoker taking larger doses of nicotine during stress to obtain

depressant effects - nicotine possesses a biphasic action on the adrenal medulla; small doses evoke the discharge of catecholamines and large doses prevent their release in response to splanchnic nerve stimulation (Goodman and Gilman, 1971). It is plausible to suggest that this particular effect may be sought after by the subject. Excessive adrenomedullary activity is avoided by the smoker since it would produce a decrement in behavioural efficiency as a consequence of the inverted U-relationship between arousal and behavioural efficiency.

(ii) Reinforcing nature

As stated earlier under 'CVS effects' the peripheral sympathomimetic effects of nicotine can be effectively blocked by a variety of agents. However, oxprenolol, which effectively blockades the β adrenergic receptors, does not appear to diminish the subjective pleasurable effects (Carruthers, 1976), which are thus presumably centrally mediated. Therefore, it is possible to regard peripheral catecholamine changes associated with cigarette smoking as reflecting more important 'CNS' effects rather than being major reinforcers for the smoking habit in their own right, although the evidence is far from conclusive.

3. EFFECTS ON THE RELEASE OF OTHER CIRCULATORY FACTORS

(i) Mechanisms

Cigarette smoking does not significantly effect plasma glucagon, insulin, alanine, glucose or beta-hydroxybutyrate (Cryer et al., 1976). However, increments in plasma growth hormone, cortisol and antidiuretic hormone (ADH) have been reported (Cryer et al., 1976; Goodman and Gilman, 1971). The mechanism of action in each case probably involves a cholinergic final common pathway in the hypothalamus for the following reason. The release of plasma growth hormone and cortisol are not susceptible to blockade by combined α and β blockade, phentolamine and propanol respectively (Cryer et al., 1976). The antidiuretic effect of nicotine,

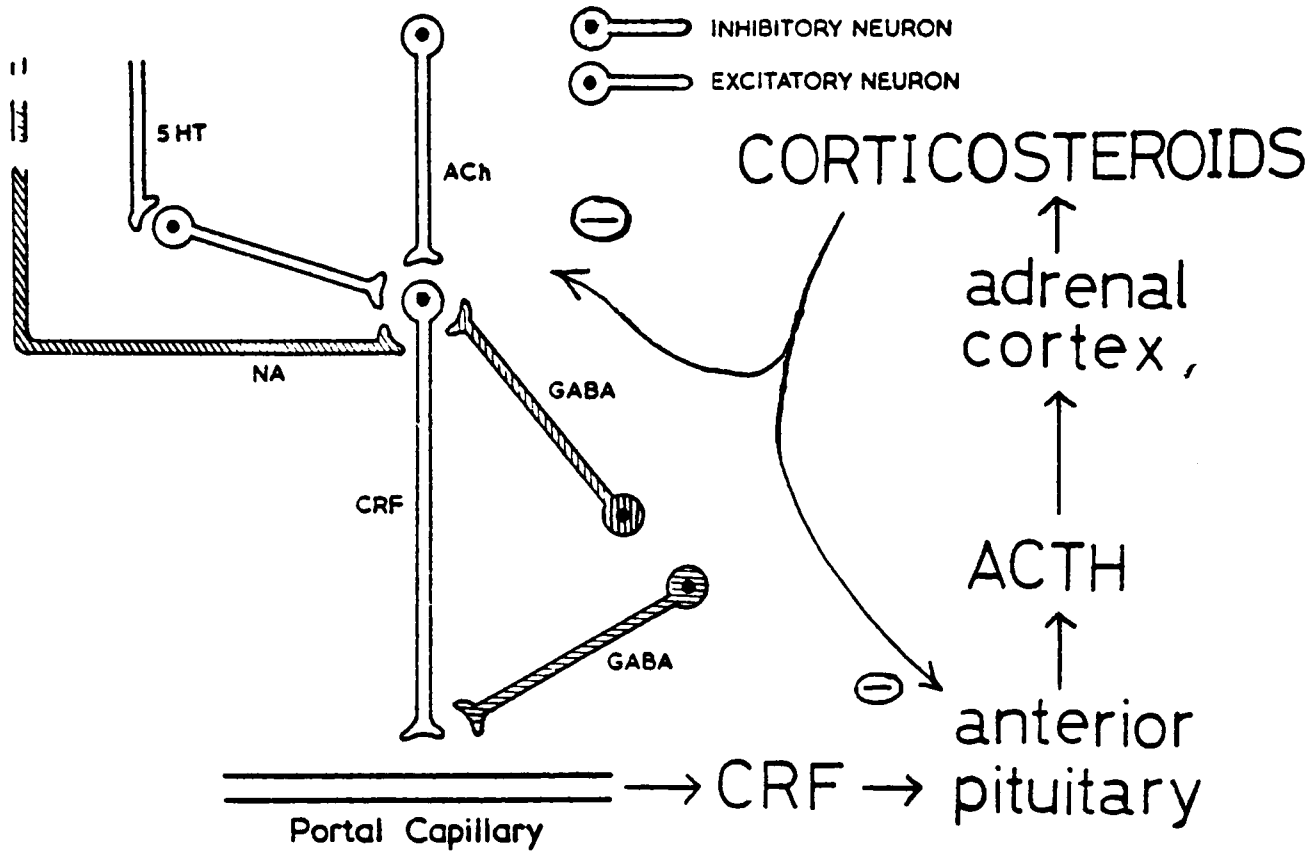
similar to that of ACh, is the result of stimulation of the hypothalamicohypophseal system with the consequent release of ADH (Goodman and Gilman, 1971). The nicotine induced release of corticosteroids can be traced through a complicated sequence of events and provides a good example of the growing power of biological techniques (cf. Figure 8).

(ii) Reinforcing nature

Release of ADH has not been suggested as in reinforcer for smoking. Similarly, the motivation for coffee or alcohol consumption, which are often associated with smoking behaviour, has not been interpreted in terms of their known diuretic effects (by inhibition of reabsorption from the kidney tubules and inhibition of ADH release from the posterior pituitary, respectively (Laurence, 1973). However, ADH is also released in the brain itself and may be involved in facilitating memory (see review in 'The Lancet', February 24th, 1979) and thus explain some of the known effects of smoking on memory.

The reinforcing aspects of growth hormone would appear to be rather long term and can probably be disregarded as being of major importance in maintenance of smoking behaviour.

By contrast, the nicotine induced release of corticosteroids has been suggested as a putative reinforcer of smoking. Stimulation of adrenocortical activity by enhanced corticotropin release (Kershbaum et al., 1968) has been suggested to act as a reinforcer for smoking by increasing the output of corticosteroids in individuals with slow or inadequate corticosteroid production in face of stress (Grant, 1968). If this is true one would predict that smokers, as compared to non-smokers, should show less corticosteroid release to stress and that smoking should 'normalise' the stress-induced corticosteroid release in the smoker.



Suggested model for the control of CRF from the hypothalamus. The model shows: (a) The CRF neuron with its axon terminating at a portal capillary. (b) A 5-HT pathway which releases CRF after excitation of a cholinergic interneuron. (c) The final common pathway to CRF release is cholinergic. Two cholinergic neurons are shown. One is the interneuron placed between the 5-HT pathway and the CRF cell (for control of the circadian rhythm?); the other cholinergic neuron does not have a 5-HT synapse and may control the stress-induced release of CRF. (d) A noradrenergic pathway (NA) which is inhibitory to CRF secretion. (e) GABA inhibitory neuron. This could be either a pre- or postsynaptic input.

FIGURE 8 : The control of corticosteroid production. Adapted from Jones, Hillhouse and Cole (1978).

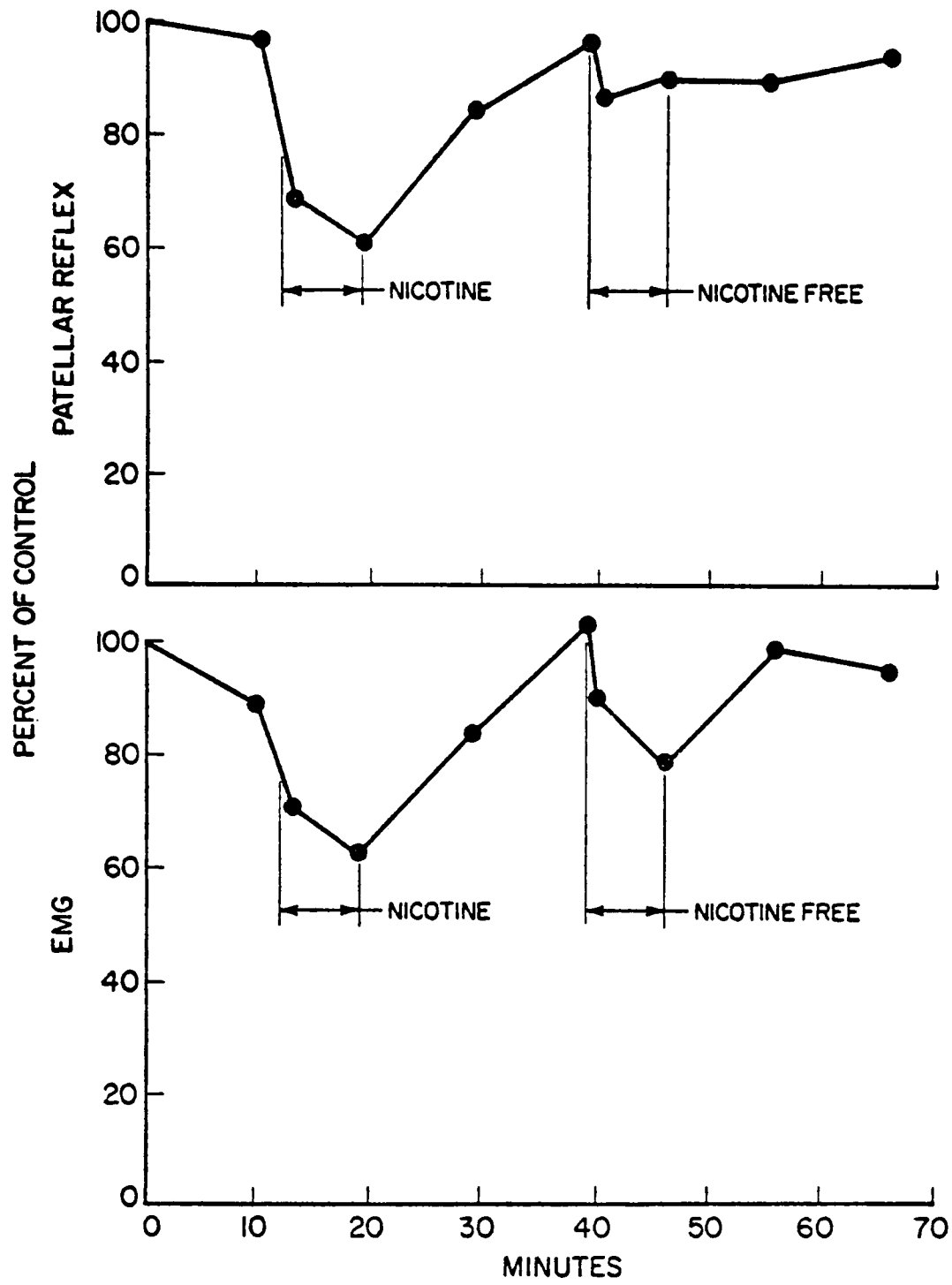
Conversely, if the corticosteroid levels of heavy smokers are substantially elevated one might argue that some of the minor withdrawal effects experienced by heavy smokers giving up the habit may be due to rebound loss of corticosteroid production. High blood levels of steroid prevent release of cortitropin (negative feedback achieved either by acting directly on the pituitary or indirectly on CRF release from the hypothalamus) which in turn results in corticosteroid hypofunction (Laurence, 1973). Some of the minor withdrawal effects of 'giving up' in a heavy smoker may thus be analogous to the catastrophe which can follow from sudden withdrawal of clinical steroid therapy. Unfortunately, there appear to be no experiments directly examining these hypotheses, although the study of Tucci and Sode (1972) on a group of 94 non-smokers and non-deprived light and heavy smokers revealed no significant differences in plasma cortisol and urinary corticosteroid between any of these groups. This type of study, although useful, illustrates the importance of including non-smoking smokers as a control, since one could postulate that the basal level of the corticosteroid production by the deprived smoker would be lower than that of the non-smoker. However, the authors note that there were no significant differences in circadian variation of corticosteroids between smokers and non-smokers. Since the smoker will not be smoking for some part of the night, this acts as a partial non-smoking smoker control and reinforces the view that corticosteroid release is not an important reinforcing factor in smoking. The same study did demonstrate a slight non-significant elevation of urinary epinephrine and depression of norepinephrine comparing heavy smokers to light smokers to non-smokers (strength of effect: heavy/light/non-smokers), as might be expected (see above: 'Catecholamine effects of smoking').

4. EFFECTS OF SKELETAL MUSCLE

(i) Mechanisms

There is evidence that smoking has a relaxing effect on skeletal muscle and that this is largely due to nicotine. A report that smoking caused a dramatic transient reduction in skeletal muscle tone in spastic patients (Webster, 1964), together with the observation that smoking a tobacco cigarette reduced the amount of electromyogram artefact during EEG recording of a very tense and anxious patient prompted Domino and his colleagues to explore this effect (Domino, 1973; Domino and von Baumgarten, 1969). They showed that smoking a single cigarette produced a marked depression of the muscular contraction elicited by the patellar reflex. This effect was dose-related and was also produced by inhalation of nicotine from an aerosol but not by lettuce cigarettes or by nicotine-free aerosol. As can be seen from Figure 9, the time course of the reflex depression roughly follows that of the blood nicotine levels found after smoking (see earlier).

Similar effects have been obtained by Isaac and Rand (1969) in dogs using intravenous nicotine, and the introduction of tobacco smoke into the lungs. The mechanism of this depression of the patellarreflex is complex, involving both central and peripheral components. Ginzel et al. (1968) concluded on the basis of their own and other worker's studies that nicotine in small doses (4-50 µg - close to 'real' smoking doses) injected intraventricularly into cat brains usually depressed the patellarand linguo-mandibular reflexes. Some degree of central involvement is certain since high spinal transection abolishes nicotine's depressant effects on reflexes and, in addition, these depressant effects can be blocked by mecamylamine (a centrally acting nicotine blocker) but not by hexamethonium (a peripheral nicotine blocker).



Effects of inhaling a nicotine aerosol and nicotine-free aerosol on the mean patellar reflex and EMG. The mean patellar reflex is shown above, and the EMG of the quadriceps femoris muscle below. Both represent 100% as the control for five to eight subjects. Note that inhaling the nicotine aerosol gave a greater depression than the nicotine-free aerosol.

FIGURE 9 : Effects of nicotine on patellar reflex and EMG. From Domino (1973).

This central mechanism is in addition to the hypothesised mechanism (Domino, 1973) of nicotine induced depression of the patellar reflex. This suggests that depression of the patellarreflex is mediated by a direct stimulant action of nicotine on cholinergic receptors of the Renshaw cells in the spinal cord (the Renshaw cell is an inhibitory interneuron in the reflex arc).

Central, rather than peripheral, mechanisms of nicotine action are likely to be of great importance in the finding that nicotine and cigarette smoking reduced masseter contractions of smokers to noise stress (Hutchinson and Emley, 1973).

(ii) Reinforcing nature

Although the relaxing effect of cigarette smoking on skeletal muscle has been suggested as reinforcing for the habit - especially in stressful situation (Russell, 1976), the evidence and its interpretation are uncertain. Firstly, although the depressant effects of cigarette smoking on muscle reflex are well proven and, in addition, unlike cardio-vascular system changes, are not subject to tachyphylaxis (Domino, 1973), it is not known for certain whether tonic muscle activity is reduced as well. The one report of cigarette smoking and tonic EMG suggests that it is not (Fagerström and Götestam, 1977).

Secondly, it is debatable as to what extent the observed increase of muscle tension (especially phasic) during stress and anxiety merely reflects what is going on in the brain and/or whether the feedback from increased muscle tension can contribute to or modulate the perception of stress. Analogously, this question also arises when considering the reasons for the effectiveness of the benzodiazepam minor tranquilisers. These are relatively selective for the limbic system which is concerned with emotional control (probably by inhibiting a protein inhibitor of

GABA - itself an inhibitor - see Review I(i)T.I.N.S. [1978]). The diazepams also have central muscle-relaxant effects (Laurence, 1973) which may be secondary to or independent from the former mechanism and so contribute to the final anxiolytic effects.

Similarly, progressive desensitisation therapies for phobias and EMG biofeedback for anxiety states take the view that reduction of muscle tension is incompatible with states of anxiety and so reduces anxiety. However, there is experimental evidence that feedback from voluntary muscle can throw 'noise' into the system and scotomatize perception of stressful situations (Murphy, 1970). This concept can be traced back to Wilhelm Reich's(1950) 'character armour' and in the Eastern martial arts where muscle relaxation is emphasised to prevent the martial art exponent from 'scotomizing' his environment, and so more effectively perceive an attack directed at him.

In summary, therefore, it is difficult to predict whether or not a reduction in tonic muscle tension in the stressed cigarette smoker will be reinforcing or not. Moreover, the well known phenomenon of response stereotypy (Eysenck, 1977; Barrell and Price, 1977) indicates that only a certain proportion of smokers will respond (tonic and phasic) extremely in the muscular system. Many individuals will tend to respond more in the cardiovascular system or viscera. However, the question of muscle tension and smoking is very interesting and certainly deserves more attention.

5. EFFECTS ON THE ELECTRODERMAL SYSTEM

(i) Mechanisms

Electrodermal activity (sweat gland activity) is a commonly used measure of autonomic excitation. Tonic (SCL, SPL) and phasic (SCR, SFs,

SPR) components of electrodermal activity are thought to largely reflect the excitation/inhibition balance of the limbic system (a major target area for nicotine), and in particular the hippocampus and amygdala (Rickles, 1972). While electrodermal activity is usually regarded as an index of central autonomic activity, in the case of cigarette smoking, or nicotine, systematic peripheral effects cannot be completely excluded. The immediate sympathetic innervation of the sweat gland is muscarinic (local iontophoresis of atropine blocks SCR and reduces SCL: Venables and Martin, 1967) and so should be unaffected by nicotine. However, peripheral actions of nicotine cannot be excluded, since studies on spinal cats indicate that close arterial injection of nicotine towards the right stellate ganglion caused cardioacceleration and/or sweat secretion from the right front foot pads (Aiken and Reit, 1968). While little work is reported regarding nicotine per se, cigarette smoking (as opposed to controls) appears to cause elevations of tonic activity (SCL) (Agué, 1974; Mangan and Golding, 1978; although Kumar et al. 1978, reported non-significant dose-related effects for intravenous nicotine). By contrast cigarette smoking appears to have depressant effects on the phasic (SCR, SFs) components of electrodermal activity (Mangan and Golding, 1978).

(ii) Reinforcing nature

The smoker's perception of smoking effects on electrodermal activity (a small increase in sweating) is unlikely to be of any major reinforcing value. Electrodermal effects are best regarded as reflecting central stimulant actions of nicotine on tonic autonomic responding, and depressant actions on phasic responding. Decreased phasic autonomic responding may be of some value in 'filtering out' the effects of distracting or aversive stimuli. Indeed, Knott (1979) presents some electrodermal, evoked potential and performance evidence to support his

contention that smokers compared to non-smokers may be rather poor at stimulus filtering, and so use cigarettes as a "stimulus barrier."

6. EFFECT OF NICOTINE AND CIGARETTE SMOKING ON THE BRAIN

(i) Mechanism

The fact that smoking doses of nicotine increase arousal is well attested from both animal (Armitage et al. 1969; Cheshire, Kellett and Willey, 1973) and human studies (Murphree, Pfeiffer and Price, 1967; Philips, 1971; Brown, 1973; Knott and Venables, 1977) arousal being measured by EEG desynchronisation, attenuation, or frequency shift of alpha activity. A similar inference might also be derived from studies reporting decreased arousal as one consequence of smoking deprivation (Knapp et al. 1963; Ulett and Itil, 1969; Hall, Rappaport, Hopkins and Griffin, 1973; Knott and Venables, 1977). This cortical arousal is probably secondary to the effect of nicotine of the reticular activating system and the hippocampus (Domino, 1973) where particularly high levels of nicotine occur after absorption (see earlier under: 'Distribution of nicotine in the body'). Bilateral lesions of the midbrain reticular formation in cats will completely abolish the cortical desynchronisation produced by nicotine even in (high) doses 100 µg/Kg, (20 µg/Kg being normally sufficient [Domino, 1973]). In addition, iontophoretic injection of nicotine in the brainstem activates some neurones, providing direct evidence of nicotine action. Unlike most other stimulant drugs the arousal due to nicotine or tobacco smoking closely resemble normal arousal produced by stimulating conditions (Domino, 1973; Russell, 1976). In a very well controlled study, Cheshire et al. (1973) found that intravenous nicotine at 1 or 5 µg/Kg/minute produced a dose-related EEG desynchronisation in monkeys which was indistinguishable from 'normal arousal' as produced by visual or auditory stimulation. In contrast,

other stimulants such as D-amphetamine (.1mg/Kg and .5 mg/Kg p.o.) and caffeine (50 mg/Kg p.o.) whilst producing the same order of overall desynchronisation over a larger time course were significantly different on particular EEG bands from normal arousal and from arousal produced by nicotine.

ACh release and EEG

Nicotine also causes a release of ACh from the cortex. This, too, is secondary to effects in other areas, since ACh is not released when nicotine is applied directly to the cortex. The EEG arousal is short lived, whereas the cortical ACh release is more prolonged, lasting an hour or more, suggesting that these two effect of nicotine are mediated by two different mechanisms (Armitage, Hall and Seller, 1969).

Although activation of the EEG is emphasised in the literature concerning nicotine and smoking, there are reports of depressant effects. These may be interpretable both in terms of (a) the known biphasic dose-response curves of nicotine at the synapse and (b) in terms of the starting states of the organism:

(a) Thus Armitage et al (1969) found that whereas the most common effect of small frequent doses (2 µg/Kg every 30 seconds) of intravenous nicotine in anaesthetised cats was desynchronisation of EEG and an increase of cortical ACh, larger doses given less frequently (4µg/Kg every 30 seconds) could increase or decrease EEG activity with corresponding increase or decrease in ACh release. These ranges of dose are are equivalent to those obtained from cigarette smoking.

Although human smoking studies have generally regarded EEG activation as being the rule, the exceptions, in terms of smoking producing EEG synchronisation, may be more frequent than is generally admitted. Thus, Murphree et al. (1967) noted that some subjects showed increases

in EEG alpha to cigarette although stimulant effects predominated in the sample. Similar 'mixed' stimulant and depressant effects have been reported by Knott (1978), Remond et al. (1979).

(b) Starting state is known to modify the effect of many drugs on the CNS, including nicotine (Domino, 1973). This has been suggested by Murphree et al. (1967) to explain some paradoxical depressant effects of nicotine.

It is plausible to suggest that under some conditions (such as a high basal state of arousal) depressant actions of nicotine may predominate. This is supported by the observation that starting state, whether in terms of personality differences (Ashton et al. 1974; Eysenck and O'Connor, 1979) or situation (Ashton and Watson, 1970) may both direct rate of nicotine intake and (consequently) physiological outcome.

The complexity of analysis of the final outcome of cigarette smoking in terms of the biphasic dose-response effects of nicotine interacting with the starting state of the brain is further compounded by consideration of smoking behaviour itself. The behavioural as opposed to nicotine contribution of smoking to EEG effects can be considered at three levels:

(i) Effects from the initiation of the behaviour (whether driven by internal attempts at nicotine homeostasis or arousal modulation; or direct external cues - the social suggestion of other smokers).

(ii) The direct effects of activity - motor and sensory feedback from lighting up, taste, inhalation and smell of smoking.

(iii) Conditioning of the feedback stimuli from smoking behaviour to the direct pharmacological effects of nicotine.

Any or all of these possible contributions to the EEG effects of smoking are important and are often considered together as the 'secondary reinforcing' effects of smoking. Thus mecamylamine, a centrally acting nicotine antagonist, will completely block EEG desynchronisation in the cerebral cortex and olfactory bulb of both alert and encéphale isolé cats caused by nicotine injection, but will not totally blockade those effects when nicotine is administered via smoke into the lungs (Hall, 1970). It would appear from this result that the stimulus of the smoke itself is sufficient to cause some degree of EEG arousal. Olfactory bulb stimulation by tobacco smoke is likely to be important since this is the only sensory route into the brain which is "direct" -

> 'The olfactory system breaks all the laws that seem to govern the organisation of other sensory mechanisms. It is, as we have noted, the only system known in which the primary sensory neurons lie at the body surface. There is no transducing element, as there is in, say, Corti's organ; the olfactory epithelial cell itself is buffeted by the external environment.' from Nauta and Feirtag (1979).

Similarly, in humans, there is evidence that smoking behaviour as opposed to nicotine is providing some of the observed effect of smoking on EEG. Thus, controls such as inhalation of nicotine free smoke or 'sham smoking' with a glass tube filled with cotton wool can produce similar effects to those found when humans smoke cigarettes containing nicotine; upward shift of dominant 'α' frequency by 1 or 1 Hz (Hauser, Schwarz, Roth and Bickford, 1958) and reduction of EEG 'α' (Murphree et al. 1967).

The picture is complicated by individual differences in the degree to which these 'secondary reinforcing' effects occur; Hauser et al. (1958) noted that whilst over 80 per cent of all subjects showed

this alpha frequency shift after cigarette smoking, only 30 per cent of the subjects showed the shift during the initial inhalation (i.e. before nicotine could arrive at CNS). These subject differences may reflect some conditioning of smoking behaviour to pharmacological effects and may help to explain why pharmacological control of central nicotine levels, whether by using nicotine blocking agents or by preloading subjects with nicotine, does not affect smoking rates to the extent one might predict (see later under 'Addiction and Arousal Theories of Smoking').

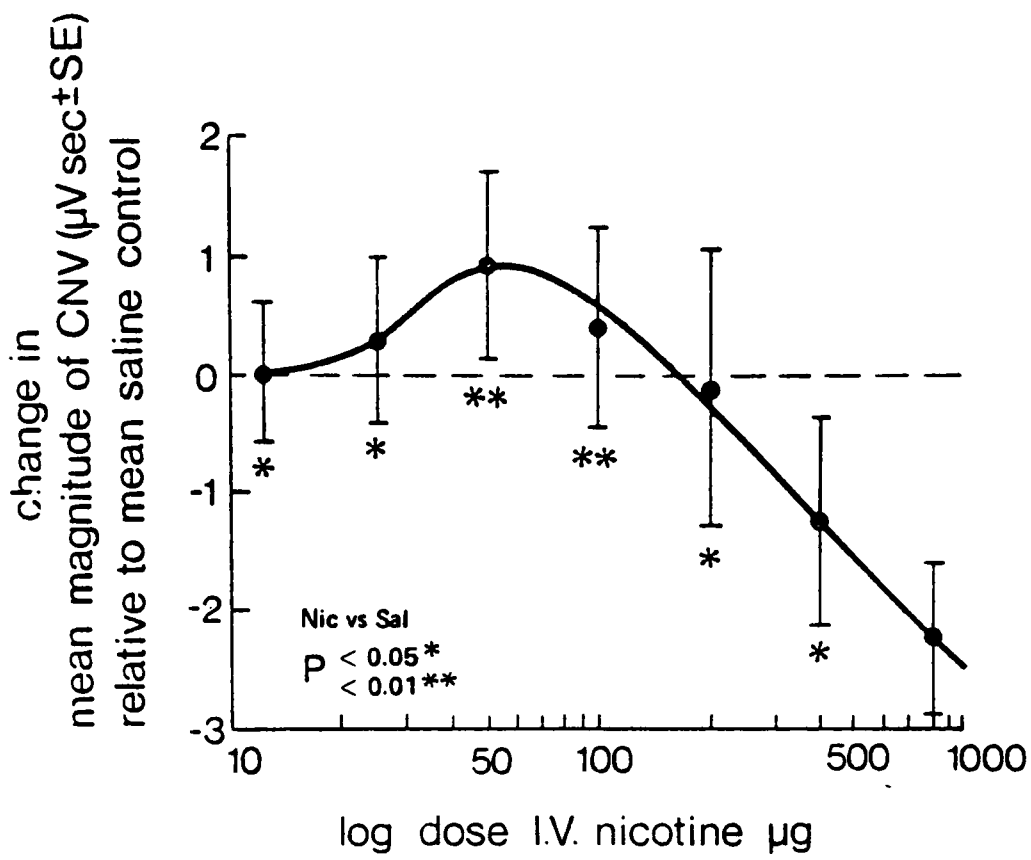
Phasic EEG, evoked potentials, photic driving, CNV

In contrast to the generally stimulant effects of nicotine and cigarette smoking on tonic EEG, depressant effects as well as stimulant effects have been reported using phasic EEG measures. Both stimulant effects (Hall, Rappaport, Hopkins and Griffin, 1973; Friedman, Goldberg, Horvarth and Meares 1974) and depressant effects (Vasquez and Toman, 1967; Knott and Venables, 1978) of smoking compared to smoking deprivation of average evoked potential amplitudes have been reported. Depressant effects of smoking can be inferred from Vogel, Broverman and Klaiber's (1977) study on photic driving. The latter found that smokers, after 3 hours deprivation, exhibited a greater incidence of EEG 'driving' responses to photic stimulation than non-smokers and that smoking one cigarette resulted in a reduction of EEG driving responses to a level comparable to that of non-smokers. These findings in humans are congruent with animal studies; smoking dosages of nicotine (12.5 µg/Kg) reduce evoked potential envelopes in cat auditory cortex whilst simultaneously increasing general CNS excitation (Pradhan and Guha, 1976).

Knott and Venables (1978) suggest that smoking may be able to stimulate CNS inhibiting mechanisms (without simultaneous reductions in CNS excitatory processes) resulting in the 'screening out' of irrelevant

and irritating sensory input into consciousness. This suggestion is congruent with the finding that tobacco smoking increases habituation rate to intense auditory stimuli as measured by EEG alpha blocking response (Friedman, Horvarth and Meares, 1974). In addition, animal work suggests a possible site of action of nicotine on these inhibitory processes. Relying on previously reported studies (Bhattacharya and Goldstein, 1970; Nelsen, Pelley and Goldstein, 1973) which had implicated the hippocampal limbic system as the major target area for nicotine. Nelsen, Pelley and Goldstein (1975) examined the hypothesis that if reticular formation and limbic arousal systems are mutually inhibitory (Routtenberg, 1968), then nicotine-induced limbic (hippocampal) system arousal should counteract the behavioural disruption resulting from electrical stimulation of the reticular formation. Administration of nicotine (100 µg/Kg) did, indeed, attenuate the behavioural disruption - in rats executing a visual performance task - caused by stimulation of the reticular formation and from these results the authors suggested that a possible reinforcement for smoking is its ability to reduce reticular activation when this is manifested as over-arousal in excessively stimulating environments.

However, the two studies mentioned at the outset clearly indicated stimulant and not depressant effects of cigarette smoking on the evoked potential. One possible explanation for these results may be that, given the variations in subject population and smoking style, these smokers absorbed doses of nicotine which were in fact stimulant. Support for this contention comes from the studies of Ashton et al. (1974), Ashton et al. (1978), concerning the effect of cigarette smoking and dosages of nicotine on the contingent negative variation in man. The results of this work clearly demonstrate that smoking can produce stimulant or depressant effects on the CNV, the direction of which are



Mean dose-response curve in six subjects showing effect of intravenous nicotine (each dose given as five 'shots') expressed as change in mean magnitude of CNV relative to mean saline control. Note biphasic shape of curve so that smaller doses produce an increase in CNV magnitude (stimulant effect) and larger doses produce a decrease in CNV magnitude (depressant effect) relative to saline control.
Abscissa: log dose I.V. nicotine μg.
Ordinate: change in mean magnitude relative to mean saline control (μVs $\pm$ 1 S.E.)
Correlated t test for significance of difference between mean CNV with nicotine and mean CNV with saline for each dose * $p<0.05$ and ** $p<0.01$.

FIGURE 10 : Biphasic stimulant-depressant dose-response curve for intravenous nicotine on the CNV.

From Ashton et al. (1978).

dependent on the rate of smoking or nicotine dose (cf. Figure 10).

(ii) Pharmacological basis of CNS effects and their reinforcing nature.

Although the smoking behaviour itself may effect changes in the CNS, these can be considered as secondary in importance compared to the postulated primary reinforcer, nicotine. The EEG changes and the behavioural arousal that follow nicotine injections are blockaded by mecamylamine. This shows that they are mediated by cholinergic mechanisms (Domino, 1967; Hall, 1970). However, as mentioned earlier, this direct nicotinic cholinergic action can lead to the release of ACh, noradrenaline, 5-HT, dopamine, etc. Considering the rapid clearance of nicotine from the brain - of the order of a few minutes - compared with the normally much longer time intervals between smoking successive cigarettes, it is plausible to argue that these secondary changes are the main determinants of smoking behaviour.

Nicotine induced noradrenaline release (Bhagat, 1970; Hall and Turner, 1972) is of particular interest since activity in hypothalamic reward system seems to involve catecholamine release (Stein and Wise, 1967). Not only do smoking doses of nicotine release catecholamines in these areas (Hall and Turner, 1972) but nicotine actually influences hypothalamic electrical self-stimulating behaviour in a biphasic dose-dependent manner (Domino, 1973). We might thus view the reinforcing nature of nicotine as being due to secondary release of central catecholamines signalling reward in an analogous manner to the reinforcing nature of amphetamine.

Whilst at a crude level of analysis this view of the major reinforcing effect of nicotine is attractive, it ignores the still little

understood relationship between arousal and reward-punishment systems. Since the immediate effects of reward are well known to be arousing (Gray, 1971), although ultimately de-arousing in the classic 'Drive Reduction' sense of appetitive behaviour, one can account for the stimulant effects of nicotine on tonic EEG measures. Similarly, increased arousal does focus attention (Wachtel, 1967) and thus inhibits responses to irrelevant stimuli which could account for the increase in habituation rates found by Friedman et al.(1974) and the 'stimulus filter' model proposed by Knott and Venables (1978) on the basis of their own and other workers' experiments on evoked potentials and photic driving.

However, the reverse viewpoint is equally plausible - that nicotine by virtue of its biphasic stimulant and depressant effects can shift arousal to a hypothetical 'arousal optimum' (Berlyne, 1971), and thus signal reward. The resolution of these two viewpoints may lie in the exact nature of the stimuli impinging upon the smoker. Thus the nicotine induced shift from reticular to limbic system control of cortical activity found by Nelsen, Pelley and Goldstein (1973) may reflect the activation of an arousal system which focuses mainly on those stimuli in the environment which have rewarding value according to the two arousal system theory of Routtenberg (1968). This would simultaneously account for the hypothesised directly rewarding effects of nicotine by stimulation of 'reward systems' and also the filtering out of irrelevant or unpleasant stimuli which in its turn would signal reward.

At a pharmacological level the relationship between the attentional aspects of arousal and reward-punishment systems becomes even closer, even though imperfectly understood. The relationship between noradrenaline and reward is probably much more complex than the original experiments of Stein and Wise (1967), relating noradrenaline

release to electrical self-stimulation behaviour in the 'reward pathways' of the hypothalamus, would suggest. There is evidence that specific lesioning of noradrenergic pathways with 6-hydroxydopamine does not interfere with the ability of rats to learn simple behaviours for food reward, nor avoidance of direct and indirect punishment, but does interfere with extinction and those tasks involving complex environmental stimuli. Mason (1979) suggests that the noradrenergic pathways are not directly involved with reward and punishment, per se, but in the direction of attention - 'stimulus sampling' - by reward and punishment systems. Further pharmacological analysis of this issue in terms of smoking behaviour awaits a fuller understanding of the precise mechanisms involved which, no doubt, include dopamine, 5HT, peptides, etc.

The pursuit of the pharmacological basis of EEG effects of nicotine leads the discussion of the central effects of nicotine to consideration of the interaction of smoking and performance.

7. EFFECTS OF NICOTINE AND TOBACCO SMOKING ON PERFORMANCE

For simplicity, performance variables are divided into the following categories:

1. Learning - acquisition of behaviour
2. Consolidation of memory in the absence of overt behaviour
3. Performance of established behaviour

1. Effects on learning

Nicotine has a biphasic dose-dependent effect on animal learning (mainly rats), which is in keeping with its known biphasic effects at EEG and synaptic levels. Provided the "correct" dosage is chosen (usually within weighted equivalent dosage levels obtained by smokers) which may depend upon the particular starting state (individual

differences, strains and species of animal), nicotine can be shown to facilitate the acquisition of shock avoidance (Domino, 1973; Evangelista, Gattoni and Izquierdo, 1970), operant behaviour such as bar pressing to obtain water (Morrison, 1967, 1968), visual discrimination (Bovet-Nitti, 1969) and maze learning (Garg, 1969). Whilst dosage comparisons between different experiments are difficult to evaluate, primarily because different investigators have employed different routes and rates of nicotine injection, one finding in particular seems relatively unambiguous and clear-cut. Small doses of nicotine (40 µg/Kg subcutaneously) facilitate and larger doses (80 µg/Kg subcutaneously) inhibit acquisition of active avoidance (pole-jump response) in the rat (Domino, 1973).

With human subjects there is some evidence that smoking impairs verbal learning but improves subsequent recall (Andersson, 1975), although Mangan and Golding (1978) found little significant effect on acquisition of verbal paired associate or serial learning (in contrast to a significant improvement in subsequent recall). There is also evidence that smoking interferes with incidental learning in an immediate serial recall task whilst having no effect on immediate serial recall of the words (Andersson and Hockey, 1977). These results suggest that smoking is having clearer effects on consolidation (as measured by subsequent recall) as opposed to acquisition (as measured by immediate recall).

The effect of smoking on acquisition in man is probably explicable in terms of nicotine's known biphasic effects on animal learning and also its effects of narrowing attention (Johnston, 1965, 1966). Thus, whilst acquisition of simple verbal rote learning is impaired by cigarette smoking (Andersson, 1975), the results of Andersson and Hockey (1977) and Mangan and Golding (1978), based on more complex learning tasks, would suggest that, with the inclusion of more 'irrelevant material' in the

learning task, the major effect of smoking is to focus the subject's attention on the immediate task and to prevent the subject from attending to these background stimuli. In the above experiments, this effect was evidenced by a smoking induced impairment of incidental learning - memory for the position of words on a screen - whilst having no effect on immediate serial recall of the words themselves (Andersson and Hockey, 1977), and by a non-significant impairment of acquisition of Low Interference Paired Associate word lists and non-significant improvement of High Interference Paired Associates (Mangan and Golding, 1978). The possible physiological basis for this attentional focussing effect of cigarette smoking has been discussed in the previous section.

2. Consolidation

"Consolidation" refers to the postulated transfer of memory traces from the 'short-term memory stores' (STM) to the 'long-term memory stores' (LTM). The former operate over time-scales of seconds, the latter over time-scales of minutes to days. In practice, the consolidation process can be examined by the re-testing for the required behaviour at various intervals after acquisition.

Whilst learning and memory have been tested on smokers - mainly by smoking prior to acquisition - it is entirely possible that the findings of improved recall in experiments detailed earlier are less an effect on the acquisition process, which mainly involves short-term memory and attention, but more an effect on the postulated consolidation process occurring between acquisition and subsequent re-testing. Provided the initial training is short in duration relative to the clearance of nicotine and subsequent transmitter release, cigarette smoking prior to acquisition may be acting directly upon this consolidation process. This possibility has been systematically studied in animals but not in humans.

Post-trial injections of nicotine have been shown to facilitate retention of maze learning in rats (Garg and Holland, 1968; Evangelista, Gattoni and Izquierdo, 1970). However, nicotine is not alone in possessing this property since the same experimenters have found that post-trial injections of amphetamine, strychnine, picrotoxin and hexamethonium to be effective in facilitating retention. Evangelista et al. (1970), make the unusual suggestion that improved consolidation may be mediated by stabilisation of autonomic reflexes, by ganglion blocking peripherally. Some such explanation has to be provided to explain the effects of hexamethonium, which is only a peripheral ganglion-blocker. Presumably, the process of consolidation can be improved by removing interfering stimuli during the consolidation process - in this case autonomic feedback. However, with the current ignorance of the physiological basis of memory there is no need to put forward a unitary mechanism encompassing all these drug effects. Thus, nicotine is known to release ADH (see earlier), which has been implicated in consolidation (Lancet - Review [1979])[4] and, in addition, both nicotine and amphetamine can cause release of NA (see earlier), which has been implicated in the most gross form of learning possible - cortical plasticity during development (Pettigrew, 1978).

Bearing on this latter mechanism, nicotine has been shown to induce theta activity in the hippocampus (EEG activity related to arousal, the orienting response and learning), and to increase hippocampal RNA levels (Daroqui and Orsingher, 1972). Whilst the former effect is probably more related to acquisition rather than consolidation, the latter increase of RNA, in an organ implicated in attentional and memory processes is suggestive of a possible of nicotine action on consolidation through prior NA release, since RNA and associated protein synthesis has

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[4] ADH & memory (Lancet, 1979, 24th, February).

been suggested as the final stage of consolidation (see Cooper, Bloom and Roth, 1978, for a recent review). These EEG and RNA changes in the hippocampus have been shown to depend on noradrenergic pathways since both changes are prevented by alpha-methyl-tyrosine, which is a specific inhibitor of catecholamine synthesis and predictably reverses the amphetamine or nicotine-induced facilitation of learning (Orsingher and Fulginiti, 1971). However, understanding of the mechanism by which cigarette smoking and, by implication, nicotine, affects the consolidation process awaits a greater knowledge of the physical basis of memory which no doubt involves all the known transmitters, including peptides, and also Ca^{++}, cyclic GAMP, before the final RNA and protein synthesis stages. This advance will be at least as important as the understanding of the encoding of "evolutionary memory" - DNA.

3. Effects on performance of established behaviour

Acute: Acute injections of nicotine have been shown to produce mixed effects of facilitation and depression on a number of operant response measures in the rat, including electrical self-stimulation of the lateral and posterior hypothalamus (Olds and Domino, 1969; Pradhan and Bowling, 1971; Newman, 1972; Domino, 1973), bar-pressing for water reward (Morrison, 1967, 1968; Armitage, Hall and Morrison, 1968), conditional pole-jump behaviour in the rat and shock-avoidance behaviour in the monkey (Domino, 1965). The range of dosages employed were typically 25-600 µg/Kg subcutaneously and 100-800 µg/Kg intraperitoneally (for comparison 25-50 µg/Kg subcutaneously is quite similar to dosages produced by inhalation of cigarette smoke in man [Domino, 1973]). These mixed stimulant and depressant effects on operant responses can be explained in terms of nicotine's known biphasic dose response effects at synaptic and EEG levels (e.g. Armitage, Hall and Morrison, 1968; Domino, 1973). In general, it

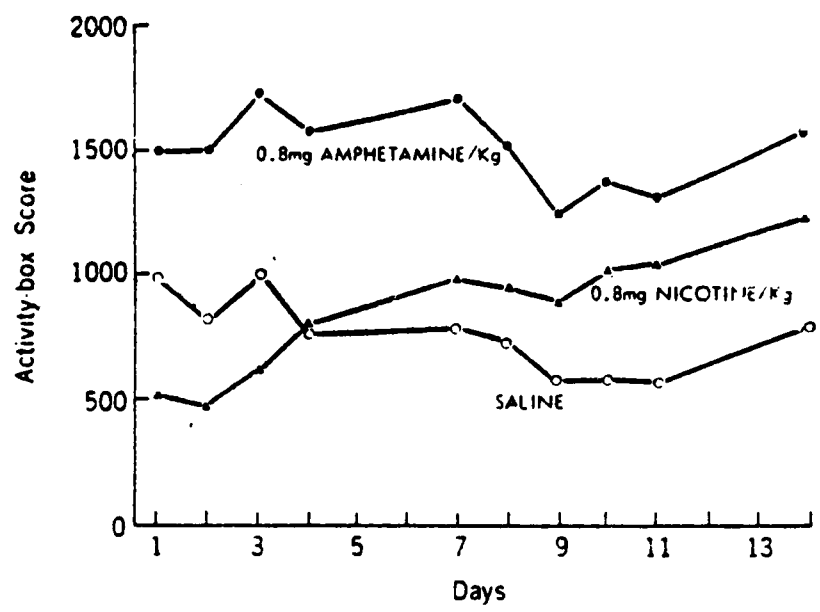
would appear that whilst small doses produce a stimulant effect, larger doses will produce depressant actions. As discussed earlier, starting state of the animal also appears to mediate the direction of nicotine effects. Domino (1973) suggests that nicotine will tend to reduce the self-stimulation rate in rats with high rates of response and vice-versa. This effect is not exclusive to nicotine but also occurs for amphetamine.

The direction of nicotine effect is often time-dependent - medium doses producing initial depression followed by facilitation after a few minutes (Domino, 1973). This is crudely explicable in terms of nicotine's biphasic response curve since a few minutes post-injection the brain levels of nicotine rapidly fall - having a half-life of 5 minutes post-intravenous injection in the mouse brain (Stahlhandshake, 1970). However, "active" i.e. involving transient adaptation to secondary transmitter release, e.g. NA, acetycholine, etc., followed by rebound effects, cannot be excluded since time-based rebound effects of CNS activity in the opposite direction to those at the behavioural level have been found in the EEG of the cat (Domino, 1973): a transient EEG activation occurring within one minute after intravenous injection of nicotine 20 µg/Kg was followed by spindle bursts within 4 minutes, often more pronounced than before nicotine injection. Presumably the reverse type of rebound, i.e. depressant effects followed by stimulant ones after acute nicotine injection, can also occur. They certainly do occur over the longer time-scales involved in chronic nicotine administration (Morrison and Stephenson, 1972; Stolerman, Fink and Jarvik, 1973). Although these latter effects are usually described in terms of long-term tolerance to nicotine depressant effects, it is not unreasonable to suggest that a short-term reversible tolerance - tachyphylaxis - to nicotine depressant

effects may be contributing to the observed initially depressant and then stimulant effects on operant response after acute nicotine injection.

The pharmacological bases of these depressant and stimulant effects appear to be primarily central acetylcholine and noradrenaline release (although other transmitter systems are no doubt involved). Thus, physostigmine (a reversible inhibitor of cholinesterase, which crosses the blood-brain barrier) but not neostigmine (a peripheral cholinesterase inhibitor) will potentiate the depression of operant response rates caused by high doses of nicotine (Morrison, 1968). Since, similarly, the stimulant effects of even small doses of nicotine on operant response rates were reduced or abolished it is possible that nicotine's depressant actions are mediated largely by acetycholine release and that the stimulant effects may be mediated by different mechanisms, e.g. noradrenaline. Some evidence for this view is evidenced by the differential interactions with nicotine of a variety of nicotinic and muscarinic agonists and antagonists, and an adrenergic agonist (methamphetamine) on electrical self-stimulation behaviour (SS). Newman (1972) suggests that nicotine may be stimulating a central 'GO' mechanism (as measured by increased SS rates) via release of noradrenaline, probably post-synaptic, i.e. via prior ACh release, but that any decreases in SS rates (e.g. as observed by Domino, 1973) at higher dosages of nicotine are mediated by nicotine-induced release of ACh onto muscarinic, as opposed to nicotinic, receptors, a so-called 'NO-GO' system.

Chronic: There is some evidence that chronic as opposed to acute nicotine injection in rats will have additional effects. Firstly, tolerance to the depressant effects of chronic nicotine administration appears after a few days (cf. Figure 11). This tolerance has also been found by Stolerman, Fink and Jarvik (1973). It would appear that chronic nicotine



Mean activity-box scores for groups of eight rats tested for 30 minutes during 10 trials. Animals were tested immediately after the injection of nicotine, (0.8 mg/kg), amphetamine (0.8 mg/kg) or saline (control).

FIGURE 11 : Mean activity box scopes for rats, effects of (chronic) nicotine, amphetamine or saline (i.v.).

From Morrison and Stephenson (1972).

administration by drinking water through implanted subcutaneous reservoirs or i.p. injections within equivalent weighted human dosage ranges produces a tolerance lasting for at least 90 days after the end of regular treatment with nicotine (as measured by spontaneous locomotor activity in a Y maze). Although Stolerman et al. (1973) suggest that this long-lasting tolerance may be related to relapse to tobacco usage in man, they also state that a nicotine abstinence syndrome was not detected.

A stronger 'animal model' for relapse to tobacco in smokers who have 'given-up' is provided by Hall and Morrison (1973). Rats which have been helped by nicotine to learn a difficult and stressful shock avoidance task more rapidly and perform it more efficiently seem to depend on the continuation of nicotine to maintain their proficiency. When nicotine is withdrawn their ability to perform the task deteriorates progressively until they eventually do it no better than when they were novices. This is not simply a learning dissociation phenomenon (State-Dependent Learning) whereby the animal is unable to remember what was learned under the influence of nicotine because the disruption was relatively slight on the first day of withdrawal and deteriorated progressively. Nicotine may be acting as a tranquilliser in this situation since if a conditioned 'safety-signal' is presented during saline withdrawal then the decrement in performance does not occur. This suggests that the nicotine may be reducing the stressful aspects of the shock avoidance situation and can thus be compared to other tranquillisers, although it is arguable whether an analogy should be drawn with 'Major' tranquillisers, e.g. chlorpromazine, opiates, or 'Minor' tranquillisers, e.g. alcohol, barbiturates and valium, etc., (e.g. cf. Domino, 1973; Gray, 1971).

In addition, chronic nicotine administration (100 µg/Kg,

injection, 3 x daily) appears to have effects on what might be loosely termed 'attention' in rats performing a visual discrimination task for food reward (Nelsen and Goldstein, 1973). It would appear that, whilst impairing acquisition by increasing 'omission' errors, after criterion performance has been reached, nicotine causes a significant decrease in errors of 'commission' (bar pressing when the cue light signalling reward availability was not on), although having no significant effect on 'omission' errors (failure to make correct response when cue light signalling reward availability was on). This finding is explicable in terms of Routtenberg's (1968) 2-system theory of cortical activation, in which the reticular formation and limbic system are mutually inhibiting and control 'Drive Orientated Arousal' and 'Incentive Orientated Arousal' respectively. Chronic nicotine administration has indeed been found to favour limbic system versus reticular system control of the cortex in the rat (Nelsen, Pelley and Goldstein, 1973) and the rabbit (Bhattachrya and Goldstein, 1970). This provided support for the view that chronic nicotine may be favouring 'Incentive Orientated Arousal', i.e., base-rate operant response via the limbic system, whilst conversely inhibiting 'Drive Orientated Arousal', i.e., acquisition of new learning.

MAN

The effects of cigarette smoking on human performance can be viewed from the various angles discussed earlier as regards the effect of nicotine on animal performance. However, the task is further complicated by the fact that it is difficult to establish what is the human's baseline performance on some particular task, i.e., is one studying the effect of smoking deprivation (cf. the chronic nicotine studies referred to above) or is one studying the effects of smoking per se (cf. acute nicotine administration)? The two may not be the same. Unfortunately there is

insufficient data to draw any firm conclusions as to whether cigarette smoking is genuinely improving the performance of the smoker or merely preventing 'nicotine-hunger' disrupting a deprived smoker's level of performance efficiency..

Cigarette smoking (and by implication nicotine) has been demonstrated to act as stimulant drug on critical flicker fusion (Warwick and Eysenck, 1963), and in keeping with stimulant properties, to prevent the drop in performance associated with long, monotonous vigilance tasks; driving stimulation (Heimstra, Bancroft and De Kock, 1967); monotonous reaction-time task (Myrsten and Andersson, 1978); visual and auditory vigilance tasks (Wesnes and Warburton, 1978). In keeping with the viewpoint of smoking as being purely stimulant are the findings that smoking deprivation does not effect smokers' performance on simple tasks (Bowden test and Proof Reading) but actually improves performance on more complex tasks (Raven's Progressive Matrices, Letter Series, Mental Arithmetic), (Elgerot, 1976). An interpretation of the deleterious effects of cigarette smoking on more complex task performance can be given in terms of the 'Yerkes-Dodson Law' - optimal arousal being lower for more complex tasks and hence the observed decrement in performance with an over-arousing dosage for drug;nicotine. This is analogous to the decrement in performance seen with high dosages of nicotine in animal studies. However, this finding (Elgerot, 1976) poses difficulties for the view that nicotine, as a biphasic stimulant and depressant drug, should be able to lower arousal and thus increase performance for complex tasks - perhaps lowered arousal can only be seen when cigarettes are smoked in high stress situations. Some evidence for this interpretation is offered by Myrsten, Andersson, Frankenhaeuser and Elgerot (1975) who used questionnaire methods to divide smokers into two groups and to test

them in boring and stressing situations: 'high arousal' smokers who felt they needed to smoke when over-excited or stressed and 'low-arousal' smokers who needed to smoke during low-stimulation, boring situations. The results of this study support the view that smokers can increase their performance (on a complex sensori-motor task) but only when the smokers' starting states are taken into account (cf. Domino, 1973 - nicotine interaction self-stimulation rates in rats) - smoking during low situational arousal (boredom) improving 'low-arousal' smoker's performance and, conversely, improving 'high-arousal' smoker's performance during high situational arousal (stress).

Also predictable from viewing smoking as being generally stimulant is the finding that visual attention is narrowed (Johnston,1975, 1976). This is congruent with the finding of 'narrowed attention' in verbal learning mentioned earlier (see under 'Effects on Learning'), and with the general finding that increased arousal, whether produced by pharmacological or non-pharmacological means, will narrow attention (Wachtel, 1967).

Narrowed attention and reduced distractability probably explain the finding that nicotine tablets (0, 1 mg, 2 mg, oral nicotine given to deprived smokers and non-smokers) decrease the interfering effects of colour and word (e.g., 'BLUE' written in red colour) in the Stroop Test (Wesnes and Warburton, 1978). It may also explain the finding that smoking improves vigilance by suppressing 'false positives' (Mangan and Golding, 1978), although this type of result may be better explained in terms of a nicotine induced shift to limbic system arousal (cf. Nelsen et al., 1973). In practice, the class of interfering stimuli that smoking suppresses may have to be broadened to include preoccupations with failure acting as distracting stimuli which will interfere with the

main task in anxious subjects (Warburton and Wesnes, 1978). This type of action can be viewed as depressant, i.e., anxiolytic. It is entirely possible,given the evidence reviewed earlier (cf. under Phasic EEG, Evoked Potentials, etc.), that the subject may be able to dose himself with the correct dosage of nicotine to inhibit interfering stimuli, both emotional and non-emotional, whilst leaving cortical excitation undiminished for the main task.

Some such self-titration must be occurring to account for the surprising lack of evidence that smoking produces deficits as well as improvements in performance, which animal research with varying nicotine dosage definitely indicates. At high dosages nicotine will produce deficits in operant response through depressant actions. What little research has been carried out relating self-titration in smokers across different task demands does indicate that smokers do in fact take less and smaller puffs and so presumably obtain stimulant nicotine effects during monotonous driving simulation (Ashton and Watson, 1970).

8. EFFECTS OF NICOTINE AND TOBACCO SMOKING ON (1) APPETITE AND (2) AGGRESSIVENESS

(1) Nicotine and appetite

It is often observed that smokers gain in weight after giving up smoking. This gain in weight is probably derived from two sources.

Firstly, appetite increases upon giving up smoking, partly as a consequence of the ability of smoking to prevent feedback of 'hunger-stimuli' such as hunger contractions of the stomach (Schendorf and Ivy, 1939) and perhaps, more importantly, by central nicotine action to 'switch-off' the feeding centres of the hypothalamus (Münster and Bättig, 1975). As such, the nicotine provided by cigarette smoking, may be regarded as highly rewarding in the classic 'Drive Reduction' sense for the hungry smoker.

Secondly, giving up smoking may be causing weight gain because smokers seem to expend calories less efficiently than non-smokers. Thus, weight gains after giving up smoking tend to occur even if calorie intake is reduced (Lincoln, 1969). This may be because smoking or nicotine increases metabolic rate, perhaps by short-term increases in serum free fatty acids and triglycerides (Russell, 1976). Giving up smoking will consequently lower metabolic rate and so cause weight gain irrespective of whether the ex-smoker attempts to curb his or her increased appetite.

The weight gain of the smoker who gives up, caused by increased appetite and lowered metabolic rate,may be a serious deterrent to giving up smoking, especially for women.

(2) Nicotine and aggressiveness

There is evidence that nicotine reduces aggressiveness in animals

as measured by predatory biting attack in the cat (Bernston, Beattie and Walker, 1976), post-shock biting attack in the squirrel monkey (Hutchinson and Emley, 1973) and social aggressiveness in rats (Silverman, 1971). There is some evidence that the mechanism of this nicotine-induced reduction of aggressiveness involves the activation of the (inhibitory) nicotine part of a mutually-inhibitory nicotinic-muscarinic system controlling aggression (Bernston et al., 1976). (However, recent evidence suggests that other transmitters, such as noradrenaline , 5HT and GABA, may also be involved [Mandel, Mack, Kemf, Ebel and Simlers, 1978].)

Congruent with the previously cited animal experiments is the observation that heavy smokers have high 'chronic anger scores' (Thomas, 1973) and that smoking prevents the increase in self-rated feelings of aggressiveness observed when non-smokers and deprived smokers performed stressful and monotonous tasks (Heimstra, 1973). Similarly, when smokers are deprived of cigarettes, they not only score higher on an aggression inventory but they also display more aggression on an 'aggression machine', with which they administer 'shocks' to other people (Schechter and Rand, 1974).

Thus, reduction of aggression in smokers with high chronic anger scores may be an important motivational factor for smoking, and, as such, nicotine in this respect may be regarded as acting similarly to other tranquillisers (Hutchinson and Emley, 1973).

9. SUMMARY AND CONCLUSIONS OF PHYSIOLOGICAL EFFECTS OF NICOTINE AND CIGARETTE SMOKING, EFFECTS ON PERFORMANCE, AND EFFECTS ON APPETITE AND AGGRESSIVENESS

1) Nicotine has biphasic dose-related effects at nicotinic cholinergic receptors, being stimulant in small doses and depressant at larger doses.

2) However, it is difficult to predict, exactly, whether a given dose of nicotine, that is stimulant or depressant at the receptor level, will similarly be stimulant or depressant at higher levels of neural organisation. This is because nicotine action leads to the release of a wide variety of central and peripheral neurotransmitters and hormones (ACh, NA, 5HT, Ad, ADH, ACTH, etc.), which themselves may have excitatory or inhibitory actions. Thus, depressant effects may be caused by stimulation of inhibitory systems and vice-versa.

3) In terms of the reinforcing nature of nicotine, central, rather than peripheral effects are probably most important, regardless of whether the exact site of nicotine action is central or peripheral or both (e.g. nicotine-induced tachycardia).

4) For the cigarette smoker, probably the most important reinforcing feature of nicotine, obtained from a cigarette, is its dual nature as both a tranquilliser and a stimulant. There is some evidence that smokers may alter their puffing behaviour so as to obtain stimulant or tranquillising actions as appropriate to their prior state of arousal.

5) The ability of nicotine and cigarette smoking to increase performance (e.g. learning, vigilance, etc.) probably derives from nicotine's effects on focussing attention, and, when absorbed by the smoker in

appropriate dosages, to bring the smoker to the optimum portion of the 'inverted U curve' relating arousal to performance efficiency.

6) Smoking behaviour, as opposed to direct pharmacological actions of nicotine, may produce some of the observed central effects, both by virtue of the effects of smoke and physical activity per se, and perhaps by virtue of smoking behaviour stimuli (CS) becoming classically conditioned to direct nicotine actions (US) - the so-called 'secondary reinforcing' nature of smoking.

CHAPTER 2

AROUSAL MODULATION AND NICOTINE ADDICTION

MODELS OF CIGARETTE SMOKING

Currently, the most widely accepted theories of smoking maintenance are the addiction and arousal modulation theories.

A) Physiological addiction theories (Schachter, 1978, for example) postulate that certain CNS receptors, probably located in the medial forebrain bundle, become addicted to nicotine, i.e., they signal punishment when the nicotine level at these sites falls below a critical level. From this point of view, we might regard the desire to smoke as a consequence of nicotine 'hunger' in the classical drive sense, the purpose of smoking being to maintain nicotine homeostasis, just as regular heroin injections maintain opiate homeostasis at the CNS opiate receptors.

There are two main lines of evidence supporting an addiction model;

(1) 'withdrawal effects' following cessation of smoking;

(2) variations in smoking rate following experimental manipulation of nicotine levels in the smoker.

(1) Despite the fact that behavioural effects, such as increases in irritability, in eating, mannerisms, laziness, and depression, are commonly reported, especially in heavy smokers (Ryan, 1973; Schachter, Silverstein, Kozlowski, Perlick, Herman, and Liebling, 1977), as well as psychophysiological effects, usually in the direction of decreased arousal - lowered frequencies of dominant EEG (Ulett and Itil, 1969; Knott and Venables, 1977), decreased evoked potential envelopes (Hall et al 1973) and reductions in pulse rate and diastolic blood pressure (Knapp, Bliss and Wells, 1963) - there is no evidence of withdrawal effects in any way comparable with those reported by Subjects going 'cold turkey' in heroin addiction, or by alcoholics 'drying out'. On this basis, it is also difficult to account

for the fact that some smokers can abstain for a day or more with little consciously experienced craving.

Even if significant withdrawal effects were to be demonstrated, however, it is a moot point whether this would constitute direct support for an addiction hypothesis insofar as the total population of smokers is concerned. While such effect may be a 'rebound' phenomenon, suggesting that nicotine tolerance has occurred, particularly in long-term, heavy smokers, it is equally plausible that these effects may signal a return by some Subjects to a more 'normal' constitutional level of functioning.

This possibility is strongly suggested by Brown's (1973) data, comparing EEG characteristics of groups of heavy and light smokers, ex-smokers and non-smokers which show that smokers and ex-smokers share some EEG characteristics not seen in non-smokers. Indeed, Brown's (1973) findings may be cited as indirect evidence for an arousal modulation theory of smoking maintenance.

There is also other evidence that the 'normal' constitutional level of functioning of the smoker is different from that of the non-smoker. Longitudinal studies indicate that the teenager who eventually becomes a smoker is more emotionally labile than the future non-smoker (Cherry and Kiernan, 1978) and it is plausible to suggest that cigarette smoking for these individuals may have value as a 'psychological tool' in order to regulate mood. This view of smoker/non-smoker differences gains further credence in light of the evidence for a fair degree of genetic determination for smoking (Strickenberger, 1968) just as there is, to a lesser extent, for coffee and also alcohol consumption.

(2) More convincing empirical support comes from studies in which nicotine levels in the smoker are artificially manipulated, and the effects on smoking rate assessed. These may be roughly divided into those studies

concerned with internal, and those concerned with external manipulation of nicotine delivery.

Internal: Direct pharmacological control of nicotine supply to postulated mid-brain receptors has been obtained by intravenous or oral administration of nicotine or lobeline (Lucchesi, Schuster and Emley, 1967), of nicotine receptor antagonists such as mecamylamine, which readily pass the blood-brain barrier (Stolerman, Goldfarb, Fink and Jarvik, 1973) or through varying nicotine excretion rates by manipulating urinary pH (Schachter et al., 1977). These studies claim to demonstrate that the smoker will adjust his smoking rate in the appropriate direction. Observed changes, however, have been relatively small.

A number of factors, however - two in particular - could have depreciated treatment effects;

(i) In the case of oral ingestion of nicotine or lobeline, since there is considerable degradation by the liver of nicotine before the active molecule can reach the brain, nicotine dosage levels to mimic smoking may have been radically underestimated by experimenters;

(ii) With regard to cigarette smoking, nicotine may have to arrive at the CNS receptors in a concentrated bolus form, which suggests the method of pulsed microinjections into the carotid to mimic the in vivo effects of cigarette smoking. While Russell (1976) reports minimal effects on smoking of discrete, rapid, intravenous nicotine injections, at a rate designed to mimic in vivo 'boli', this may be in part a function of bolus dispersion due to venous mixing.

External: Attempts to vary smoking rate by manipulating the maximum possible nicotine delivery of a cigarette have produced conflicting results. While Frith (1971) and Schachter (1978) report significant variations in number of cigarettes smoked under these conditions, Mangan and Golding (1978), and

Goldfarb, Jarvik and Glick (1970) report no relationship (cf. Stepney, 1980, for recent comprehensive review of sixteen published experiments utilising this paradigm, suggesting that for a 50% decrease in nicotine delivery, a cigarette consumption increase of only 9% will be observed, on average). There is, however, some relevant evidence concerning smoking style. It has been reported that the number of puffs increases as the nicotine delivery of the cigarettes is reduced (Frith, 1971; Ashton and Watson, 1970). It may be that other aspects of smoking style, such as puff strength, for example, are also critical in determining amount of nicotine extracted from a cigarette. Some such explanation must be advanced to account for the recent observation that cigarette smokers appear to be able to maintain their plasma nicotine levels within fairly tight limits ± 10% (approximately) with only slight changes in cigarette consumption, in the face of variations in predicted nicotine delivery of cigarettes of ± 40% (approximately) from their habitually smoked medium nicotine cigarettes (Ashton, Stepney and Thompson, 1979).

Another factor, which has general relevance in studies involving manipulation of nicotine delivery, is that smoking quickly acquires secondary reinforcing properties - nicotine is a potent drug, the latency between CS (lighting up, lip contact, taste, inhalation) and US (arrival of nicotine at the appropriate CNS receptors) is short - approximately 8 to 10 seconds - and the smoker has experienced many thousands of CS-US pairings. Secondary reinforcement undoubtedly operates as a confounding variable when we attempt to measure the effects of manipulation of nicotine on smoking rates.

B) Arousal modulation theories suggest that the smoker uses nicotine to maintain a steady state, approximating an 'optimal arousal state' (Berlyne, 1971). Nicotine clearly has both a stimulant and depressant

effect on animal brains (Armitage et al., 1969) depending on dosage (Paton and Perry, 1953; Armitage et al., 1969). Data from human EEG studies generally support the view that nicotine and smoking have stimulant effects (Philips, 1971, for example) but there is some recent evidence for dose-related biphasic stimulant and depressant effects of nicotine on the CNV (Ashton et al., 1978, or cf. earlier "Effects of nicotine and cigarette smoking on the brain").

Nicotine addiction theorists regard these postulated beneficial effects - relaxation or stimulation - as a subjective rationalisation for the feeling of relief produced by the arrival of nicotine at depleted CNS sites. Thus, in learning theory terms, nicotine can be regarded as producing reward more or less directly (arousal modulation), or by avoiding punishment (addiction). Since omission of punishment is regarded by some theorists (e.g. Gray, 1971) as equivalent to reward, the only way to resolve the relative contribution of beneficial arousal effects, compared with avoidance of aversive withdrawal effects, on smoking maintenance, is to compare the effects of smoking on naive smokers, ex-smokers and current smokers. Critical studies on this issue, however, are lacking.

In addition to maintenance of optimal arousal level, and perhaps as a consequence of this, nicotine and cigarette smoking facilitate performance in a number of tasks - vigilance (Frankenhaeuser et al., 1971), acquisition and retention, in both animal (Garg, 1969, for example) and humans (Andersson, 1975, for example). The precise mechanisms involved are unknown (cf. earlier "Effects of nicotine and tobacco smoking on performance"). It may be that the effect can be accounted for simply in terms of increased arousal, leading to narrowing of the attentional focus (Wachtel, 1967), with consequent improvement in performance. Additionally, cigarette smoking may be improving performance by bringing the smoker to

the optimal part of the 'inverted U curve' relating cortical efficiency to arousal. However, this would hardly account for improved memory consolidation as opposed to acquisition, and the mechanism of nicotine action in this case may involve enhanced RNA production (cf. earlier: "Effects of nicotine and tobacco smoking on performance; (2) Consolidation").

Whatever the case, it seems obvious that an arousal modulation theory of smoking maintenance needs to be broadened to accommodate such effects on behaviours which can have adaptive significance.

The area of research covered in this thesis focusses on the central tenet of an arousal modulation theory of cigarette, namely that (i) the smoker can use cigarettes to obtain stimulant effects when drowsy and conversely depressant effects when anxious, (ii) the resultant stimulation or tranquillisation, as appropriate to the situation, is the major source of reinforcement for smoking maintenance, (iii) the biphasic dose-related stimulant and depressant actions of nicotine are the ultimate means by which these effects are obtained, although smoking behaviour, per se, may possess considerable secondary reinforcing properties.

Experiments 1, 2 and 3 examine the physiological effects of cigarette smoking in two extreme arousal situations: stress and sensory isolation. Experiment 4 examinesthe physiological effects of cigarette smoking in neutral, 'boring' conditions. Experiment 5 examinesthe effects of varying predicted nicotine delivery of cigarettes. Experiment 6 examines some effects of cigarette smoking and the CNV.

All the experiments have a major design feature in common; they attempt to examine the effects of cigarette smoking during the activity itself and for a short period afterwards. This design was adopted on the prediction that smoking effects will be maximal during smoking and for

only a short period afterwards, since nicotine has a short CNS half-life. This was taken to its logical conclusion in Experiment 6.

C H A P T E R 3

THE EXPERIMENTS

EXPERIMENT 1 : Psychological effects of smoking under conditions of stress and mild sensory isolation.

EXPERIMENT 2 : Further observations on variations in smoking style and psychophysiological effects of cigarette smoking under conditions of stress and sensory isolation.

EXPERIMENT 3 : Additional observations on the effects of cigarette smoking during conditions of stress and sensory isolation: the use of plumbed cigarette holders and EMG.

EXPERIMENT 4 : Cigarette smoking during 'Mild Boredom'.

EXPERIMENT 5 : Effects of variations in predicted nicotine delivery of cigarettes on psychophysiological responding and smoking behaviour.

EXPERIMENT 6 : Some effects of cigarette smoking on scalp DC potentials: Contingent Negative Variation (CNV).

E X P E R I M E N T 1

PSYCHOLOGICAL EFFECTS OF SMOKING UNDER CONDITIONS OF STRESS AND MILD SENSORY ISOLATION

Rationale

Arguing from arousal modulation theory (Berlyne, 1971), and in view of the reported findings from animal studies that the effects of nicotine are biphasic, i.e. can be stimulant or depressant, depending on dosage (Armitage et al., 1969; Ashton et al., 1978), it was hypothesised that under conditions of stress and mild sensory isolation, the smoker will attempt to manipulate his level of arousal to maintain an optimal state through self-titration with nicotine.

As to actual method of self-titration, a number of possibilities suggest themselves. The most obvious is that the smoker attempts to bring himself to the stimulant (low nicotine) or depressant (high nicotine) portions of the biphasic dose-response curve by manipulating one or more of the smoking style variables- frequency, strength and duration of puffing.

Design - General

In order to maximise the hypothesised 'arousal modulating' effects of cigarette smoking, two extremes of arousal were experimentally induced in the subjects. A lower arousal condition, 'sensory isolation', was induced by relaxing the subjects and a high arousal condition, 'stress', induced by high intensity bursts of white noise. It was hypothesised that subjects would use cigarette smoking as a 'tool' to lower their arousal in the stress condition and, conversely, to elevate their arousal

in the sensory isolation condition. Physiological arousal was assessed using as wide a range of response systems as possible. This was judged to be advisable since the concept of 'General Arousal', whilst still useful, has over the last twenty years been modified in order to account for the observation that different individuals tend to respond maximally in different systems - 'response stereotypy' (Lacey, 1956, 1967; Eysenck, 1977; Barrell and Price, 1977). Response systems monitored were EEG alpha, EKG, Respiration, EMG and Electrodermal (SCR and SCL).

The Response Systems :

It has long been known that ongoing alpha activity usually will be blocked when an awake individual is presented, for the first time, with almost any type of environmental stimulation (Berger, 1930). Reductions in alpha activity have also been noted during more prolonged conditions of postulated increased arousal, for example, performance of mental tasks (Dolce and Waldeier, 1974), anxiety states (Lindsley, 1950), etc. (cf. Eysenck [1967], Lader and Noble [1975] for reviews). Although reduction in alpha abundance is usually associated with a shift to higher frequency EEG activity (β), (together with an upward frequency shift in dominant frequency of remaining alpha), the reverse is possible with prolonged eyes-closed conditions. Thus, closing the eyes, which normally produces an increase in alpha activity, can, if prolonged too long, favour sleep and, consequently, reduce alpha activity by decreasing the predominant brain wave frequency (Plotkin, 1976). This possible error in utilising alpha as an index of arousal can be eliminated by instructing subjects to keep their eyes open. The reported effects on alpha of cigarette smoking have generally indicated stimulant effects; decreased alpha activity (Hauser et al., 1958) and elevations of dominant alpha frequency (Knott, 1978), although the latter study showed no significant effect on alpha

amplitude.

Elevation of Electrodermal activity (Skin Conductance Level [SCL]; Skin Conductance Response [SCR]) and elevations of pulse rate (HR) are well documented as indices of increased arousal (Eysenck, 1967; Lader and Noble, 1975; Naliboff, Rickles, Cohen and Naimark, 1976). HR elevation to cigarette smoking is well documented as being the single most reliable psychophysiological measure of cigarette smoking (as opposed to changes in blood pressure, peripheral blood flow, dominant frequencies of the EEG power spectrum, cortical evoked response, CNV, EMG, respiration rate and depth, SCL/SCR, etc.), this smoking-induced HR elevation being almost exclusively attributable to the dose-related effects of nicotine rather than any other associated physical or chemical component of cigarette smoking (Lucchesi et al., 1967; Herxheimer et al., 1967; Elliot and Thysell, 1968). Whilst being subject to tachyphylaxis, HR elevation to cigarette smoking occurs under almost any conditions, including electric shock stress (Schachter, 1973).

In contrast to the large body of evidence regarding the effects of cigarette smoking on heart rate, there is very little published work concerning the effects of cigarette smoking on electrodermal responding. What evidence there is suggests a stimulant effect - SCL increasing (Agué, 1974; Mangan and Golding, 1978)

Various measures of respiration have been correlated with levels of arousal, although compared to other psychophysiological measures, respiration appears to be relatively little used, perhaps because of the complexity of its relationship with other response systems including reflex relationships with cardiovascular and electrodermal systems. In general terms, whilst respiration rate is suggested to be elevated by

excitement, the depth of respiration is stated by some authors to depend on whether the increased arousal is pleasant (depth increases) or aversive (depth decreases): (Dunbar, 1954; Woodworth and Schlosberg, 1954). Woodworth and Schlosberg (1954) suggest that the 'I' fraction (ratio of the duration of inhalation (i) to the duration of the whole respiratory cycle (i + e); = I/(i + e) is perhaps the most useful indicator of whether a person is pleasantly or unpleasantly aroused, although the 'I' fraction is useless for assessing the level of arousal as opposed to emotional affect, as can be seen from the following data drawn from Woodworth and Schlosberg (1954): laughter:- I = 0.23; resting:- I = 0.43; fright:- I = 0.75. This suggestion is not contradicted in a recent selective review by Sayers (1975), dealing mainly with performance, although the latter author suggests that depth of inhalation, whilst decreasing with increasing task difficulty, is not a very sensitive measure as compared to a cardiovascular variable such as H.R.

Christiansen (1965), reviewing the published literature and much Scandinavian work otherwise generally inaccessible, emphasised two further points. Firstly, a general point, that the effects of various experimental manipulations, e.g. stress, performance tasks, appear to vary according to the type of subject; normals, neurotics and schizophrenics (various sub -groups), for example. Secondly, that the single best respiratory index for measuring the effects of experimentally-induced stress and of trait anxiety between various clinical groups is an elevation of respiration amplitude variability (period variability being a poor measure, by contrast).

Given the conflicting experimental data reviewed by Christiansen (1965), two respiratory measures were chosen. Firstly, respiration rate, which, although perhaps a poor indicator of arousal, has the merit of

being that measure of respiration most commonly used. Secondly, amplitude irregularity of respiration which is arguably the most sensitive respiratory indicator of stressful arousal.

Respiration rate appears to be slightly depressed by cigarette smoking (Dock, 1963)), and by injection of a nicotine analogue - lobeline (Bevan and Murray, 1963). However, the definitive assignation of this respiratory depression to the effects of nicotine obtained from cigarette smoking is equivocal, since injections of nicotine into the human ascending aorta have been observed to have no effect on respiration rate but to increase significantly depth of respiration (Burgess and Rapaport, 1968).

Muscle activity (EMG) whether phasic or tonic has a complex relationship with arousal. Thus, to take the extreme case, during slow wave sleep muscle activity reduces compared to wakefulness. Nevertheless, muscle tone decreases even further during paradoxical sleep, apart from ocular muscle activity, when fast low voltage cortical activity, indicative of cortical arousal, is also present. The mechanism of this spinal reflex and sensory input suppression is of some interest for cigarette smoking research since there is evidence that it is cholinergic and could, therefore, theoretically be activated by nicotine (Hobson and McCarley, 1978). As regards the suggestion that muscle activity increases with arousal, the situation is complicated by response stereotypy. Thus, although increased (irrelevant) EMG activity has been associated with mental effort in performance tasks (Venables and Martin, 1967), clinical anxiety Sainsbury and Gibson, 1954), shock-stress (Barrell and Price, 1977), the use of EMG as an arousal correlate is made difficult by the fact that some individuals will respond differentially to stress in various response systems, e.g. cardiovascular versus muscle (Barrell and Price, 1977) and even differentially between various muscle groups (Lader and Noble, 1975).

Nevertheless, given the known muscle relaxing effects of minor tranquilisers such as alcohol and diazepam (Laurence, 1973), and the current clinical usage of various progressive relaxation and EMG biofeedback techniques to counter some forms of anxiety and tension induced symptoms, such as headache, it is of interest to use EMG as one of the psychophysiological measures in this experiment. There is some evidence that cigarette smoking or nicotine reduces muscle activity; the patellarreflex (Domino, 1973) and stress-produced jaw contractions (Hutchinson and Emley, 1973), However, the situation as regards EMG is not clear-cut since recent evidence suggests that tonic EMG may be increased by cigarette smoking (Fagerström and Götestam, 1977).

Subject Characteristics

General "background" data was routinely collected from all subjects participating in the experiments presented in this thesis. The subject characteristics recorded were: age, sex, personality (Eysenck Personality Questionnaire - EPQ; Eysenck and Eysenck, 1975) and smoking habits (average cigarette consumption per day, and usual brand of cigarette smoked).

There is some evidence that these subject characteristics bear a small but significant relationship to each other and to psychophysiological responding. Thus to take a simple example, "extraversion" (i.e. the personality dimension subsuming such traits as sociability and impulsivity) is said to be positively related to cigarette consumption (Eysenck, 1973), and in addition, there is some evidence that the extraverted smoker obtains stimulent rather than depressant CNS effects from cigarette smoking (Ashton et al., 1974; Eysenck and O'Connor, 1979). Indeed, this type of relationship has been predicted on the basis of an Arousal Modulation model of cigarette smoking (Eysenck, 1973) - extraverts being relatively cortically underaroused (Eysenck, 1967), smoking in order to obtain stimulant effects and thus raise their CNS arousal towards a postulated 'optimum' (for a fuller discussion cf. Chapter 4)

Characteristics of the subject sample for each experiment are detailed at the beginning of the respective "Results" sections. However, for ease of presentation, the main analysis and discussion of this (pooled) data is deferred until Chapter 4: 'Smoking, Personality and Physiology - Interactions.' This strategy is deemed appropriate since the 'n' of the sample and its variance on a particular characteristic in each experiment is often too low to make meaningful analysis possible. For example, as regards the relationship between personality and psychophysiological responding - although significant relationships between these variables have been found (Eysenck, 1967), correlations are usually low and necessitate the use of a fairly large subject 'n' before significance is achieved.

Experimental Procedures

Twenty-four subjects were randomly allocated to one of three groups (N = 8 in each case).

(1) 'Real smoking' group, where each subject smoked a cigarette during a 5-minute period, the beginning and end of which were indicated by light flashes.

(2) 'Activity control' group, where each subject sham smoked an unlit cigarette during the period indicated by light flashes. The subject puffed and inhaled as in normal smoking, whilst smoke floated around, from a lit cigarette in the ash-tray.

(3) 'Situation control' group, where the subject did nothing but was told that he was one of a control group and that the two light flashes (at the beginning and end of the 5-minute smoking period) were presented to equate conditions between groups.

There were two conditions within the experiment. In the sensory

isolation condition, the subject lay on a soft bed with the head supported by a low pillow, and with the eyes open. After 20 minutes relaxation, the last 5-minutes of which were taken as the baseline period, the subject smoked a cigarette for 5-minutes (or sham smoked or did nothing), onset and termination of this period being indicated by light flashes. The subject then relaxed for a further 7-minutes.

In the stress condition[1] the subject sat upright in a comfortable armchair whilst bursts of white noise were relayed through headphones at randomly determined points throughout a 15-minute period. The subject smoked (or sham-smoked or did nothing) during the middle 5-minute period, the beginning and end of which was indicated, as in the sensory isolation condition, by light flashes.

1

In an earlier experiment, randomly inflicted painful electric shocks were used to produce stress. However, recruitment of volunteers was difficult. In addition, the prospect of electric shocks probably deterred the more nervous 'relaxation' smoker from participating. For this reason, the more 'innocuous sounding' White Noise bursts at an (aversive) intensity of 106 dB was used. This strategy proved more successful in persuading subjects to volunteer. In fact, electric shock or white noise seem to be equally effective at producing stress if heart rate elevation is taken as an indicator of stressful arousal. Comparing the mean heart rates in the 5-minute pre-smoking periods during sensory isolation or stress conditions it can be seen, from the tabulated data (Table 1) that heart-rate elevation due to stress (ΔHR_{ST-SI} = Mean HR pre-smoking stress - Mean HR pre-smoking sensory isolation) is +9.8 b.p.m. for electric shock and +10.3 b.p.m. for white noise. However, the use of white noise bursts as opposed to electric shock necessitates a design in which subjects act as their own controls between conditions (stress, sensory isolation) but not between activities (real, sham or situation control). This is because the phasic reactions to white noise as measured by SCR habituate to some extent - see graph (Figure 8) - although the tonic measures of heart rate and EEG alpha do not - see graphs (Figures 1 and 6). This phasic habituation does not appear to occur to the same extent with electric shock, presumably since pain receptors do not adapt so easily as sensory receptors.

Table 1:

Heart rate elevations (ΔHR_{ST-SI}) due to Electric Shock Stress and due to White Noise Stress

(N = 5)	Mean HR pre-smoking (5 mins.)
Sensory Isolation (SI)	65.4 bpm
Electric Shock Stress (ST)	75.2 bpm
$\Delta HR_{ST - SI}$	+9.8 bpm

(N = 24)	Mean HR pre-smoking (5 mins.)
Sensory Isolation (SI)	62.9 bpm
White Noise Stress (ST)	73.2 bpm
$\Delta HR_{ST - SI}$	+10.3 bpm

The total duration of white noise during the 15-minutes stress period was 61 seconds distributed randomly in twenty-three episodes of duration 1, 2, 3 or 4 seconds. Noise onset and duration were controlled by a tape programmer and solid state logic and displayed on a polygraph marker channel from associated relay equipment. White noise was at an intensity of 106 dB as rated by a Dawe sound level meter located at the headphones.

The order of the two conditions (SI and WN)[2] was randomised between subjects to avoid serial order effects. During the 30-minutes interval between conditions the subject relaxed and talked with the experimenter.

Response Measures

Skin Conductance (SC), EEG, EKG, Respiration and Puff frequency were recorded throughout the session. EMG was also recorded but not reported because of EKG artefacts.

Equipment

All responses were recorded using a Device M19 recording system. SC was recorded using an 'Electronic Developments' SC unit wired through to the physiograph.

Recording

SC was recorded using a preamplifier sensitivity of 1 mm per deflection equal to 500 ohms, although in some cases of hyper-responsivity it was necessary to lower the sensitivity to avoid constant adjustment of back-off. After thorough cleaning with 10% alcohol, Ag-AgCl cup electrodes, in contact with standard electrolytic jelly (SNP Limited), were fixed by adhesive discs on the whorls of the fingertips to the first and third fingers of the subject's non-dominant hand. The electrode area was 0.7 cm^2 and an impressed current of 8 µA DC produced a current density of 11.4 µA cm^2.

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[2] Abbreviations used: Sensory Isolation = SI; Stress of White Noise = ST or WN

EEG was recorded using SLE miniature electrodes placed in the midline frontal and left occipital areas (F_z and O_1, Jasper, 1958), referenced to the opposite mastoid (A_2). This was reversed for left-handers. The recording channel was filtered for 8 - 13 H_z activity using a band-pass filter built by the experimenter. Sensitivity was

set to yield a pen deflection of 1.5 cm for an average peak 'alpha' burst. This calibration was performed during the 'eyes-open' baseline period preceding the relevant experimental condition.

EKG was recorded from the left wrist, left and right ankles using plate electrodes secured with elastic straps. The skin was rubbed with electrolytic jelly to ensure good electrical contact.

Respiration was recorded using Hg in rubber strain gauge, from around the mid-thorax.

EMG was recorded from a variety of positions on the neck and shoulder but is not presented due to gross EKG and movement artefacts and EMG module breakdowns.

Puffing frequency was observed through a one-way window and was recorded using a hand held push button displaying on the physiograph paper.

Scoring Procedures and Data Analysis

S.C.

Skin Conductance Level (SCL) was read at every 10 seconds event mark throughout the 17-minute Sensory Isolation period, except where such points coincided with the subject's actual smoking. Mean SCL values for successive 60 second periods were derived from these readings. Units of measurement were Skin Resistance in K ohms converted to $\log_{10}$SCL using the formula

$$\log_{10}\text{SCL } (\mu\text{mhos}) = \log_{10}\left\{\frac{1000}{\text{Skin Resistance (K ohms)}}\right\}$$

Skin Conductance Response (SCR) to white noise bursts during the Stress Conditions was scored as the maximum rise from the running SCL baseline, occurring 1.5 - 3.5 seconds after the white noise burst onset (i.e. timed from the event marker channel for white noise bursts). Log_{10}SCR µmhos was calculated from this change in Skin Resistance (K ohms), using as baseline values tonic SCL in the 5 second period preceding the stimulus, according to the formula

$$= \log_{10}\left\{\frac{\log_{10}\text{SCR } (\mu\text{mhos})}{\substack{\text{Min. Skin Resistance (K ohms)} \\ \text{1.5 - 3.5 sec. POST-STIMULUS}}}\right\} - \log_{10}\left\{\frac{1000}{\substack{\text{Skin Resistance (K ohms) 5 sec.} \\ \text{PRE-STIMULUS}}}\right\}$$

A criterion was used as a cut-off point for accepting an SCR for data purposes: Amplitude criterion for evoked SCRs was change in log conductance 0.5 K ohm equivalent to a pen deflection of 1 mm at the lowest resistance expressed by any subject in the sample (20 K ohms). The criterion was 0.011 log µmhos. (This is equivalent to a 0.5 K ohm decrease in Skin Resistance Level at 20 K ohms tonic Skin Resistance Level.)

$$\frac{\log_{10}\text{SCR}}{\text{(change in log conductance µmhos)}} = \log_{10}\frac{1000}{19.5} - \log_{10}\frac{1000}{20}$$

$$= 0.010995$$

$$\underline{\Omega}\ 0.011$$

EEG

With the EEG gain amplifier set to yield a pen deflection of 1.5 cm (half-wave), for an average peak alpha burst during the eyes open baseline period preceding the relevant experimental condition, an arbitrary criterion of 0.75 cm was employed so that alpha activity had to at least 50% of the average peak amplitude to be counted. Bursts of 8-13 Hz alpha

waves during one second intervals constituted an alpha unit[3].

The total record for each condition was utilised (the scoring made slightly easier by the fact that the record was the product of an 8-13 Hz bandpass filter and by the use of an illuminated magnifier). The first 2-minutes of the 5-minute pre-smoking baseline preceding the two experimental periods were employed to establish starting point values. Percentage alpha deviation from starting point values were plotted in one-minute blocks.

EKG

Heart Rate (HR) was scored in beats per minute (b.p.m.) by counting the number of peaks on the EKG trace in minute periods. HR elevation due to smoking was calculated as the difference between HR observed in the minute period following the end of smoking and HR averaged over the relevant 5-minute baseline pre-smoking. This particular measure of HR elevation was calculated because plasma nicotine usually reaches a peak about the end of cigarette smoking (Armitage, 1978), and thus HR is being observed during the period of predicted peak plasma nicotine. (Inclusion of the minute period prior to finishing smoking would not be "activity-free".)

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[3] Samples of EEG record were scored independently by Dr. G. Mangan (to whom I am indebted) as well as by the author and the inter-observer reliability obtained was 80% to 90%. This check was felt necessary owing to the possibility of scoring eye-movement artefact in the 10 - 13 Hz bandpass filtered EEG trace as data.('α' activity is particularly susceptible to eye-related artefact - some authors even claiming EEG 'α' activity recorded from the scalp to be totally eye generated electrical activity owing to the retinal corneal D.C. potential interacting with the 10 Hz ocular muscle tremor e.g. see Lippold [1970], although this is an extreme view, many workers in the field disagreeing - see Cavonius [1973], for example). Eye related artefact was considered to be any 'spike' as opposed to any relatively longer (i.e. > one second) duration of 'alpha burst' activity.

Respiration

Two measures were obtained from the respiration record. Firstly, Respiration Rate was scored in breaths per minute by counting the number of inhalation peaks in minute periods. Secondly, a measure of respiratory irregularity - 'Deep Breaths' - was scored in Deep Breaths per minute by counting the number of inhalations which were greater or equal to an arbitrary criterion - twice the average amplitude of the inhalation/ exhalation cycle during the relevant 5-minute baseline period.

Puffing Frequency

Puffing frequency was scored in puffs per minute as the number of puffs in each 1-minute epoch of the 5-minute real smoking or sham smoking period. The 'lighting-up' puffs were scored as one puff. Similarly, closely spaced double puffs, followed by one inhalation, as observed on the respiration channel, were scored as one puff.

RESULTS

(i) Personality and Smoking Habits Data

(ii) Heart Rate

(iii) Respiration

(iv) SCL

(v) SCR

(vi) EEG

(vii) Smoking Style

(viii) Intercorrelations

(i) Personality and Smoking Habits Data

The means by groups for personality scores (PENL) and smoking habits (cigarette consumption per day), as tested by Kruskall-Wallis non-parametric one-way ANOVA, do not differ significantly. To this extent the

Table 2 Personality & Smoking Habits Data for subjects by groups: Means & S.D.s

M = Mean
SD = Standard deviation

GROUP	n	CIGARETTE CONSUMPTION (cigs. smoked per day)		PERSONALITY : EPQ SCORES							
				P		E		N		L	
		M	SD	M	SD	M	SD	M	SD	M	SD
REAL SMOKING	8	12.60		7.63		13.63		13.00		2.13	
			4.41		1.77		3.20		6.30		2.59
SHAM SMOKING	8	12.80		6.30		13.50		13.90		2.10	
			3.99		2.19		2.67		4.89		2.03
SITUATION CONTROL	8	10.30		6.80		14.50		13.40		2.10	
			4.77		2.49		1.48		2.88		2.53
COMBINED	24	11.88		6,91		13.87		13.43		2.10	
			4.37		2.15		3.17		4.80		2.29

Table 3 Kruskall-Wallis 1-way ANOVA for Smoking Habits (Cigarette Consumption per day) and Personality Scores (Eysenck's P,E,N,L) across all Groups (Real, Sham, Control)

Variable	H	df	p
Cigarette Consumption	2.09	k = 3, n = 8,8,8	NS
P	2.40	k = 3, n = 8,8,8	NS
E	1.74	k = 3, n = 8,8,8	NS
N	0.16	k = 3, n = 8,8,8	NS
L	2.71	k = 3, n = 8,8,8	NS

groups represent similar samples of the smoking population, an important factor when dealing with independent control groups (n = 8 in each case; see Table 2, 3).

(ii) Heart Rate (HR)

There are two main effects: firstly, between conditions and, secondly, between groups. These are illustrated graphically (see Figures 1 and 2).

Between conditions effects: This is a validation of the arousal conditions. Thus, heart rates were significantly higher during white noise than sensory isolation (cf. Table 4). These rates are scored in the 5-minutes prior to activity (real smoking, sham smoking or situation control) and therefore are activity-free rates.

The differences in mean baseline Heart Rate (HR) between groups are not significant. This homogeneity of groups is further underlined by the fact that the mean HR elevations by groups due to the aversive qualities of white noise are also not significantly different (see Tables 5a, b).

Predictably, cigarette smoking produces tachycardia in both stress and sensory isolation conditions. Examination of Table 6 shows that while real smoking significantly elevates HR there is no significant change (Post-Pre) for the sham and situation control groups. This suggests that the major effect of smoking is due to the nicotine and not to any of the associated behaviour of smoking - inhalation, smell of smoke, arm movements, etc.

The difference in HR elevation due to cigarette smoking during stress (+8.48 b.p.m.) and sensory isolation (+11.20 b.p.m.) is fairly small and when tested not significant (non-parametric sign test for n = 8).

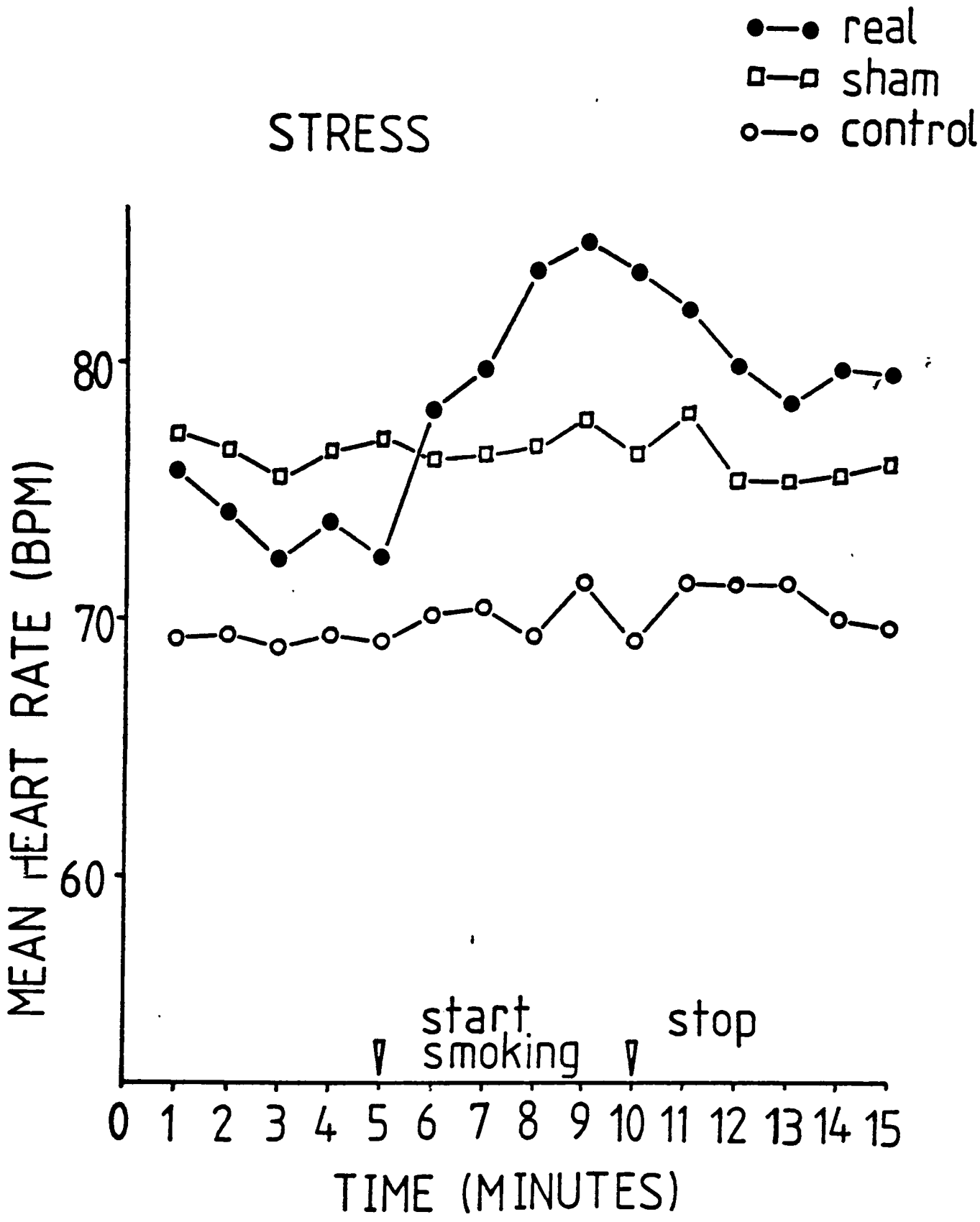


FIGURE 1 : Mean Heart Rates for Real, Sham and Control Groups (n = 8,8,8) during the white noise stress condition

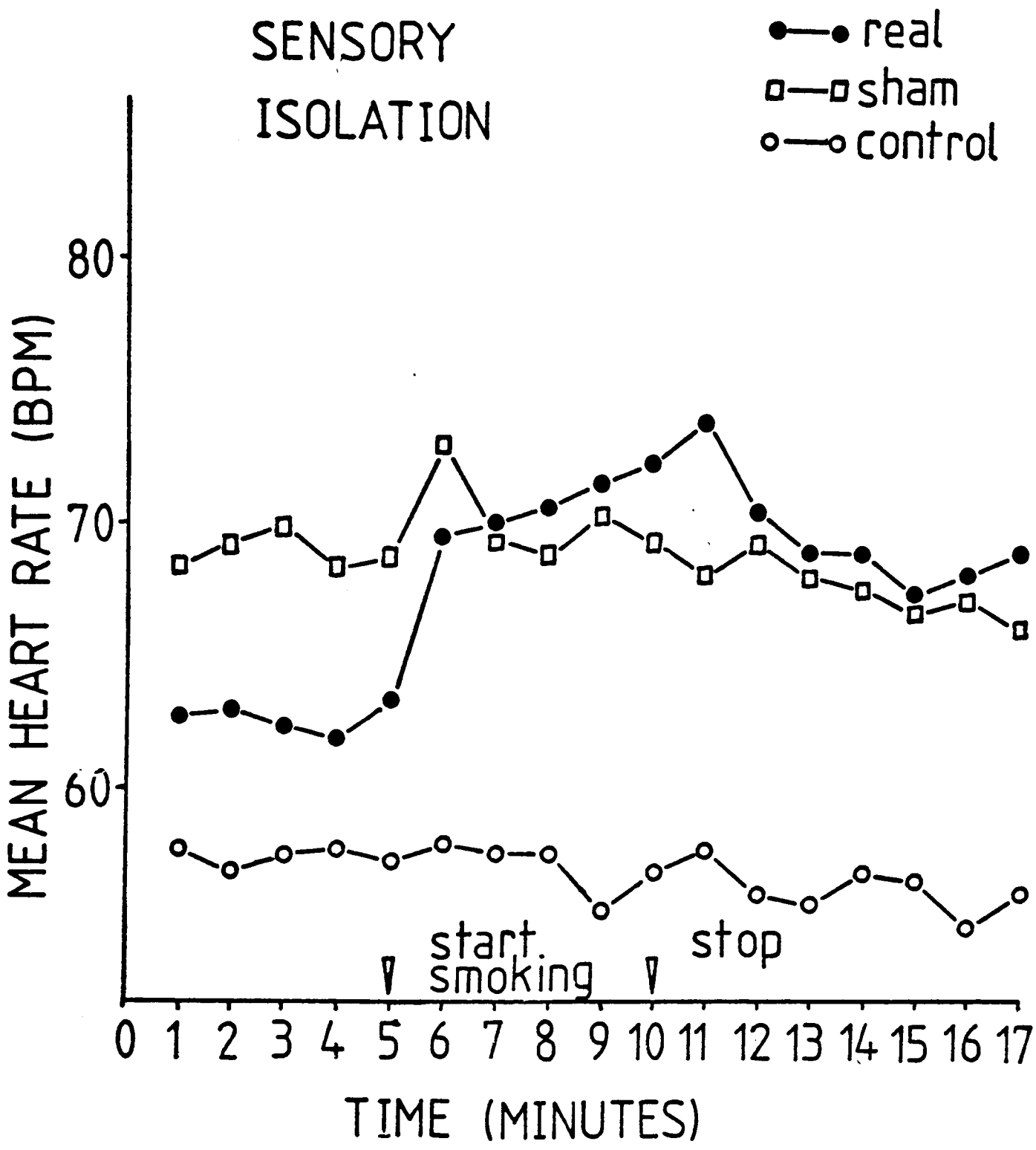


FIGURE 2 : Mean heart rates for real, sham and control groups (n = 8,8,8) during sensory isolation condition.

Table 4 — Mean Heart Rate Differences between Sensory Isolation and Stress (white noise) Conditions during pre-smoking baseline (mins. 1 - 5)

GROUP	n	Mean (S.D) Baseline H.R. (b.p.m.)				Δ H.R. ST-SI	P Sign-test 1-tailed
		Stress = ST		Sensory Isolation = SI			
Real Smoking	8	73.78	13.16	62.68	7.74	+11.10	< .004
Sham Smoking	8	76.65	9.23	68.65	8.60	+ 8.00	< .004
Situation Control	8	69.13	8.10	57.43	8.33	+11.70	< .004
Combined Groups	24	73.19	10.42	62.92	9.16	+10.27	< .001

Table 5a — Kruskall-Wallis 1-way ANOVA between three groups (Real, Sham and Control) for each Condition (Stress, Sensory Isolation) : Test hypothesis that baseline H.R. for the three independent Groups are from different populations.

Condition	H	df	P
Stress	1.93	k = 3, N = 8,8,8	N.S.
Sensory Isolation	4.79	k = 3, N = 8,8,8	N.S.

Table 5b — Kruskall-Wallis 1-way ANOVA for baseline H.R. elevation due to white noise (Δ H.R.$_{ST-SI}$) across all Groups (Real, Sham, Control)

H	df	P
1.02	k = 3, N = 8,8,8	N.S.

Table 6

Heart Rate elevations for Real Smoking, Sham Smoking and Situation Control Groups in two Conditions - (Stress & Sensory Isolation).
Δ H.R. = (H.R. 1 Min Post-Activity - Mean H.R. over 5 Mins Baseline).

GROUP	STRESS Δ H.R. b.p.m.	P sign test post-pre	SENSORY ISOLATION H.R. b.p.m.	P sign test post - pre
Real Smoking	+8.48 (2.73)	< .004	+11.20 (4.62)	< .004
Sham Smoking	+1.75 (4.51)	NS	- 0.53 (4.45)	NS
Situation Control	+2.50 (3.88)	NS	+ 0.33 (4.41)	NS

Table 7

HR Elevation : HR during the 4th minute of smoking - HR over 1-5 minutes baseline pre-smoking.

SMOKING GROUP	STRESS HR ELEVATION (BPM)	SENSORY ISOLATION HR ELEVATION (BPM)	Sign test on difference
REAL (n=8)	+ 11.10	+ 8.82	NS
S.D.	3.54	4.08	

Given that HR elevation is one of the most reliable physiological indicators of nicotine absorption from cigarette smoking (obviously plasma nicotine is the method of choice) the result would indicate that smaller quanitites of nicotine were extracted and absorbed by subjects during stress *than* sensory isolation. However, there are various reasons for supposing that actually this may not be the case. Firstly, the elevated pre-smoking HR baselines during stress may be depreciating the smoking-induced HR elevation during the stress condition, due to a Law of Initial Values effect (ceiling effect). Secondly, it is surprising that although subjects took more puffs (not significant) during the stress condition (see smoking styles results), the mean HR elevation due to cigarette smoking during stress is slightly lower than during sensory isolation (of course, puff intensity may be an uncontrolled factor here). Thirdly, it would appear that HR reaches a maximum at an earlier stage for the stress group - 3 to 4 minutes post light-up - as compared to smoking during sensory isolation (mean HR reaching a maximum after finishing smoking; 6-minutes post light-up [cf. Figures 1 and 2 'real group']). However, the greater HR elevation in the fourth minute of smoking for stress versus sensory isolation fails to achieve significance (cf. Table 7), although of course it represents a reversal of the trend when HR is taken post-smoking (cf. Table 6).

Smoking style data supports this interpretation (see Figure 10); subjects tending to smoke more intensely, as measured by puffing rate, at the beginning of the 5-minute smoking period during the stress as opposed to sensory isolation. This point is important since it may be that, although the total quantities of nicotine absorbed by the smokers (real smoking) during stress and sensory isolation conditions are similar, the smokers are obtaining their dose of nicotine more rapidly under stress.

Thus Armitage, Hall and Morrison (1968) observed that the same dose of nicotine injected into cats would produce stimulant (slow injection) or depressant (fast injection) effects depending upon the rate of nicotine injection.

(iii) Respiration

Results for Respiration Rates and Deep Breaths (> 2 x normal respiration depth) as a function of time are displayed graphically (cf. Figures 3, 4, and 5a, b). The most striking feature of these results are the slowing of Respiration Rates and the increase in the number of Deep Breaths during the Real or Sham Smoking time period (minutes 5 - 10) for Real and Sham Smoking groups, as compared to Situation Control group. This occurs for both Stress and Sensory Isolation conditions. However, although dramatic, these particular effects will not be analysed in detail since they merely serve to underline the physical processes of cigarette smoking or sham smoking, i.e. the interruption of the normal respiratory cycle by repeated inhalations of smoke or air (for real or sham smoking respectively), with the consequent slowing of overall respiratory rate (breaths per minute) and increase in respiratory irregularities (Deep Breaths). This decrease in Respiration Rate and increase of Deep Breath rate is maximal in the first minute of smoking (minute 6) but gradually dwindles towards the end of smoking (minutes 7 - 10). The reason for this 'tailing off' can be found by examining Figure 10 (Mean Puffing Rates) which can be seen to decline gradually over the 5-minute smoking period.

Whilst it does appear that baseline Respiration Rates (minutes 1 - 5; cf. Figures 3 and 4) vary considerably between groups (real, sham, control) for both sensory isolation and stress conditions, these between-group differences in baseline Respiration Rate (cf. Table 8) are not significant when tested using Kruskall-Wallis one-way ANOVA (cf. Table 9).

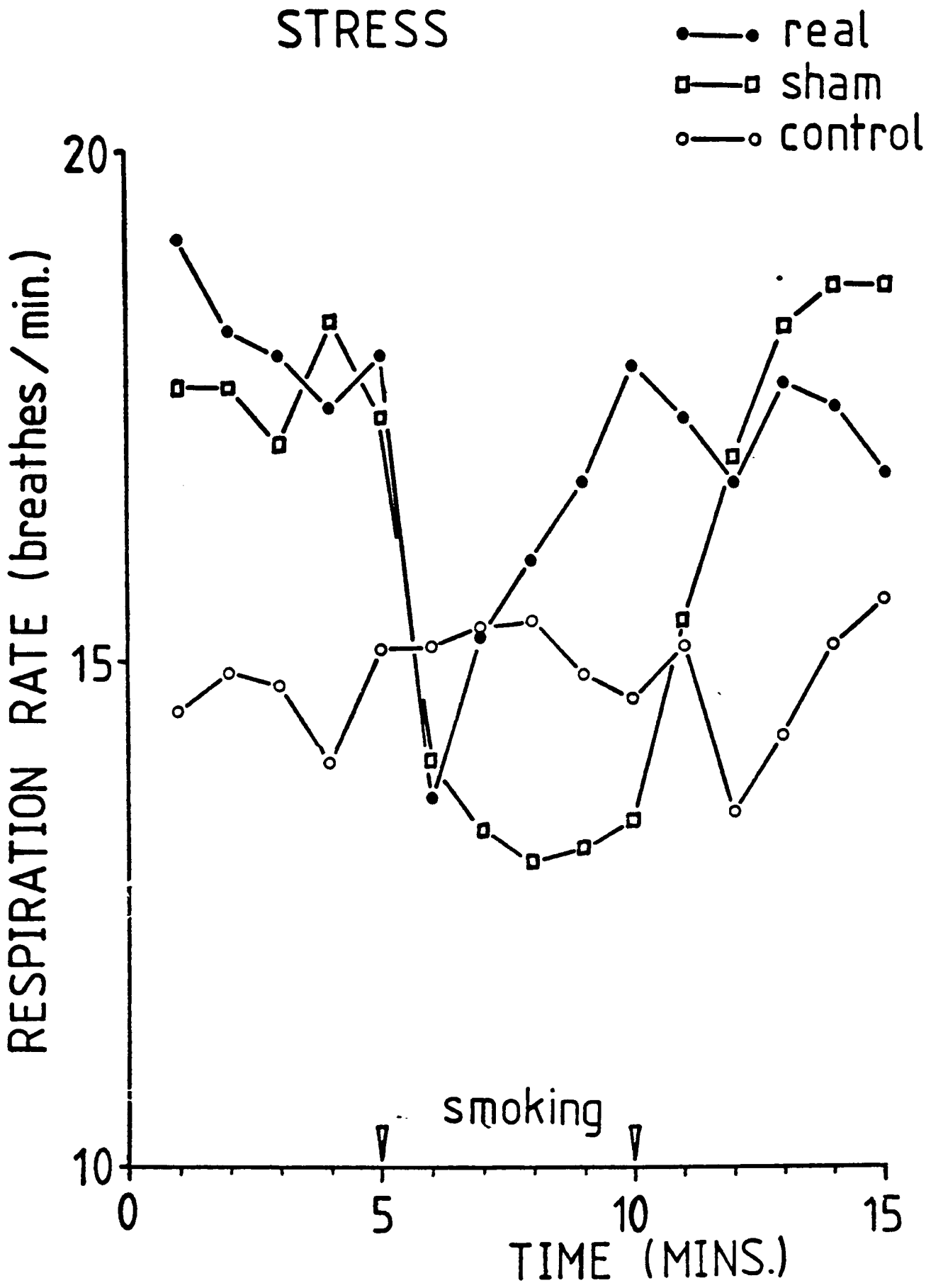


FIGURE 3 : Mean respiration rates during stress condition for real, sham and control groups (n = 8,8,8)

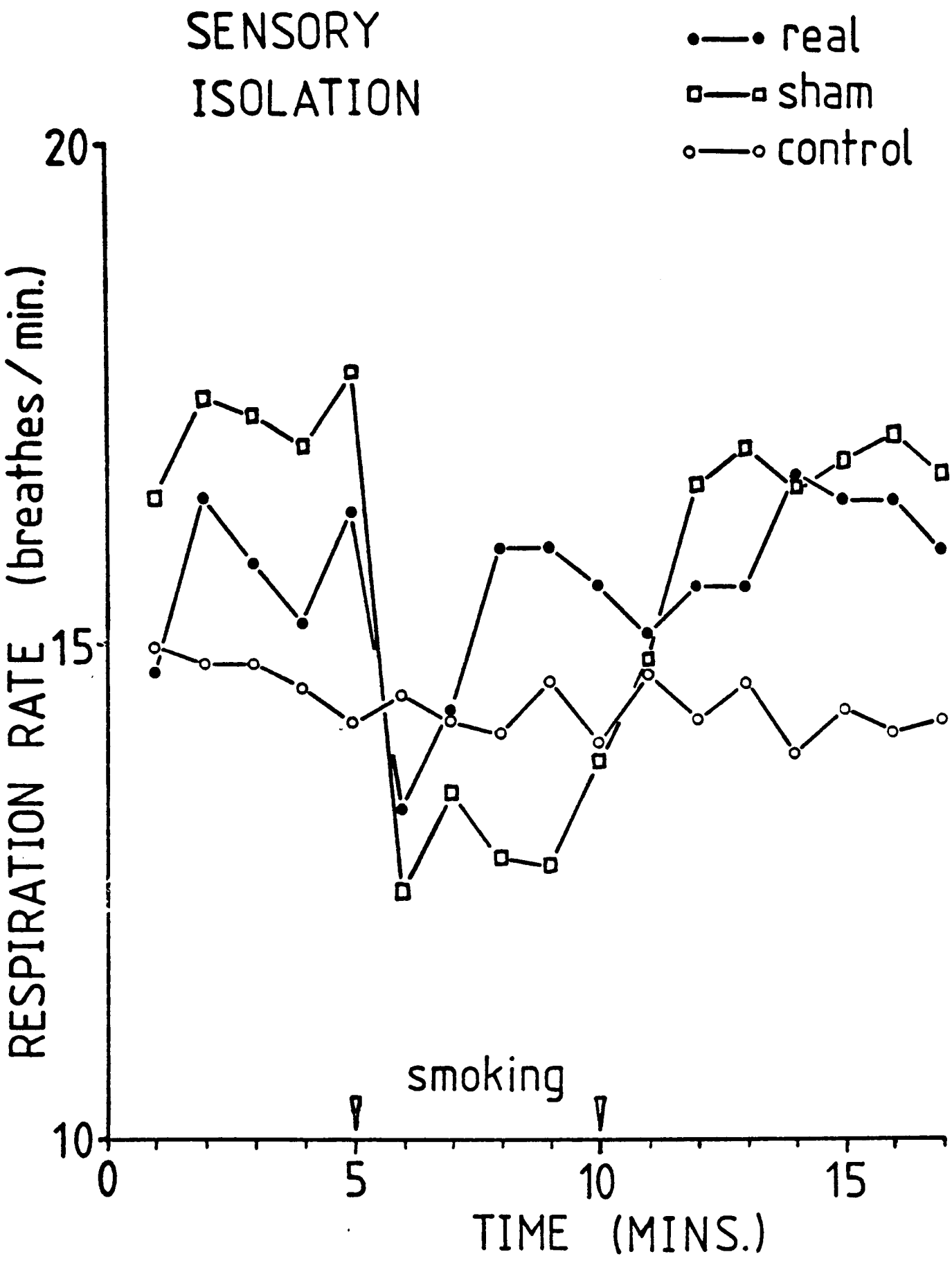
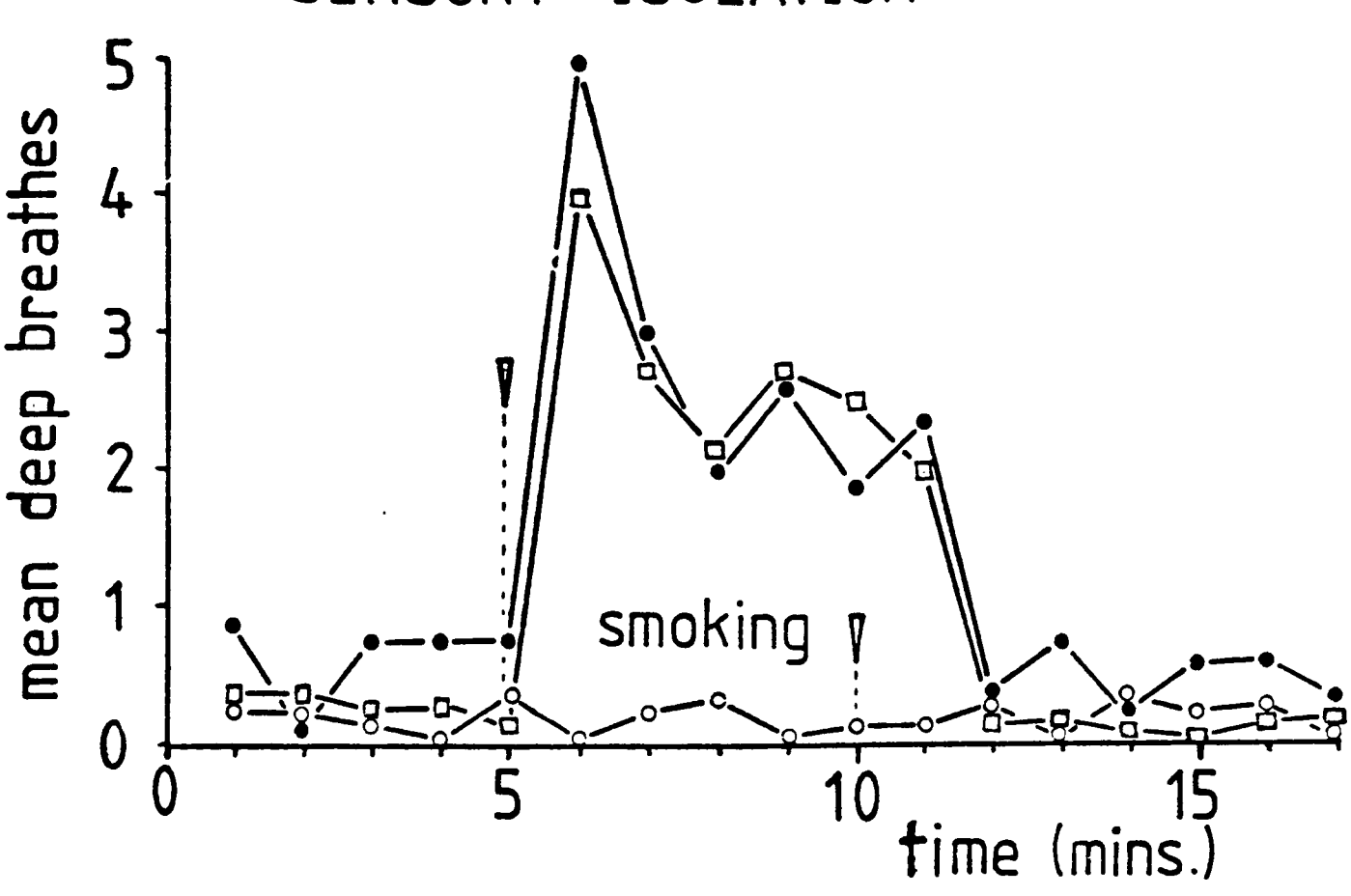


FIGURE 4 : Mean respiration rates during sensory isolation condition for real, sham and control groups (n = 8,8,8)

5a



5b



FIGURES 5a,b : Mean Breathing Irregularities (Deep Breaths) during (a) Stress (b) Sensory Isolation Conditions for Real, Sham and Control Groups (n = 8,8,8)

Table 8 Mean Respiration Rates (breathes per minute) of all groups (Real, Sham, Control) during the baseline (mins. 1 - 5) period for STRESS & SENSORY ISOLATION conditions.

GROUP	n	STRESS (ST) Mean. Resp.Rate mins. 1-5		SENSORY ISOLATION (SI) Mean Resp. Rate mins. 1-5		Δ ST-SI	'P Sign test
		m.	SD.	m.	SD.		
Real	8	18.18	(1.81)	15.75	(4.19)	+2.43	NS
Sham	8	17.66	(2.29)	17.23	(2.30)	+0.43	NS
Control	8	14.65	(2.70)	14.73	(2.91)	-0.08	NS
Combined	24	16.83	(2.72)	15.90	(3.16)	+0.93	NS

Table 9 Kruskall-Wallis 1-way ANOVA of baseline (pre-smoking) Respiration Rates (Real, Sham, Control) for two conditions (STRESS, SENSORY ISOLATION).

CONDITION	H	d f	P
Stress	5.73	K = 3, N = 8,8,8	.1 > p > .05
Sensory Isolation	2.78	K = 3, N = 8,8,8	N.S.

Table 10 Mean Differences in Respiration Rates POST-PRE smoking for Real, Sham, Control groups during STRESS & SENSORY ISOLATION Conditions.

Group	n	STRESS (ST)				SENSORY ISOLATION (SI)			
		PRE m. SD	POST m. SD	Δ ST-SI	P	PRE m. SD	POST m SD	Δ ST-SI	P
Real	8	18.18 (1.81)	17.25 (1.33)	- .93	NS	15.75 (4.19)	15.93 (4.13)	+.28	NS
Sham	8	17.66 (2.29)	17.63 (1.97)	- .03	NS	17.23 (2.30)	16.40 (3.29)	-.83	NS
Control	8	14.65 (2.70)	14.73 (2.91)	+ .08	NS	14.73 (2.54)	14.38 (2.49)	-.35	NS

p = Sign Test, 2-tailed

Table 11 Mean Deep Breathes per minute for all Groups (Real, Sham, Control) during the baseline period (mins.1-5) for Stress & Sensory Isolation conditions.

GROUP	n	STRESS		SENSORY ISOLATION		Δ ST-SI	P sign test
		m.	SD	m.	SD		
Real	8	0.725	(0.453)	0.650	(0.819)	+0.075	NS
Sham	8	0.571	(0.454)	0.275	(0.399)	+0.296	NS
Control	8	1.150	(1.125)	0.200	(0.262)	+0.950	NS
Combined	24	0.815	(0.766)	0.375	(0.560)	+0.440	NS

Table 12 Kruskall-Wallis 1-way ANOVA of baseline Deep Breathes per minute across all groups (Real, Sham, Control) for two conditions (Stress, Sensory Isolation).

Condition	H	df.	P
STRESS	3.89	K = 3, n = 8,8,8	NS
SENSORY ISOLATION	1.35	K = 3, n = 8,8,8	NS

Table 13 — Mean differences in Deep Breathes POST-PRE smoking (mean 5 min. baseline period - mean 5 min. period PRE activity) for all groups (Real, Sham, Control) during STRESS and SENSORY ISOLATION conditions.

GROUP	n	STRESS (ST)				SENSORY ISOLATION (SI)			
		PRE	POST	Δ POST-PRE	P sign test	PRE	POST	Δ POST-PRE	P sign test
		m. SD	m. SD			m. SD	m. SD		
Real	8	0.725 (.453)	1.100 (.513)	+.375	.004	0.650 (.819)	0.875 (.692)	+.225	NS
Sham	8	0.571 (.454)	0.857 (.846)	+.286	NS	0.275 (.399)	0.475 (.385)	+.200	NS
Control	8	1.150 (1.125)	0.975 (.671)	-.175	NS	0.200 (.262)	0.225 (.271)	+.025	NS

These baseline differences can thus be regarded as due to the small group sizes (n = 8, 8, 8). Nevertheless, before dismissing this sampling effect it is interesting to observe that the control group, which stands out as having a particularly low Respiration Rate (cf. Table 8) as compared with the real and sham smoking groups, also stands out as having the lowest heart rates (cf. Table 4, and Figures 1 and 2) compared with the real and sham smoking groups. The control group would thus appear to be, albeit non-significantly, less aroused in the heart-lung system. This may be because the control group appeared by simple observation to be a 'healthier', more 'sporting' sample of the smoking population (e.g. subject M.M. from the control group - baseline HR - 54.6 (ST), 46.8 (SI), Respiration Rate = 13.6 (ST), 11.0 (SI), was a keen footballer). In addition, we might note from Table 2 that the control group smoked less cigarettes overall (mean cigarette consumption = 10.30 per day) than real or sham groups (mean cigarette consumption = 12.60, 12.80 per day, respectively), although as with the HR and RESP variables these cigarette consumption differences are not significant overall (cf. Table 3).

Respiration rates (unlike HR) do not appear to be sensitive to the effects of stress as opposed to sensory isolation (cf. Table 8). It might be reasonably supposed that stress should increase respiration rates (cf. HR) but even the overall result for combined groups (n = 24) showed only a small (NS) mean elevation of +0.93 breaths per minute due to the effects of stress compared to sensory isolation. Similarly, the effects of smoking, sham smoking or doing nothing (control) are all non-significant (cf. Table 10). Evidence of other studies (Dock, 1963; Bevan and Murray, 1963) showed that smoking single cigarettes or lobeline injections (i.v.) in smokers and non-smokers causes a small drop in respiration rate. (Mean Respiration Rates of 14.5 PRE- compared to 13.5 POST-cigarette, in contrast to a mean respiratory depression of 31.4% [smokers] and 18.1% [non-smokers] due to

lobeline, the authors suggesting that the effect of lobeline appears to be additive with residual nicotine in the case of smokers versus non-smokers.)

There is some (non-significant) evidence for a depression of respiration rates caused by cigarette smoking during stress (- 0.93 breaths per minute, mean POST-PRE, cf. Table 10). However, this effect reverses (non-significantly) during sensory isolation (+ 0.28 breaths per minute, mean POST-PRE, see Table 10). This type of result is perhaps not unexpected; thus Dock (1963) found that some subjects showed no respiratory depression or even respiratory excitation, against the overall trend for a small smoking-induced respiratory depression. An alternative viewpoint of these respiration rate results might be couched in terms of Arousal Modulation; smoking decreasing arousal during stress (lowered respiration rate) and, conversely, increasing arousal during sensory isolation (increased respiration rate). However, given the lack of sensitivity in respiration rate as a measure of arousal (e.g. cf. Table 8 - no significant baseline stress versus sensory isolation differences) the smallness of effect is predictable.

Data for Mean Deep Breaths across Stress and Sensory Isolation conditions are given in Table 11. Although, as we might expect, breathing irregularities are increased by stress these differences are small and non-significant. Thus, just as in the case of Respiration Rate, this irregularity measure of respiration appears to be relatively insensitive to the effects of stress-induced increases of arousal.

Differences between real, sham and control groups in baseline breathing irregularities (mean deep breaths per minute for baseline period, minutes 1 - 5) are non-significant (cf. Table 12).

The effect of real cigarette smoking and, to a lesser extent, sham smoking, but not control, is to increase the number of deep breaths. However, this smoking-induced increase in deep breaths is small and achieves significance only for the real smoking group during stress (cf. Table 13).

Interpretation of this data is somewhat conjectural. Thus if we were able to take the view that breathing irregularities are an indicator of elevated arousal (they may be but the data from this experiment are non-significant, cf. Table 11), the significant smoking-induced elevation of deep breathing during the stress condition would indicate a smoking-induced arousal during stress. This would run counter to an Arousal Modulation theory of smoking. Nonetheless, perhaps the best way of viewing this result is that cigarette smoke, although depressing respiration rate somewhat, increases irregularities merely by irritating the lungs, this effect being most pronounced with smoking during stress since the subjects take more puffs during stress (see later - smoking style variables).

In addition, nicotine may be having a direct effect to produce deep breaths; thus 2.5 µg/Kg nicotine into the ascending aorta of 25 patients undergoing cardiac catheterization produced a significant increase in mean respiratory volume with no significant change in respiration rate (Burgess and Rapaport, 1968).

(iv) Skin Conductance Level (SCL)

SCL results are illustrated graphically (cf. Figure 6). One record was lost from the situation control group because of partial electrode detachment. Inspection of Figure 6 and Table 14 and 15 suggests that the main effect is real smoking during both the smoking and post-smoking periods. This is supported by ANOVA (Rothamsted Experimental Station ANOVA program, ICL 1900 conversion by Oxford University Computing Service) cf. Table 16.

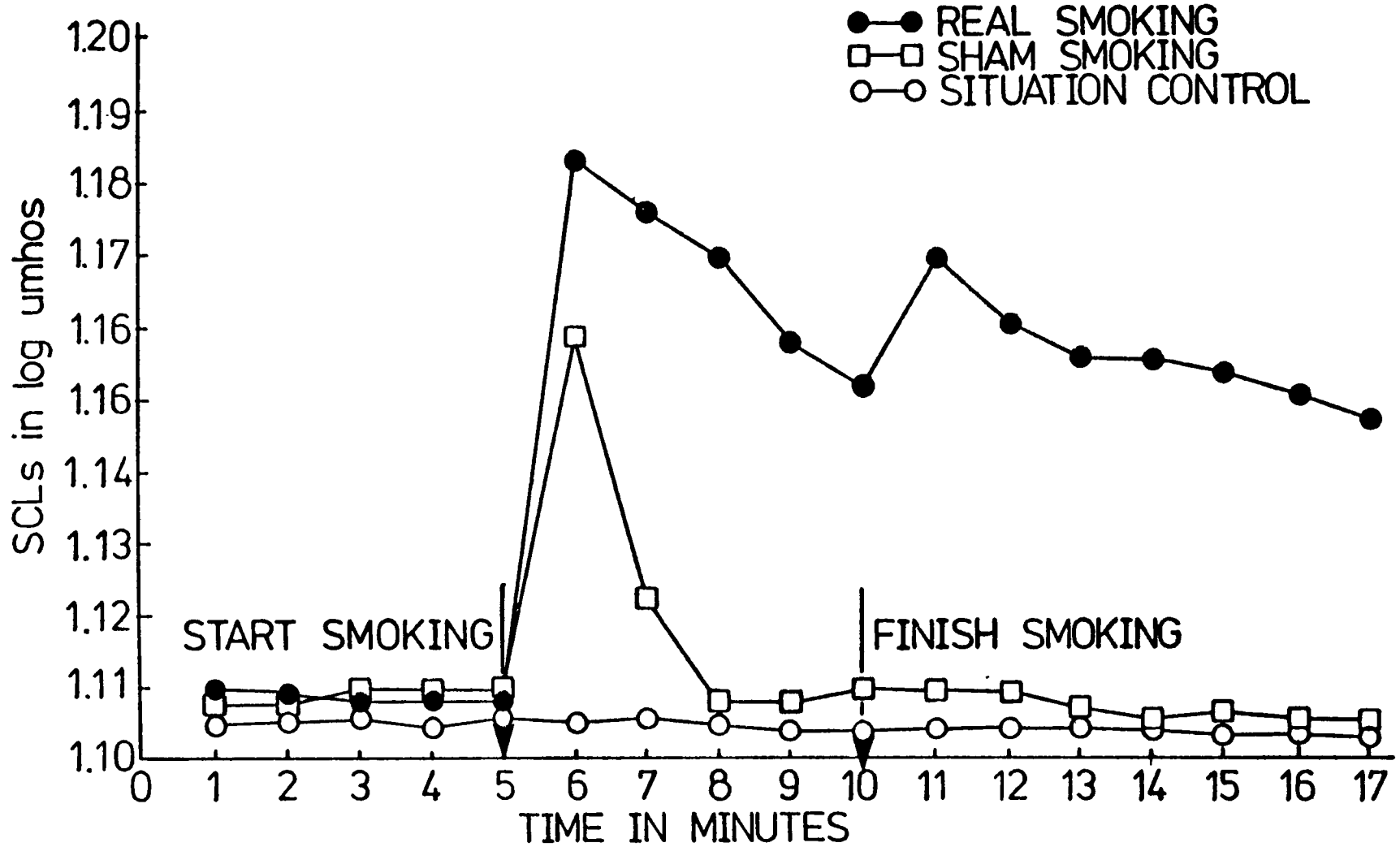


FIGURE 6 : SCL - Sensory Isolation, Mean Skin Conductance Levels (SCLs) during Sensory Isolation for Real, Sham and Control Groups (n = 8,8,7)

Table 14 Means & SDs for SCL (log umhos) by period (pre-smoking, smoking, post-smoking) for (activity) real, sham, control groups, during sensory isolation.

Period		SCL log µmhos PRE-SMOKING		SCL log µmhos SMOKING		SCL log µmhos POST-SMOKING	
GROUP (Activity)	n	m.	SD	m.	SD	m.	SD
Real	8	1.0893	0.3396	1.1671	0.3287	1.1654	0.3714
Sham	8	1.0951	0.2592	1.1164	0.2504	1.0668	0.2471
Control	7	1.0498	0.2462	1.0496	0.2552	1.0333	0.2564

Table 15 Sign Tests for differences in mean SCL given in Table 14 (see above) between PRE-SMOKING versus POST-SMOKING for each group (Real, Sham, Control).

Period GROUP (Activity)	n	PRE-SMOKING v. SMOKING		PRE-SMOKING v. POST-SMOKING	
		mean Δ SCL	P (1-tailed)	mean Δ SCL	P (1-tailed)
Real	8	+0.0778	.035	+0.0761	0.035
Sham	8	+0.0213	NS	-0.0283	NS
Control	7	-0.0002	NS	-0.0165	NS

Table 16 ANOVAS for SCL during sensory isolation by period (pre-smoking, smoking, post-smoking) and activity (real, sham, control groups).

Source of Variation	DF	SS	MS	F	P
Subject Stratum :					
Activity	2	1,355,463	677,731	0.232	NS
Residual	20	58,473 ,040	2,923,902	1219.494	
Total	22	59,833 ,503	-	-	
Subject, Period, Stratum :					
Period	2	142,511	71,255	2.905	NS
Period x Activity	4	332,990	83,247	3.394	5%
Residual	40	981,149	24,529	10.230	-
Total	46	1,456,650	-	-	-
Subject,Period, *Units*,Stratum	736	I764659	2398	-	-
Grand Total	804				
Grand Mean	1094.1				
Total N Of Observations	805				

(*Units* = Repeated Observations)

Examination of Figure 6 and Tables 14 and 16 reveals firstly that the baseline values for SCL are not significantly different between real, sham and control groups (main effect for Activity: F = 0.232, df 2,20; NS). Secondly, since the Period x Activity interaction is significant at the 5% level (F = 3.39: df 4,40) but only real smoking produces a significant rise in SCL (cf. Sign Test, Table 15: PRE versus SMOKING, p = 0.035, PRE versus POST, p = 0.035; N = 8, 1-tailed), this would suggest that although sham smoking produces a transient increase in SCL over minutes 5 - 8 (cf. Figure 6), the sham smoking effect is minor and non-significant over the whole 5-minute smoking period.

The size of effect caused by smoking a single cigarette is very close to that reported by Agué (1974) - mean SCL rise POST-PRE $\underline{\Omega}$ +0.09 log µmhos (Agué) as compared to a value POST-PRE = +0.0761 for REAL smoking (cf. Table 15).

(v) Skin Conductance Response (SCR)

SCR, to White Noise (WN) bursts during STRESS: data for real, sham and control groups are presented graphically (cf. Figure 7), and as Means (SDs) in log µmhos in Table 17.

SCR data is analysed in two ways. Firstly, by sign tests for differences between pre-smoking baseline (PRE), smoking and post-smoking (POST) periods (cf. Table 18) and, in addition, by ANOVA (Rothamsted Experimental Station ANOVA program, ICL 1900 conversion by Oxford University Computing Service), (cf. Tables 19a, b).

Consideration of Figure 7 and Tables 17 and 18 shows that significant habituation of SCRs to the WN stimuli over the 15-minute STRESS condition is occurring, irrespective of whether subjects smoke, sham smoke or do nothing at all (control). In terms of the ANOVA this is by far the largest effect - main effect for period is significant p < 1% (F = 32.42;

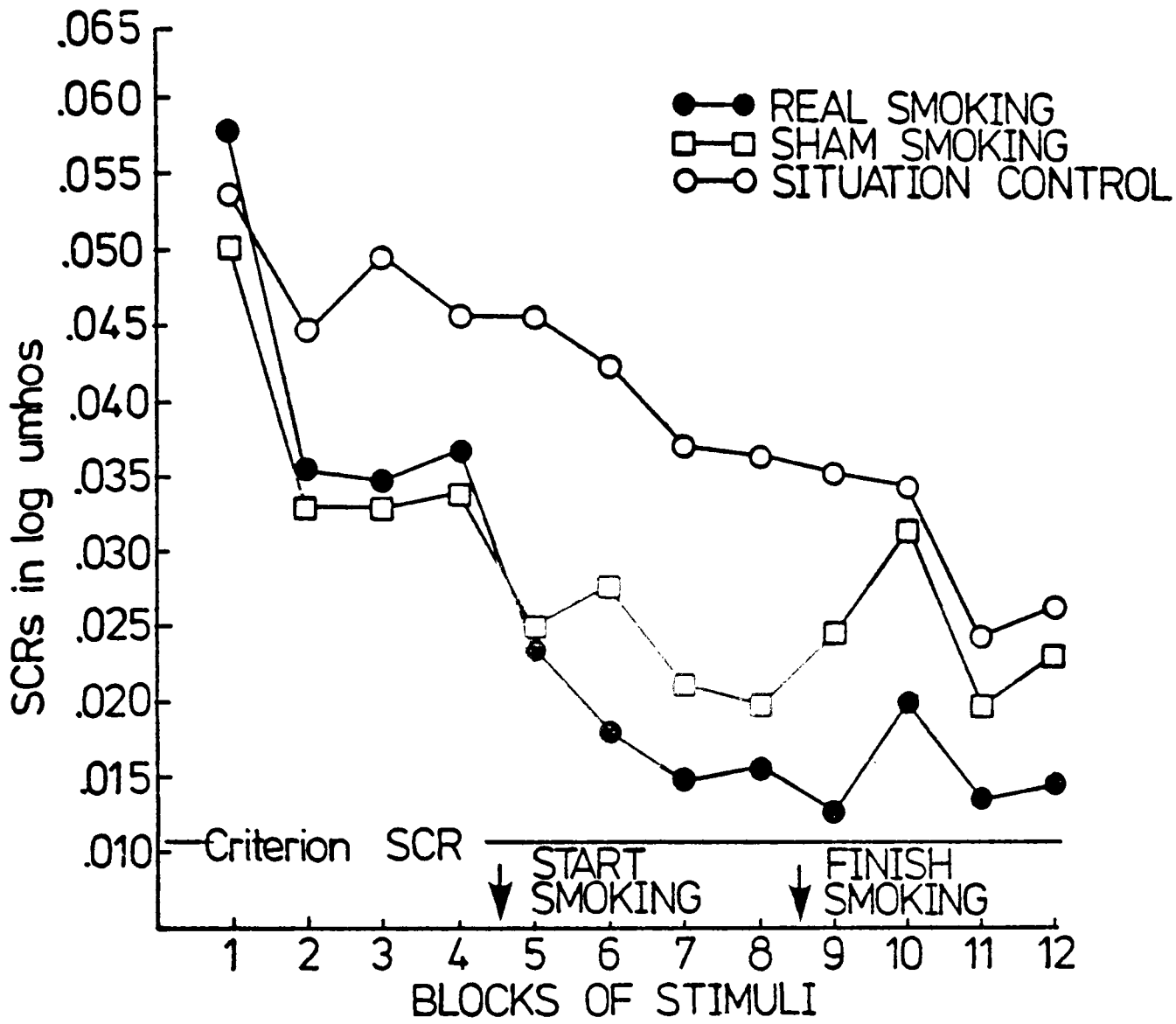


FIGURE 7 : Mean Skin Conductance Responses (SCRs) to White Noise Bursts During the Stress Condition for Real, Sham and Control Groups (n = 8,8,8). Stimuli are presented in blocks of 2 for each of viewing, except for Stimuli 1, which is SCR to First WN Stimulus (PRE = 7 WN bursts, SMOKING = 8 WN bursts, POST = 8 WN bursts).

Table 17 — Mean SCRs to WN bursts (change in log µmhos) during Stress for Real, Sham, Control groups according to period (PRE, SMOKING, POST)

Period:		SCRs log µmhos PRE-SMOKING (Stimuli 1-7)		SCRs log µmhos SMOKING (Stimuli 8-15)		SCRs log µmhos POST-SMOKING (Stimuli 16-23)	
GROUP	n	m.	SD	m.	SD	m.	SD
R e a l	8	0.0421	0.0212	0.0215	0.0145	0.0142	0.0101
S h a m	8	0.0330	0.0090	0.0250	0.0101	0.0243	0.0136
Control	8	0.0514	o.0125	0.0411	0.0092	0.0317	0.0107

Table 18 — Sign Tests on differences for mean SCRs in Table above between PRE, SMOKING & POST, for (activity) REAL, SHAM, CONTROL groups, during STRESS.

GROUP (activity)	n	S C R Difference log µmhos (Smoking-PRE)	P Sign test 1-tailed	S C R Difference log µmhos (POST-PRE)	P Sign test 1-tailed
R e a l	8	-0.0206	0.004	-0.0279	0.004
S h a m	8	-0.0080	0.035	-0.0087	0.035
Control	8	-0.0103	NS	-0.0197	0.004

Table 19 ANOVAs for SCR during STRESS by period (PRE-SMOKING, SMOKING, POST-SMOKING) and (activity) REAL, SHAM, CONTROL groups.

Source of Variation	df	SS	MS	F.	P
Subject Stratum					
Activity	2	271.344	135,672	4.781	5%
Residual	21	595,978	28,380	12.153	-
Total	23	867,322	-	-	-
Subject, Period, Stratum					
Period	2	326,483	163,242	32.420	« 1%
Period x Activity	4	62,939	15,735	3.125	5%
Residual	42	211,481	5,035	2.156	-
Total	48	600,903	-	-	-
Subject, Period, *Units*, Stratum	480	1120944		2335	
Grand Total	551	2589169			
Grand Mean	3112				
Total N Of Observations	552				

(*Units* = Repeated Observations)

Table 20 Kruskal-Wallis 1-way ANOVA between REAL, SHAM & CONTROL GROUPS for the PRE-SMOKING baseline mean SCRs to WN stimuli.

H	df.	P
5.46	k = 3, N = 8,8,8	0.10 > p > 0.05

df 2,42) (cf. Table 19b). Habituation to neutral stimuli is a well known phenomenon even in the most primitive of organisms, although habituation to stressful stimuli (in this case 106 dB white noise) is slower than for less intense stimuli, e.g. complete SCR habituation to non-aversive tones at 60 dB occurs on average after roughly eight trials (cf. Mangan and Golding, 1978, Experiment 2, p. 95).

As detailed earlier, in the footnote to the Design section, this effect had been anticipated and necessitated the use of independent groups of subjects for real, sham and control.

It would appear that the habituation of SCRs to WN stimuli during the PRE-SMOKING baseline period is less for the control group than for the real or sham smoking groups (cf. Figure 7, PRE-SMOKING STIMULI SCRs). However, a Kruskal-Wallis one-way ANOVA during the pre-smoking baseline indicates that the mean SCR differences between real, sham and control groups are not significant (cf. Table 20).

Activity main effect (i.e. real, sham, control) over the whole stress period is significant ($F = 4.781$, df 2,21 - cf. Table 19a). With consideration of Table 20 this implies that the major contribution of variance to the significant activity main effect over the whole stress period is occurring during the SMOKING and POST-SMOKING periods. The significant PERIOD x ACTIVITY effect ($F = 3.125$, df 4,42 - cf. Table 19b) can be interpreted in terms of increasing the SCR habituation to WN bursts over and above that SCR habituation revealed in the control group. This interpretation is supported by the sign-tests presented in Table 18 although significant SCR habituation does occur overall for the control group (control mean SCR POST-PRE = -0.0197 log μmhos, $p = 0.004$, 1-tailed). The crucial difference between groups appears during the actual smoking period. Thus, whereas both real and sham smoking groups have a significant

drop in mean SCR SMOKING versus PRE-SMOKING periods (p = 0.004, real; p = 0.035, sham - cf. Table 18), the drop in mean SCR SMOKING versus PRE-SMOKING periods for the control group, although of comparable size to sham-smoking (-0.0103 log μmhos, control; -0.0080 log μmhos, sham), is not significant using a simple sign test (cf. Table 18). As expected the real-smoking group experiences the two largest and significant drops (cf. Table 18) in mean SCR amplitude over the three periods (pre,smoking, post) compared to drops in mean SCR amplitude for sham and control groups over the three periods.

(vi) EEG 'alpha' (EEG 'α')

Results for EEG 'α' are presented graphically (Figures 8 and 9) and as mean scores of the three groups (real, sham, control) for three periods (pre-smoking, smoking, post-smoking) during the stress and sensory isolation conditions in Table 21.

Note that SDs are of the same order of magnitude - or even larger than the mean scores they refer to. This is because the means are generated from deviation scores above (+) or below (-) the baseline EEG 'α' value for each subject (see "Scoring Procedures and Data Analysis" earlier).

Reference to Figures 8 and 9, together with Table 21 suggests that the effect of cigarette smoking (real group) is to increase EEG 'α' above the baseline value during stress and conversely to reduce EEG 'α' below the baseline value during sensory isolation. The effects of sham smoking are similar but smaller than those seen during real smoking (roughly 50%) and by contrast the control group appears to show little systematic effect. These suggestions are confirmed by statistical tests with results shown in Tables 22 and 23: sign tests for differences in mean EEG by period (pre-smoking, smoking, post-smoking) for all groups (real, sham, control) during both sensory isolation and stress conditions (cf. Table 22). In

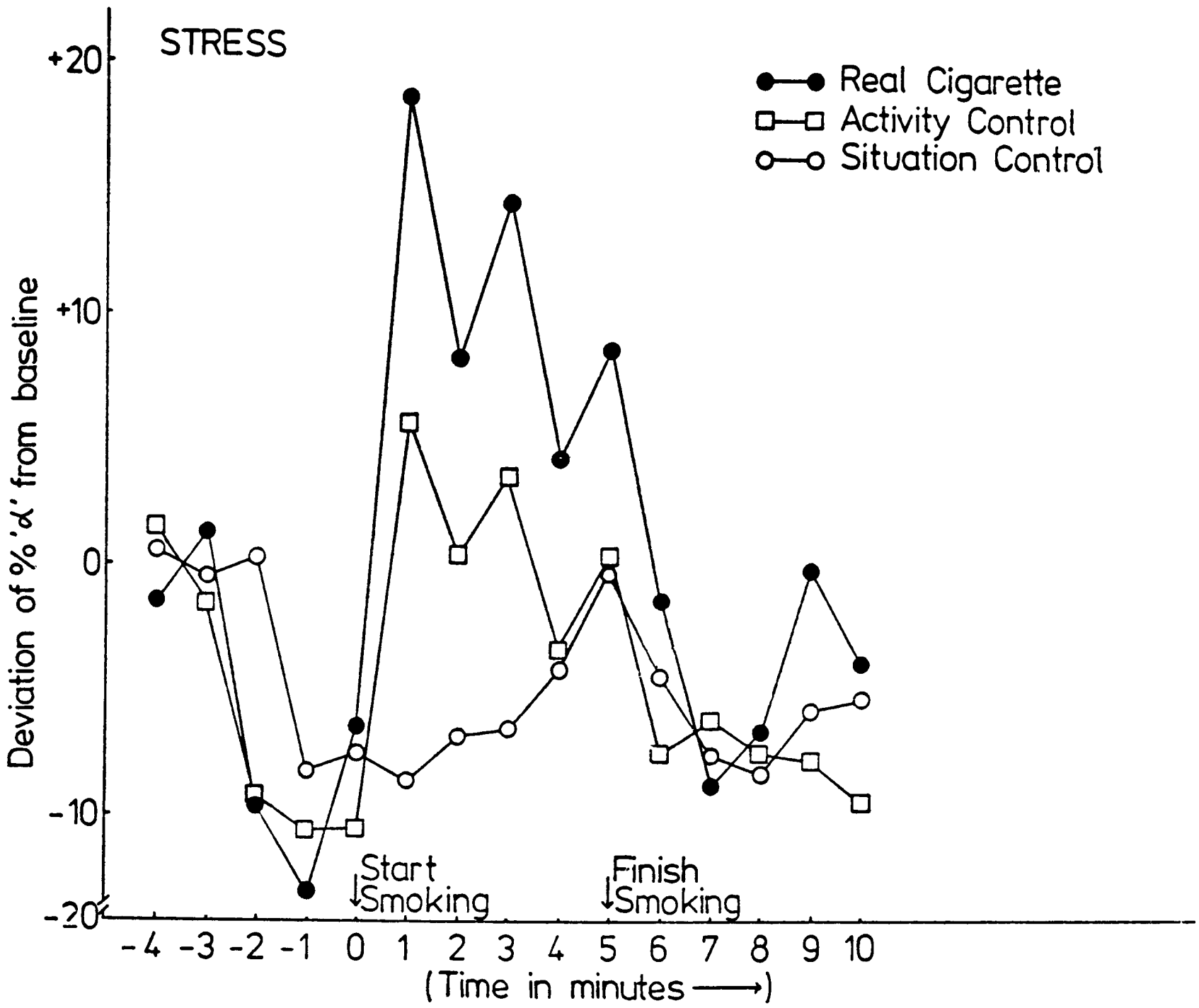


FIGURE 8 : Mean EEG 'α' During Stress Condition
for Real, Sham and Control Groups (n = 8,8,8)

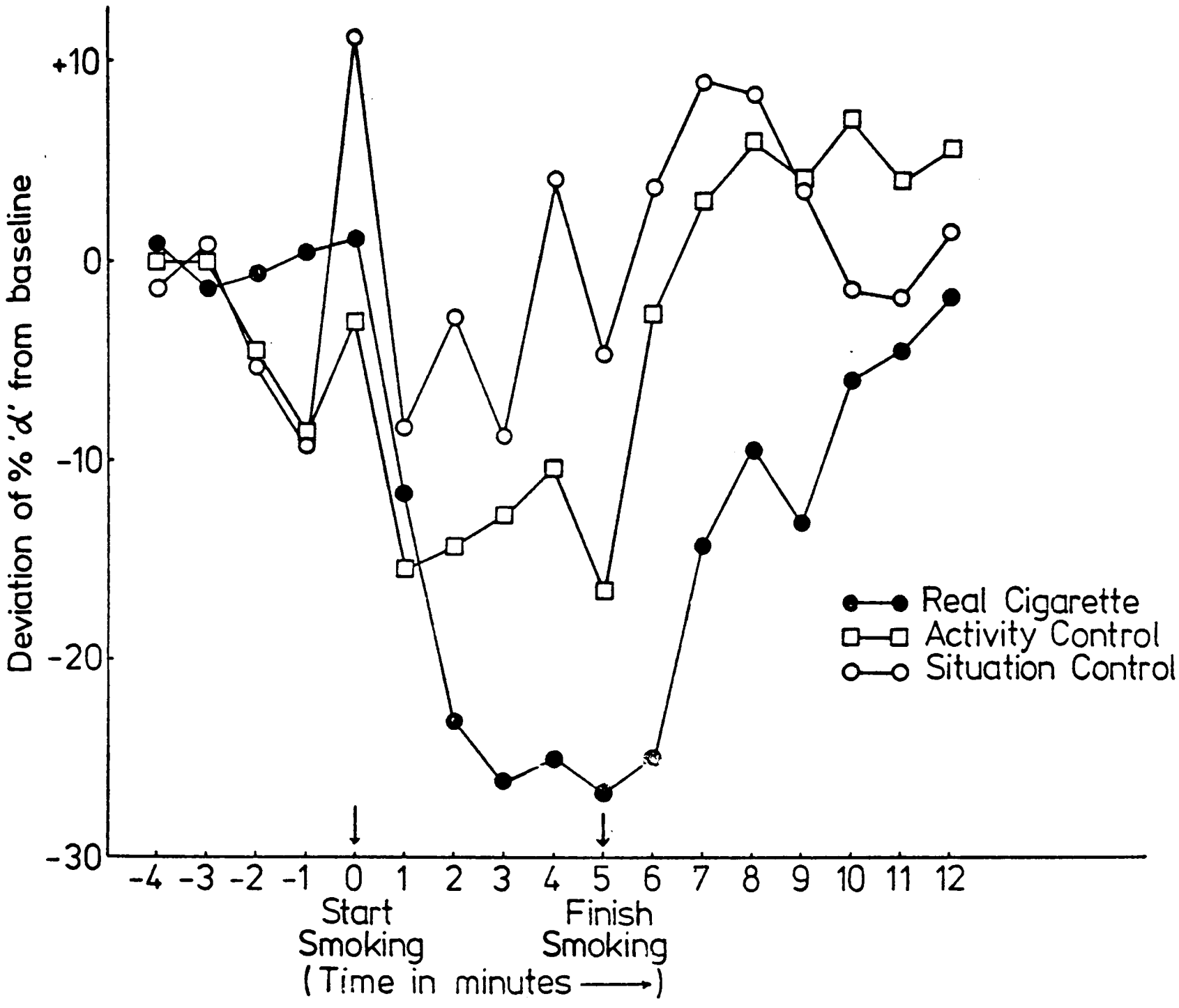


FIGURE 9 : Mean EEG 'α' During Sensory Isolation Condition for Real, Sham and Control Groups (n = 8,8,8)

Table 21 Means & SDs for EEG α of all groups (real, sham, control) by period (pre-smoking, smoking, post-smoking) during stress and sensory isolation conditions.

Condition	Group (activity)	n	EEG α Pre-smoking		EEG α Smoking		EEG α Post-smoking	
			m.	SD	m.	SD	m.	SD
S T R E S S	Real	8	-5.75	(7.07)	+10.67	(10.04)	-4.41	(12.59)
	Sham	8	-5.24	(8.51)	+2.17	(12.02)	-6.20	(10.41)
	Control	8	-3.17	(8.94)	-5.20	(14.41)	-6.20	(15.67)
SENSORY ISOLATION	Real	8	-0.31	(4.88)	-22.84	(23.52)	-9.93	(12.03)
	Sham	8	-2.70	(6.26)	-14.22	(18.18)	+5.19	(7.63)
	Control	8	+0.32	(8.80)	-4.58	(23.65)	+4.51	(27.34)

Table 22 Sign tests for differences in mean EEG ∝ between PRE-SMOKING versus SMOKING and PRE-SMOKING versus POST-SMOKING by group (real, sham, control) during s t r e s s and sensory isolation conditions.

CONDITION	Group (activity)	n	Difference in mean EEG ∝ (Smoking) - (Pre-Smoking) Δ EEG ∝	P sign test 1-tailed	Difference in mean EEG ∝ (Post-Smoking) -(Pre-Smoking) Δ EEG ∝	P sign test 1-tailed
STRESS	Real	8	+16.42	0.035	+1.34	NS
	Sham	8	+ 7.41	NS	-0.96	NS
	Control	8	- 2.03	NS	-3.03	NS
SENSORY ISOLATION	Real	8	-22.53	0.035	-9.62	.035
	Sham	8	-11.52	0.035	+7.89	NS
	Control	8	- 4.90	NS	+4.19	NS

Table 23 ANOVAs for EEG ∝ by Activity (real, sham, control groups) by Order (Stress or Sensory Isolation condition presentation order) by Condition (Stress, Sensory Isolation) by Period (Pre-Smoking, Smoking, Post-Smoking

Source of Variation	dF.	S.S.	M.S.	F	P
Activity	2	1897.3	948.7	0.333	NS
Order	1	4272.8	4272.8	1.501	NS
Activity x Order	2	68.4	34.2	0.012	NS
Residual	18	51237.6	2846.5	21.487	-
Total	23	57476.1	-	-	-

(Table contd. overleaf)

Table 23 (contd.)

Source of Variation	dF.	S.S.	M.S.	F	P
Condition	1	694.4	694.4	0.532	NS
Condition x Activity	2	8702.1	4351.0	3.333	NS
Condition x Order	1	1816.2	1816.2	1.391	NS
Condition x Activity x Order	2	3975.5	1987.7	1.523	NS
Residual	18	23494.7	1305.3	9.853	-
T o t a l	24	38682.8	-	-	-

Source of Variation	dF.	S.S.	M.S.	F	P
Period	2	1683.5	841.8	1.191	NS
Period x Activity	4	1818.7	454.7	0.643	NS
Period x Order	2	1740.9	870.4	1.232	NS
Condition x Period	2	18590.1	9295.1	13.153	« 1%
Period x Activity x Order	4	50.5	12.6	0.018	NS
Condition x Period x Activity	4	7436.3	1859.1	2.631	5%
Condition x Period x Order	2	310.6	155.3	0.220	NS
Residual	76	53707.2	706.7	5.334	-
T o t a l	96	85337.9	-	-	-

addition, an ANOVA (Rothamsted Experimental Station ANOVA program, ICL 1900 conversion by Oxford University Computing Service) for the same variables plus order of condition presentation (stress or relaxation condition; first or second [cf. Table 23]).

The elevation of EEG 'α' during stress by real smoking is significant during the smoking period (EEG 'α' = +16.42; p = .035, cf. Table 22) but rapidly drops back to baseline after smoking (EEG 'α' = +1.34; p = NS - cf. Table 22). Sham smoking (ST) produces similar effects but smaller - roughly half the effect of real smoking and these are not significant (cf. Table 22). Doing nothing (control group) produces no significant changes in EEG 'α' (cf. Table 22).

In general these smoking effects on EEG 'α' reverse during the sensory isolation condition. However, the results are not a complete mirror image - in contrast to the relatively transient elevation of EEG 'α' during stress by real smoking,the depression of EEG 'α' during sensory isolation by real smoking is greater in magnitude (ignoring direction +/-) (Δ EEG 'α' = -22.53; p = .035, sensory isolation; Δ EEG 'α' = +16.4; p = .035, stress - cf. Table 22) and persists after smoking (Δ EEG 'α' = -9.62; p = .035). Sham smoking during sensory isolation produces a smaller and transient depression of EEG 'α' compared to real smoking (Δ EEG 'α' = -11.52; p = .035 - cf. Table 22) which seems to 'rebound' during the post-smoking period. This 'rebound' is not significant compared to baseline. The control group likewise shows no significant changes during sensory isolation (cf. Table 22).

Inspection of ANOVA (cf. Table 23) reveals that main effects (Activity and Condition) and order effects are not significant. The following interactions were significant:

Condition x Period	F = 13.153; df 2,76; p = 1%
Condition x Period x Activity	F = 2.631; df 4,76; p = 5%
Condition x Activity interaction just fails significance:	F = 3.333; df 2,18; p ≈ 5%

From the inspection of means and from the sign tests calculated (cf. Table 21 and 22) it is clear that the main effect occurs during the smoking period, as a function of Condition and, to a lesser extent, Activity, i.e. the most powerful experimental effect is the observed reversal (across Conditions) of the direction in EEG 'α' (elevation/depression) caused by real or sham smoking. The magnitude of the relative effects of real versus sham smoking on EEG 'α' are significant but to a lesser degree. This suggests that sham smoking is making a large contribution to any observed real smoking effect.

(vii) Smoking Style

Data on puffing frequencies for real and sham smoking during stress and sensory isolation conditions are presented graphically (Figure 10) and as means, (S.D.) (cf. Table 24).

Subjects took slightly more puffs from their cigarettes (real or sham) during stress as opposed to sensory isolation but this change in puffing rate is small and not significant (cf. Table 24). It would thus appear that whether or not smokers are attempting to obtain larger (depressant) dosages of nicotine during stress as opposed to sensory isolation, they are certainly not making any major attempt to do so by means of increasing their number of puffs (the relevant variable may be puff intensity which was not measured).

Sham smokers took slightly more puffs than real smokers during both stress and sensory isolation conditions although this difference is not significant when tested statistically (Mann-Whitney U test, $n_1 = 8$,

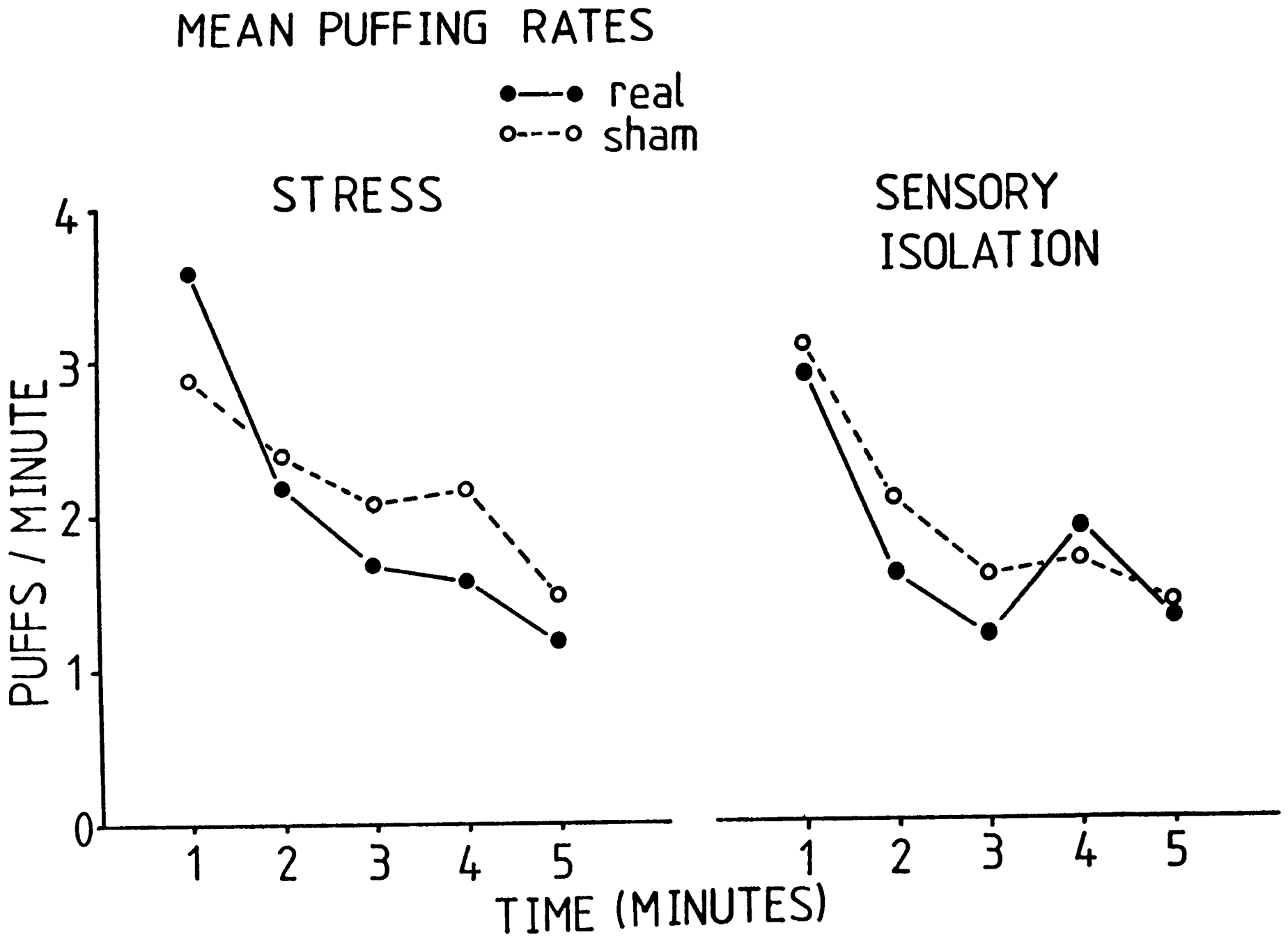


FIGURE 10 : Puffing Rates During 5 Minute Smoking Period in Stress and Sensory Isolation Conditions for Real Smoking and Sham Smoking Groups (n = 8,8)

Table 24 Mean Total puffs during 5. mins.real smoking, sham smoking,during stress and sensory isolation conditions.

Group	n	Number of puffs				Difference Δ ST-SI	P sign test 1-tailed
		S t r e s s		Sensory isolation			
		m.	SD	m.	SD		
REAL	8	10.3	1.9	8.9	2.4	+1.4	NS(.062)
SHAM	8	11.1	3.0	9.9	3.3	+1.2	NS

Table 25 Analysis of Puff Distribution during real and sham smoking.

Group	n	PUFF DISTRIBUTION RATIO = {No. of puffs in first 2 mins. of smoking / No. of puffs in last 2 mins. of smoking}				P sign-test 1-tailed ST v. SI
		S T R E S S		SENORY ISOLATION		
		m.	SD	m	SD	
R e a l	8	2.27	0.76	1.90	1.42	NS
S h a m	8	1.49	0.36	1.69	0.41	NS

Table 26 Spearman Rank Correlation (r_s) for subjects for total number of puffs between Stress and Sensory Isolation Conditions.

GROUP	n	r_s	P
Real	8	+ 0.69	< .05
Sham	8	+ 0.71	< .05

Table 27 Significance of observed drop in pufffing rate (first two minutes versus last two minutes) over smoking period

Group	n	Drop in number of puffs over duration of smoking (number of puffs during mins. 1 - 2 v. mins. 4 - 5)			
		STRESS	P sign test 1-tailed	SENSORY ISOLATION	P sign test 1-tailed
Real	8	- 3.0	.004	- 1.3	.008
Sham	8	- 1.6	NS (.062)	- 2.1	.008

n_2 = 8; U = 23 (stress); U = 26 (sensory isolation);NS under both conditions).

A more subtle analysis of the puffing rate is suggested by the heart rate (HR) results. There is evidence that, whilst HR elevation caused by real smoking does not differ significantly between stress and sensory isolation conditions, HR is peaking earlier for real smoking under stress compared to sensory isolation (cf. Figures 1 and 2 and HR results section). This may be because subjects are puffing more frequently at the beginning of the 5-minute smoking period under stress, compared with sensory isolation. This hypothesis was tested for each subject by analysing the ratio of the mean number of puffs during the first 2-minutes to the last 2-minutes of the 5-minute smoking period. This ratio gives an estimate of how the smoker is distributing his puffs when smoking a cigarette, as opposed to the total number of puffs taken (cf. Table 25). Although not significant the effect is in the predicted direction for real smoking, i.e. relatively faster rates of puffing at the beginning of smoking during stress compared to sensory isolation. This lends some credence to the possibility (suggested by the work of Armitage et al., 1968) that smokers may be obtaining some of the observed depressant effects from smoking during stress by increasing the rate of intake as compared with size of nicotine dose absorbed during smoking (again the more relevant variable may be puff intensity or inhalation).

The prior analysis has concentrated on finding significant differences in puffing patterns between conditions and activity in order to account for the observed differences in psychophysiological results between conditions and activity. The relative failure of this approach may be judged from the small and insignificant differences (cf. Tables 24 and 25) compared with the great and significant similarities (cf.

Table 26 and 27) in puffing patterns observed between conditions and activity.

Consideration of Tables 24 and 27 taken together with Figure 10 demonstrates that puffing rate declines over the 5-minute period, the differences in number of puffs (cf. Table 25) and their distribution (cf. Table 26) are not significantly different. In addition, there is a fair degree of variation amongst subjects as to how many puffs they take (cf. SDs in Table 24) and this variation is highly consistent - subjects appear to show relatively consistent idiosyncracies in puffing behaviour even when sham smoking (cf. r_s correlations between conditions - Table 26). Taken together, these results present a picture of individual puffing patterns as being relatively immutable i.e., smoking, at least in terms of puffing rates, is a remarkably consistent activity, being relatively unaffected by variations in arousal or indeed whether or not the cigarette is lit.

(viii) Intercorrelations between electrodermal and EEG measures

It has been generally accepted since the Lacey studies in the 1950's (Lacey, 1956, 1967), that the concept of 'General Arousal' was untenable if taken to mean that all physiological response measures, e.g. cardiac system, EEG, electrodermal, EMG, etc., increased or decreased in a unitary fashion. This is most obvious if the cardiac acceleration to cigarettes is considered. The data from this experiment clearly show that cigarettes accelerate Heart Rate (HR) during sensory isolation and white noise, yet the effects in the EEG and electrodermal systems are opposite in direction to that of HR during the white noise condition.

Therefore it was of some interest to see to what extent the electrodermal and EEG systems correlated in terms of their mean activities

during each period: pre-smoking, during smoking, and post-smoking, (5-minutes, 5-minutes, 5-minutes, (stress), or 7-minutes (Sensory Isolation), respectively. Negative correlations between SCR/SCL and EEG 'α' would be expected from a synergistic arousal system. The correlation results obtained can be seen in Tables 28 and 29.

The most obvious results disclosed by the correlations (see 'ALL' especially) is that

(1) these systems (EEG/SCR SCL) are only partially correlated over short time periods of minutes;

(2) this partial correlation is mainly seen during sensory isolation and breaks down during white noise, even reversing to a significant level ($r = .745$, $p < .05$, $n = 8$) with the middle period of the situation control group.

The poor correlations of activity between the electrodermal and EEG systems may be due to the mode of analysis (it may be necessary to analyse within subject on a second by second basis) but given the large amount of evidence that these systems are only partially correlated (Lacey, 1956, 1967; Barrell and Price, 1977; Eysenck, 1977), it is better to see the results as supporting a model of the various response systems being partially independent in levels of activity.

It is, perhaps, not surprising that this independence of activity should be increased by the highly arousing and aversive effects of white noise (cf. positive correlations, Table 29).

Individual correlations will not be commented upon in detail since, having regard to the relatively small number of observations ($n = 8$, in each case) chance significances are likely to occur. For the 18 correlations an average of one correlation could be expected to be significant at the 5% level merely by chance - three significant

Table 28

SENSORY ISOLATION : Correlations - Mean SCL with Mean EEG ∝.

	Pre-smoking	During smoking	Post-smoking
Real smoking (n = 8)	.277	- .566	- .291
Sham smoking (n = 8)	- .631	.041	- .443
Situation Control (n = 8)	- .404	- .765 *	- .438
ALL (n = 24)	- .244	- .485 *	- .382

(* $p < .05$, Pearson Correlation Coeff.)

Table 29

WHITE NOISE : Correlations - Mean SCR with Mean EEG ∝.

	Pre-smoking	During smoking	Post-smoking
Real smoking (n = 8)	- .071	.526	- .472
Sham smoking (n = 8)	- .218	- .540	- .647 *
Situation Control (n = 8)	.110	.745 *	.108
ALL (n = 24)	.020	- .083	- .271

(* $p < .05$, Pearson Correlation Coeff.)

correlations occurred, in fact, two in respect of the situation control group during their middle period, but opposite in sign (cf. Tables 28 and 29).

The general suggestion from this analysis is that the harder two partially linked systems are perturbed (in this case, electrodermal and EEG) the more they exhibit independence. Here the perturbations are the effects of smoking/sham smoking and, especially of white noise.

DISCUSSION

The EEG and electrodermal data strongly indicate that smoking produces an increase in arousal during the sensory isolation condition and conversely a decrease in arousal during the white noise conditions. Sham smoking produced roughly 50% of the real smoking effect as measured from the situation control baselines. Thus, the main effect of the experiment - to show that smokers can manipulate their level of arousal to a hypothetical 'optimum' - was considered successful.

Overall, the most striking feature of the psychophysiological data is the reversal of the EEG effect for real and sham-smoking according to condition. It is obvious that percentage alpha is increased during stress and decreased during sensory isolation by smoking. The fact that the sham smoking group produce roughly 50% of the real smoking effect suggests that some of the effects of the latter are due simply to activity - to having an object to manipulate, for example. Many subjects stated that the reason they found smoking in a stress situation relaxing was that it diverted their attention (Freeman, 1948, reports that even irrelevant muscular activity reduces anxiety).

As regards the role of nicotine, undoubtedly this accounts for some of the difference between sham and real smoking. Under the sensory isolation condition the alpha-blocking effect from real smoking lasts well

into the 7-minute post-smoking period. This is perhaps the time required for nicotine clearance from the CNS. However, this is not the case in the stress condition, which may reflect the shorter clearance time for nicotine during stress, because of heart elevation by white noise, for example.

The trend in EEG data are generally reflected by the SC data. In the sensory isolation condition the rise in SCL caused by real smoking lasts well into the 7-minute post-smoking period whereas the initial rise in SCL caused by sham smoking drops back to near situation control levels even within the period of smoking. This occurs in spite of the fact that the rate of sham puffing declines no more slowly than real smoking during the period (cf. Figure 10).

In the case of the stress condition the difference between real and sham smoking is less dramatic but interestingly enough during the post-smoking period the effect of real smoking in attenuating SCRs to noise bursts again lasts longer than that of sham smoking. The large (but not significant, cf. Table 20) differences between situation control and the sham and real smoking groups in the first five minutes is less easily explained. It is certainly not reflected in the EEG data. This divergence between SCR and EEG data is reflected in the correlations between response modalities discussed earlier, being especially marked for the situation control group in the stress condition.

The difference between sham and real smoking may give an upper estimate of the contribution of nicotine to the effects in EEG, SC and EEG. In the case of (POST-PRE) HR elevation, it seems reasonable to suppose that nearly all the effect is due to nicotine since HR remains virtually unaltered by sham smoking or by any systematic time-course

related effects - situation control. However, in the case of EEG and SC responses, it is possible that, given the larger sham smoking effects, a potent control (i.e. nicotine free cigarettes possessing the same taste and puffability characteristics) would have accounted for an even larger proportion of the main real smoking effect. Until such cigarettes become available this question will remain unresolved.

It is noteworthy that sham smoking should account for such a large proportion of the real smoking effect on EEG, SCL, and SCR. This could be just due to the physical activity (especially plausible since sham smokers puff slightly more than the real smokers, although this is not significant: cf. Smoking Style Results). In the case of the sensory isolation condition, the behaviour is arousing, for the stress condition it is de-arousing, perhaps by distraction and diversion of attention from the noise bursts. Interestingly, object manipulation 'something to fiddle with' factors emerge in smoking questionnaires (Ikard et al., 1969). It is also entirely possible that the constellation of smoking related behaviours - sight, lip contact, taste and inhalation - form a compound CS for the UCS of nicotine. This is made even more likely given the short puff→brain arrival of nicotine (8 - 10 seconds: Russell, 1976) and the large number of CS-UCS pairings. Both these factors (speed of reinforcement, number of reinforcements) are known to be crucial in producing strong Classically Conditioned responses.

This conjecture that pharmacological effects can be Classically Conditioned is made all the more convincing by consideration of the recent work of Lal et al (1976), which demonstrated Classically Conditioned alleviation of narcotic withdrawal symptoms in rats, and Bridger et al. 1978, showing conditioned amphetamine psychosis in rats.

The question of how these postulated nicotine effects are mediated remains unanswered. Nicotine is well documented as a CNS stimulant, having an effect mainly on the ARAS. Thus the alpha-blocking caused by smoking in the sensory isolation condition is to be expected. In the stress condition it is possible that nicotine may be producing tranquillising effects on the CNS by virtue of its biphasic stimulant and depressant dose-response (cf. Ashton et al., 1978). Nicotine may also be producing tranquillisation by acting as a 'stimulus barrier' to the white noise bursts as suggested by the increased SCR habituation during and after cigarette smoking (cf. Friedman et al., 1974). Alternatively, it is possible that nicotine is producing the relaxation effect by blockading the neuromuscular junction or ganglions, an effect which has been reported by Goodman and Gilman (1971), Domino and von Baumgarten (1969), Hutchinson and Emley (1973), thus relieving some of the muscular tensions. This in turn would effect the feedback of neurones monitoring muscular tensions into the ARAS, the balance between the central and peripheral effects of nicotine leading to the direction of observed change in alpha. However, Fagerström and Götestam (1977) showed tonic EMG is increased by cigarette smoking. Unfortunately, EMG data collected in the present experiment did not resolve this question, for technical reasons discussed earlier (cf. 'Experimental Procedures: EMG', however, relevant EMG data is presented later in Experiment 3).

E X P E R I M E N T 2

FURTHER OBSERVATIONS ON VARIATIONS IN SMOKING STYLE AND PSYCHOPHYSIOLOGICAL EFFECTS OF CIGARETTE SMOKING UNDER CONDITIONS OF STRESS AND SENSORY ISOLATION.

Rationale

Some electrodermal and EEG evidence was presented in Fxperiment 1, which supported the hypothesis that smokers can use cigarette smoking as a 'tool' to manipulate their level of arousal towards a hypothetical 'optimum', i.e. to increase arousal during sensory isolation and to lower arousal during stress. There was evidence that sham smoking could account for roughly half of the observed cigarette smoking effects on electrodermal and EEG responding, demonstrating that the physical effect of smoking and smell of tobacco smoke are extremely important. In contrast, the hypothesis that cigarette smoking can be used as a 'tool' to regulate the smoker's level of arousal by virtue of the dose-related biphasic stimulant and depressant properties of nicotine remained unproven. The expected result - that smokers would attempt some degree of self-titration for nicotine by increasing their puffing rate so as to obtain depressant (large) doses during the stress condition - was small, not significant and thus unproven, although such small change as did occur in the mean number of puffs was in the predicted direction (increase). Similarly, a post hoc analysis of puff distributions and heart rate elevation with time, based upon the observation (Armitage et al., 1968) that the rate of dosage as opposed to the absolute dosage of nicotine may be the critical factor governing stimulant versus depressant effects of nicotine, produced evidence in the predicted direction but again not significant statistically. Thus smokers made a

small attempt to obtain nicotine at a faster (predicted to be depressant) rate under stress, as evidenced by the relatively increased puffing rates in the first few minutes of smoking (puff distribution ratio during stress versus sensory isolation) and consequently a faster rise in the heart rate during stress (comparison of heart rate elevation with time between stress and sensory isolation conditions).

Several explanations are possible for the failure to demonstrate significant attempts by subjects at self-titration in order to obtain stimulant (low) or depressant (high) dosages of nicotine (as appropriate to the respective sensory isolation or stress conditions). These speculations involve either rejecting the 'Arousal Modulation' model based upon biphasic nicotine effects or postulating that other smoking variables, inhalation, puff intensity, etc., are the means by which smokers manipulate nicotine intake. The simplest explanation is that nicotine may not be the most important reinforcer involved in smoking. While there may be some degree of truth in this, the observation that very low nicotine cigarettes or nicotine-free herbal cigarettes are unpopular is strong evidence for nicotine as a reinforcer for the smoking habit. Thus, nicotine would appear to be important, but not necessarily so by virtue of its biphasic stimulant and depressant properties. By default, the lack of significant statistical differences in puffing rates or in heart rate elevations when subjects smoked during stress versus sensory isolation conditions, provides some evidence in support of a 'Nicotine Addiction' model for cigarette smoking. The observed changes in electrodermal and EEG responding due to smoking (Experiment 1) could merely mean that nicotine has arrived at depleted receptor sites, so producing reward. In these terms, the reduction in arousal during stress as measured by EEG and SCR, is crudely explicable on the basis that reward and punishment

systems are mutually antagonistic, at least in learning theory terms, (Gray, 1971). Thus nicotine might reduce the aversive consequences of white noise by activating reward systems[1], whereas the increase in arousal during sensory isolation is explicable in terms of the known arousing effects of reward. In simpler terms, the smoker's feelings of relaxation during stress, or of stimulation during drowsiness when he smokes cigarettes, are merely rationalisations for the pleasurable feelings following the satisfaction of 'nicotine-hungry' receptors (cf. Schachter, 1973). However, whilst this type of explanation has a degree of plausibility, it is equally possible that the smoking variable measured (puffing rate) was not the most crucial one. To this end, inhalation and residual butt weight were studied in this experiment, in addition to puffing rates.

It was predicted that smokers would inhale more deeply and for longer time, puff more intensely (indirectly measured from butt weights) but only show a small increase in total number of puffs taken when smoking during white noise stress as opposed to sensory isolation. Since measures of changes in smoking style were the primary object of study, this experiment was a selective replication and extension of Experiment 1 for a 'real-smoking' group of subjects only.

Design

Ten subjects were recruited by advertisement, by word of mouth and from the Subject Panel (Department of Experimental Psychology, Oxford University). The experimental design and procedures including scoring were the same as in Experiment 1 for the 'real-smoking' group, with the following differences:

1) EMG recording was not attempted; EEG, electrodermal, HR and RESP were recorded as in Experiment 1.

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[1] Activation of 'reward systems' by nicotine would reciprocally inhibit 'punishment systems'.

2) Mean Respiratory Rates, but not Respiratory Irregularities, were scored. This was because in Experiment 1 Respiratory Irregularities (deep breaths) were no more sensitive than Respiratory Rate as an arousal measure.

3) EEG 'α' was scored with reference to one calibration value per subject. The amplitude scoring criterion was based on half the average peak amplitude of an alpha burst during a two-minute eyes-closed period prior to the experiment. EEG 'α' scores (% time in 1-minute blocks that the 8-13 Hz band pass filtered record showed activity > criterion) were not expressed as % deviations from pre-smoking baseline values (as in Experiment 1) but as absolute scores. This enables comparison of absolute EEG 'α' scores between conditions. Other scoring criteria (i.e. duration of α burst, deletion of eye movement artefact) were the same as in Experiment 1.

4) Puffing rates were recorded as in Experiment 1; in addition, depth and duration of inhalation and butts were registered (see below). Subjects were asked to inhale after a puff and not to blow the smoke out prior to inhalation. Since this is a slight variation from the normal smoking style of some individuals, subjects were asked to practise this during the days prior to the experiment. Inhalation of smoke was verified by observation through the one-way window into the test room and concurrently by observation of the RESP physiograph channel.

Butt weights

Subjects were asked carefully to stub out their cigarettes at the end of the five-minute smoking periods. Buttweight (g) was the mass of the residual filter, paper and unburnt tobacco as weighed at the end of each experiment on an electronic balance (by courtesy of the Histology Section, Department of Experimental Psychology). Partly charred tobacco

but, not ash was included for this purpose.

Depth of Inhalation

Difficulties in assessing depth of inhalation of tobacco smoke arise from the possibility that the signal (in effect change in electrical resistance) given by the mercury in rubber strain gauge around the subject's chest may not be a linear function of the volume of gases inhaled (e.g. errors may arise from thoracic versus abdominal expansion via the diaphragm). These non-linearities are further compounded by the possibility that the efficiency of absorption of nicotine from a given volume of smoke inhaled may itself bear a non-linear (although monotonic) relation to depth and duration of inhalation. To some extent these possible non-linearities can be ignored when simply comparing depth of inhalation between conditions using subjects as their own controls. Unfortunately, one source of error cannot be ignored on this basis, that is, in comparing depth of inhalation between conditions and within subjects, the subject's posture has changed from prone (sensory isolation condition) to upright (stress condition). Such a large change in posture inevitably leads to a compression of the abdomen upon sitting upright and thus favours chest as opposed to diaphragm (abdominal breathing) movement during inhalation. Subsidiary problems arise from movement of the mercury strain gauge between conditions.

In order to overcome these latter problems, the output of the Hg strain gauge was calibrated against actual volume of inhalation as measured directly by a spirometer.

Calibration procedure for depth of inhalation as measured by Hg strain gauge

Equipment: The spirometer (constructed by courtesy of the Oxford Physiology Department) was of standard water displacement type. Inhalation/ exhalation cycle was continuously monitored as the subject breathed into

the spirometer through a mouthpiece connected via flexible hosing. Output of the spirometer was by ink pen on to paper affixed to a rotating drum. Volume in arbitrary units was given as cms. deflection of the ink trace on paper.

Details of the Hg strain gauge and its output to the physiograph are given in Experiment 1.

Design

The calibration procedure was carried out on each subject at the end of the stress and sensory isolation conditions respectively, with the subjects adopting that posture required by the relevant condition, i.e., sitting upright or laying prone. Subjects were requested to make a series of small, medium and large inhalations, followed by exhalations, through the spirometer mouthpiece. The range of inhalations and exhalations as measured by the Hg strain gauge output on to the physiograph was checked against the range of inhalations and exhalations previously recorded from the subject when smoking during the relevant experimental condition. This ensured that a range of inhalation/exhalation cycles was obtained during the calibration procedure which was sufficient to cover the variation in depth of inhalations observed during smoking in the preceding relevant experimental condition.

The magnitude of inhalation as measured from the spirometer (arbitrary units of volume) was then plotted against the magnitude of concurrent output by the Hg strain gauge to the physiograph (cms. deflection at fixed gain). Magnitude of inhalation from each measure (spirometer, Hg strain gauge) was taken from the minimum and maximum deflections for equivalent inhalation/exhalation cycles. This ensured fixed points for comparison within any cycle.

Duration of inhalation (seconds) was measured from the beginning of inhalation following the puff to the end of the exhalation.

Calibration results

As demonstrated by examples (cf. Figure 1) the relationship between measures of inhalation given directly (spirometer) as contrasted with indirectly (Hg strain gauge) is approximately linear over the range of values for smoking inhalation. This is congruent with the reported findings of Rawbone, Murphy, Tate and Kane (1978). The differences between calibration results between conditions for the same individual tended to be less than differences between individuals, in particular, some individuals (a minority: three subjects out of ten) demonstrated marked curvilinear relationships (see Figure 1, subject PM). While Rawbone et al. (1978) admit that curvilinearity occurs near zero inhalation point, they surprisingly fail to report cases of curvilinearity over the inhalation ranges encountered during smoking. It is, of course, true that correlation coefficients between spirometer and Hg strain gauge measures of inhalation are very high (>0.90) (Rawbone et al., 1978, p.176) but a wealth of deviancy from a linear relationship can be hidden in a correlation coefficient. This could be critical when using inhalation as a smoking style measure; as reported here - three curvilinear relationships out of ten subjects is a relatively large number.

Christiansen (1965) notes that the relative involvement of upper thoracic versus lower thoracic (i.e. abdominal) in respiration may be a crucial individual difference. In countries such as Japan, China, India, etc. where breathing control (thoracic versus abdominal) is taught as one aspect of physical training, these departure from linearity in respiration measures using indirect techniques (e.g. Hg strain gauge or high frequency impedance pneumography) may be even more important

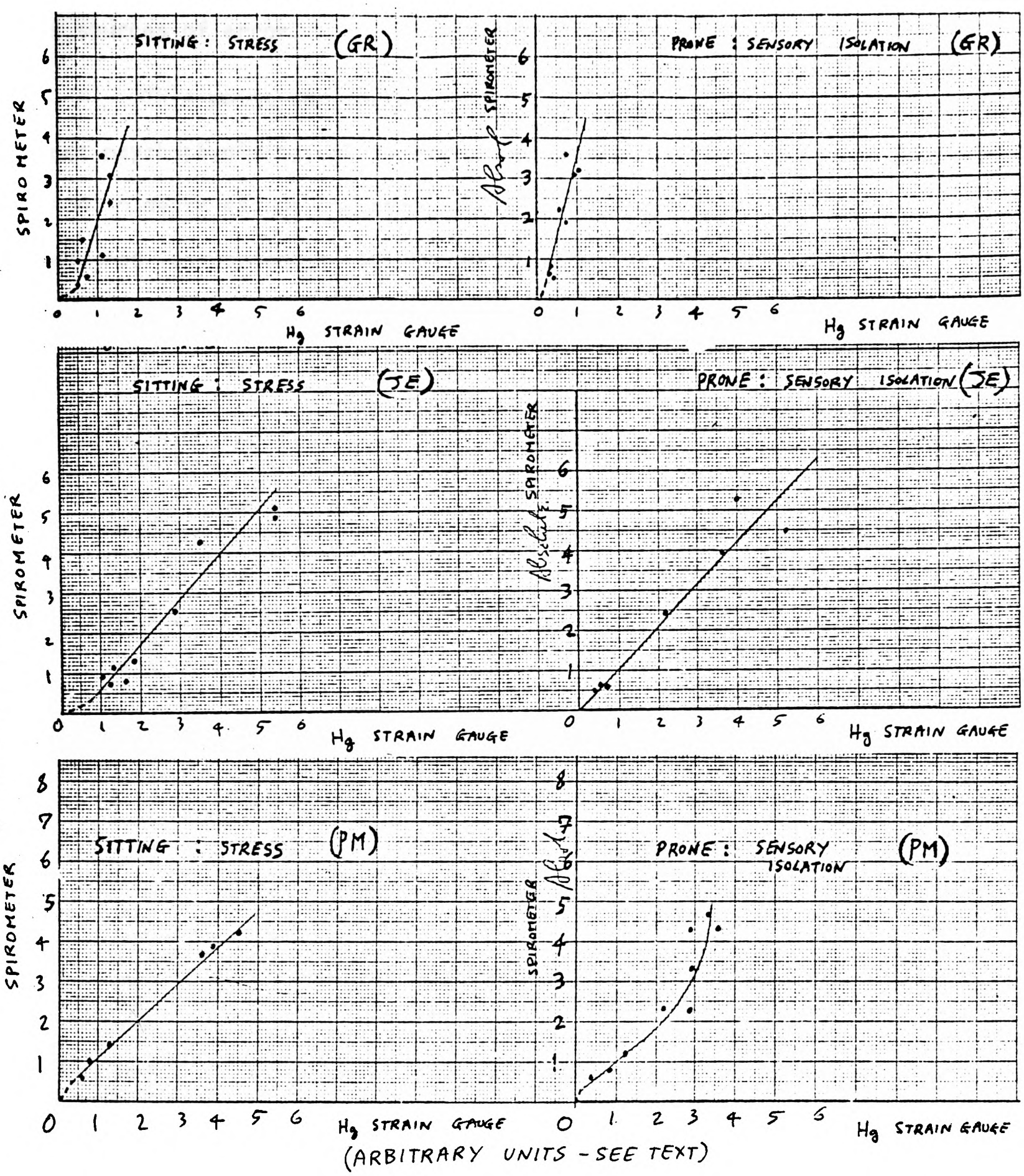


FIGURE 1 : Specimen Calibration Curves Drawn from Experimental Results to Illustrate Range of Effect Out of the Ten Subjects: for Three Subjects: Spirometer (y-axis), Hg Strain gauge (x-axis) Values of Inhalation - Subjects "GR", "JE", and "PM". (n.b. "PM" shows curvilinear relationship).

as sources of error.

This point has further ramifications. Thus the failure of most psychophysiological investigation to study this aspect of respiration in depth may be one cause of the relative failure of respiration measures (as opposed to SC, HR, EEG) as an index of arousal.

Limitations of the smoking style measures: puffs, inhalation, butt wt.

The smoking style measures detailed in the previous sections are subject to two types of limitations: firstly, the accuracy of measurement, secondly, the degree to which measurement reflects the dosage of nicotine absorbed by the subject.

Puffs: although number of puffs may be simply counted, the measure is a relatively crude index of the effort the subject makes to obtain tar/nicotine. Puff pressure and duration may be as important as number of puffs, as noted earlier (also cf. Experiment 3 - plumbed cigarette holders).

Butt Wt.: as an index of the amount of tobacco burnt whilst smoking over a fixed time period (5 minutes), it is relatively accurate, although subject to some weight measurement inaccuracy inherent in the manufacturing tolerances of cigarettes and from variations in water content (cf. Results - Experiment 3). A far more serious difficulty arises regarding the fact that the tobacco rod acts as a fractionation column throughout the course of smoking - tar and nicotine accumulating towards the butt. Consequently, a small difference in butt wt. with a short stub is equivalent to a much larger wt. difference for a longer stub, in terms of tar/nicotine extracted by the smoker. Similarly, a smoking puff from a threequarters burnt-cigarette will contain more tar/nicotine than an equivalent puff from a cigarette just lit.

Notwithstanding this difficulty, it is valid to make comparisons of butt wt. between conditions, with subjects acting as their own controls. Such comparisons give a crude estimate of the relative change in smoking vigour across conditions, but necessitate caution, for the reasons above, as regards assessment of the importance of magnitude as opposed to direction of butt wt. differences between conditions (cf. Experiment 3 and 5 for more detailed discussions of this point)

Inhalation: The calibration technique used for assessing the relationship between Hg strain gauge output and actual volume of gas in the lungs represents a small but definite advance on those employed by (Rawbone, 1978), as detailed earlier (also cf. Experiments 3, 4, 5). However, the relationship between the absorption efficiency for nicotine from inhaled smoke and depth, duration of inhalation remain unresolved. It is reasonable to assume that the greater the depth of inhalation, the more efficient the nicotine absorption, since a greater alveolar area will be exposed to nicotine/tar particles (the relationship is no doubt non-linear). Unfortunately, assessment of the importance of duration of inhalation, as regards efficiency of nicotine absorption, is more difficult. This is because the effective alveolar area for nicotine absorption is constantly changing over the time course of smoke inhalation. In the absence of any published data relating duration of smoke inhalation to consequent plasma nicotine levels, duration of inhalation was scored as the time from start of inhalation to the end of exhalation. Given that most subjects exhibited smoke inhalation/exhalation cycles roughtly approximately a sunusoidal curve, this is arguably as fair a measure as any other (cf. Appendix A : Specimen Chart Records, w.r.t. Hg strain gauge output). However, it is emphasised to the reader that this measure is very crude.

RESULTS

Personality and smoking habits

Age range and means (± SD) for EPQ variables and cigarette consumption are given in Table 1 (n = 10 subjects).

Whilst PENL personality scores and age range were almost identical for this sample of subjects (n = 10) compared to the sample in Experiment 1 (n = 24, combined groups - see Table 2a, Experiment 1), the subjects in Experiment 2 included a number of heavier smokers, as can be judged by comparing mean ± SD cigarette consumption for subjects in Experiment 1 (cigarette consumption 11.88 ± 4.37, n = 24) with those for this experiment (cigarette consumption 23.00 ± 10.87, n = 10). This represents an important extension of the range of the smoking population sampled, individual differences in cigarette consumption having implications for the strength of effect produced by smoking a single cigarette on a number of psychophysiological variables, in particular, cigarette-incuded heart rate elevation (see later Chapter on Smoking, Personality and Physiology - Interactions for combined data from various experiments).

Smoking Style Variables: Puffs, Inhalation, Butts

Mean puffing rates against time are presented graphically (cf. Figure 2) and as mean total puffs together with mean depth and duration of inhalation, Smoke Exposure Index and mean butt weights, in Table 2 for sensory isolation and stress conditions.

All smoking style variables show changes which can be interpreted in terms of subjects attempting to obtain more nicotine from the cigarettes smoked during stress as opposed to sensory isolation - more puffs, greater depth and duration of inhalation and smaller butts. The increase in puffing rate during stress (+2.7) was relatively small compared to the total number of puffs taken during the sensory isolation condition (13.5)

Table 1 Personality & Smoking Habits (n = 10)

Variable	m	SD
Age range (yrs.)	19-25	
P	5.40	(4.58)
E	13.30	(5.44)
N	12.30	(5.62)
L	4.30	(2.63)
Cigarettes: Consumption/Day	23.00	(10.87)

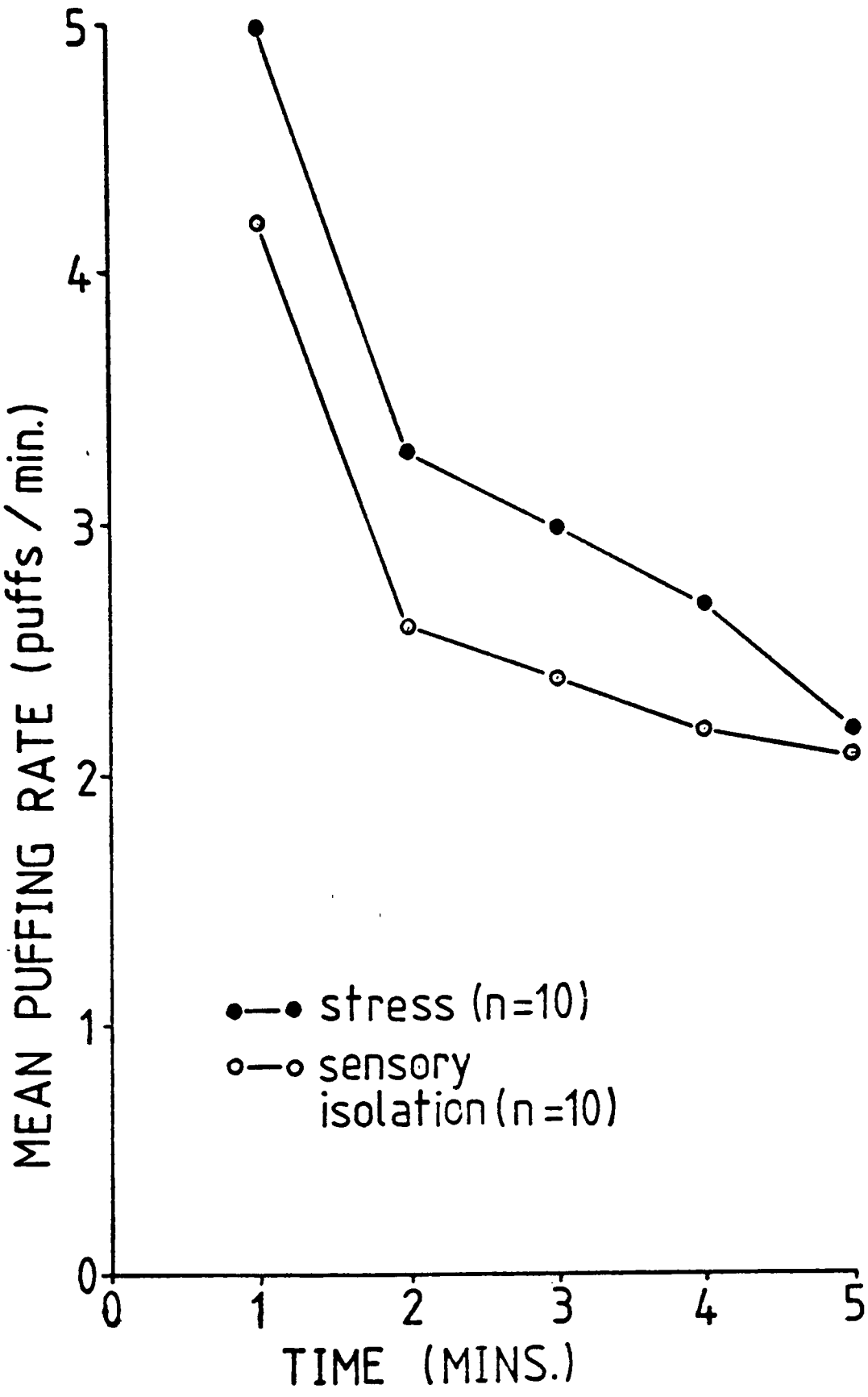


FIGURE 2 : Puffing Rates for Cigarette Smoking During Stress and Sensory Isolation.

Table 2 Smoking Style Variables: Differences & Correlations between conditions of Stress & Sensory Isolation.

Variable	n	Sensory Isolation m	Sensory Isolation SD	Stress m	Stress SD	Δ ST-SI	p sign test 1-tailed	r_s (Spearman)
Butt wt.(g)	10	.227	(.056)	.181	(.053)	-.046	.02	+.27
Puffs (number)	10	13.5	(5.30)	16.2	(6.46)	+2.7	(.055) NS	+.81**
Depth of Inhalation (volume units of spirometer)	10	1.578	(0.587)	1.767	(0.714)	+.189	NS	+.53
Duration of inhalation (secs.)	10	2.82	(0.72)	3.00	(0.97)	+.18	NS	+.83**
Smoke Exposure Index 1) (vol.secs) (=puff x mean depth x mean duration)	10	62.24	(46.51)	93.67	(75.95)	+31.43	NS	+.63*

Spearman Rank Order Correlation Coefficient = r_s	* $p < .05$ ** $p < .01$

1) Smoke Exposure Index: adapted from Rawbone et al (1978)

Table 3 **Smoking Style:**
Pearson Correlation Coefficients (r)
between measures within each condition

SENSORY ISOLATION

	Butt weight	Depth of inhalation	Puffs	Duration of Inhalation
Butt weight	-	-0.24	-0.38	-0.63 [1)]
Depth of Inhalation		-	0.12	0.04
Puffs			-	0.19
Duration of Inhalation				-

S T R E S S

	Butt weight	Depth of Inhalation	Puffs	Duration of Inhalation
Butt weight	-	-0.24	-0.59	-0.27
Depth of Inhalation		-	0.16	0.34
Puffs			-	-0.0005
Duration of Inhalation				-

1) r = -0.63 for butt wt/duration of inhalation, suggesting that increasing butt wt. associated with shorter duration of inhalation but r falls fractionally short of significance at the 5% level. Using $t = \sqrt{vr^2/(1-r^2)}$, v = n - 2 = 8 df., the 95% confidence interval for t = 2.30 is (-2.306,2.306).

and of marginal significance. This is similar to the results obtained in Experiment 1. The failure of depth or duration of inhalation (or the combined measure: SMOKE EXPOSURE INDEX) to achieve significance as smoking style measures for comparisons between conditions implies that subjects were not attempting any systematic control over their intake by these means. The only variable to achieve significance was butt weight (g).

Since the increase in puffing rate was relatively small and the total burning time was fixed (5-minutes) the implication of the observation that significantly smaller butts were left during the stress condition (cf. Table 2) is that subjects were puffing more vigorously (duration and/or negative pressure of each puff) during stress. Further, since subjects were instructed to inhale all the smoke - this was verified by observation of the subject and of the Hg strain gauge output (see Design Section) - and, since the depth of inhalation was not significantly greater during stress, the conclusion is that subjects were attempting to increase their nicotine extraction from the cigarettes during stress mainly by varying the intensity of each puff.

The correlations between conditions for puffs, duration and to a lesser extent depth of inhalation (r = +0.81, +0.83, +0.53, respectively - cf. Table 2) are relatively high compared to that for butt weight (r = +0.27 - cf. Table 2). The small and non-significant changes in puffs and inhalation measures between conditions, as compared to the significant correlations between conditions, indicates that these variables are fixed and idiosyncrative for the individual smoker (cf. Table 2). In contrast, butt weight changed significantly between conditions and the correlation between conditions was low, implying that this (logically puff intensity) is the variable of interest as regards the predicted

self-titration for stimulant or depressant dosages of nicotine.

Table 3 shows the intercorrelations between smoking style measures within each condition. Whilst most of these correlations are non-significant, some internal consistencies are revealed. Firstly, the more puffs subjects take the smaller the butt weight: (r =-0.38 [SI], NS; r = -0.59 [ST], NS). This implies that (predictably) increased puffing rates lead to burning more tobacco. Perhaps a measure of puff intensity would account for the remainder of the variance. Secondly, the negative correlations (cf. Table 3) between depth or duration of inhalation with butt weight implies that individuals who obtain more nicotine from their cigarettes (smaller butts) also inhale for a longer time and inhale to a greater depth.

These smokers would seem to be making an 'across the board' effort to obtain more nicotine both by increasing the amount of tobacco burnt and also by exposing their alveoli to the tobacco smoke to a greater extent.

Heart Rate (HR)

Mean HR results are given in Tables4 and 5.

Baseline HR (minutes 1-5, pre-smoking) was significantly greater during the stress as opposed to the sensory isolation condition (cf. Table 4). One subject (JE) showed a baseline HR decrease. (STRESS: 72 b.p.m., SENSORY ISOLATION: 74 b.p.m.). This aberrant result partly accounts for the slightly smaller stress-induced baseline HR elevation observed for this sample of subjects (mean, n = 10, HR [ST-SI] = 7.10 b.p.m.) as compared with that for Experiment 1 (mean, n = 24, HR [ST-SI] = +10.27). Considerable individual differences do exist in HR reactivity, although not statistically significant when comparing group means (e.g. for comparison the sham-smoking sub-group [n = 8] of Experiment 1 had a mean ΔHR ST-SI = +8.00).

Table 4 Mean Heart Rate differences between Sensory Isolation and Stress (white noise) Conditions during pre-smoking baseline (mins.1-5)

n	Baseline H.R. (b.p.m.)				Δ HR ST - SI	P sign test 1-tailed
	Sensory Isolation (SI)		Stress (ST)			
	m	SD	m	SD		
10	69.30	(5.74)	76.40	(6.11)	+7.10	.011

Table 5 Mean Heart Rate elevations for cigarette smoking during Sensory Isolation and Stress Conditions

HR = (HR 1 min. post cigarette smoking - mean HR over 5 mins. pre-smoking baseline)

N	SENSORY ISOLATION					STRESS				
	mean HR (bpm)		Δ HR Post-Pre		P sign test 1-tailed	mean HR (bpm)		Δ HR Post-Pre		P sign test 1-tailed
	Pre	Post	m	SD		Pre	Post	m	SD	
10	69.30	80.00	+10.7	10.08	.011	76.40	89.10	+12.7	3.89	.001

Cigarette smoking significantly elevated HR in both stress and sensory isolation conditions as can be seen from Table 5. (HR elevation [POST-PRE] smoking is not significantly different between conditions ST/SI or significantly different in this experiment compared with HR elevation [POST-PRE] for the real smoking group in Experiment 1.)

Subject JE again appeared aberrant, actually showing a drop of -2 b.p.m. (POST-PRE) smoking during the sensory isolation condition, although showing an elevation of +16 b.p.m. (POST-PRE) smoking during stress. By self-report JE was a fairly light smoker (cigarette consumption = 9 per day), but in terms of smoking style measures taken in the experiment, smoked his cigarettes extremely vigorously as compared with other subjects, taking the greatest number of puffs (PUFFS = 30 [ST], 26 [SI]), and ranking first or second in both conditions on the smallness of residual butts and greatness of depth of inhalation. However, any explanation suggesting that he obtained a sufficiently large dosage of nicotine during sensory isolation to obtain depressant cardiovascular effects fails to explain why the smoking induced HR (POST-PRE) depressed during sensory isolation but elevated during stress. Perhaps the most probable explanation lies in some curious interaction between nicotine and the individual's personality, subject JE having EPQ scores: P = 14, E = 15, N = 12, L = 2. Thus whilst E, N and L scores are 'normal', JE's 'P' score is three standard deviations above Eysenck's (1975) normal comparison and is one of the highest P scores encountered by the experimenter. Correlations between personality and psychophysiological effects of cigarette smoking are dealt with in greater detail in Chapter on Smoking, Personality and Physiology - Interactions.

Respiration

Mean and (SD) Respiration rates are given by period (PRE- and

Table 6 Respiration Rates PRE- (mins. 1-5) and POST-SMOKING (mins. 11-15) for Sensory Isolation and Stress Conditions.

Condition	n	MEAN, (SD) RESPIRATION RATES (Breathes per minute)				Δ POST - PRE	P Sign test 1-tailed
		PRE-SMOKING		POST-SMOKING			
		m	SD	m	SD		
Sensory Isolation	10	17.20	2.55	16.14	3.49	- 1.06	NS (.090)
Stress	10	17.55	2.86	17.02	3.45	- 0.53	NS

Table 7 Comparison of baseline (PRE-SMOKING mins.1-5) Respiration Rates between Sensory Isolation and Stress Conditions.

n	MEAN, (SD) RESPIRATION RATES (Breathes per minute)				Δ ST-SI	P Sign test 1-tailed
	PRE-SMOKING BASELINE					
	SENSORY ISOLATION		STRESS			
	m	SD	m	SD		
10	17.20	2.55	17.55	2.86	+0.35	NS

POST SMOKING) and condition (Sensory Isolation and Stress) in Tables 6 and 7. Respiration rates during smoking are not given since they merely reflect the physical activity of smoking (see Experiment 1 - Respiration Results).

Perusal of Tables 6 and 7 reveals that, as in Experiment 1, respiration rates are not significantly effected either by the effects of condition (stress versus sensory isolation) or by the effect of smoking a cigarette (PRE- versus POST-SMOKING).

Skin Conductance Level (SCL)

SCL data is presented graphically as a function of time (Figure 3) and as means and SDs by conditions and period (cf. Tables 8, 9, and 10).

Baseline SCL (pre-smoking, minutes 1-5) was significantly higher during stress as opposed to sensory isolation (Table 8). This is predictable given that SCL usually increases during stimulating conditions (noise, performance tasks, etc.). Two subjects showed small drops in SCL during stress, one of these being subject JE to whom attention has already been drawn in another context.

Cigarette smoking elevated SCL levels but this only achieves significance for the sensory isolation condition (see Tables 9 and 10).

The significant elevation of SCL during and after smoking in the sensory isolation condition is similar to that observed in Experiment 1. Since this experiment did not include its own sham-smoking control, effect of smoking on SCL during stress is analysed for comparison. The non-significance of the SCL rise attributable to cigarette smoking during stress is unlike that of the other autonomic variable monitored, the significant cigarette induced HR elevation, which occurs irrespective of condition. This could be interpreted in terms of Arousal Modulation,

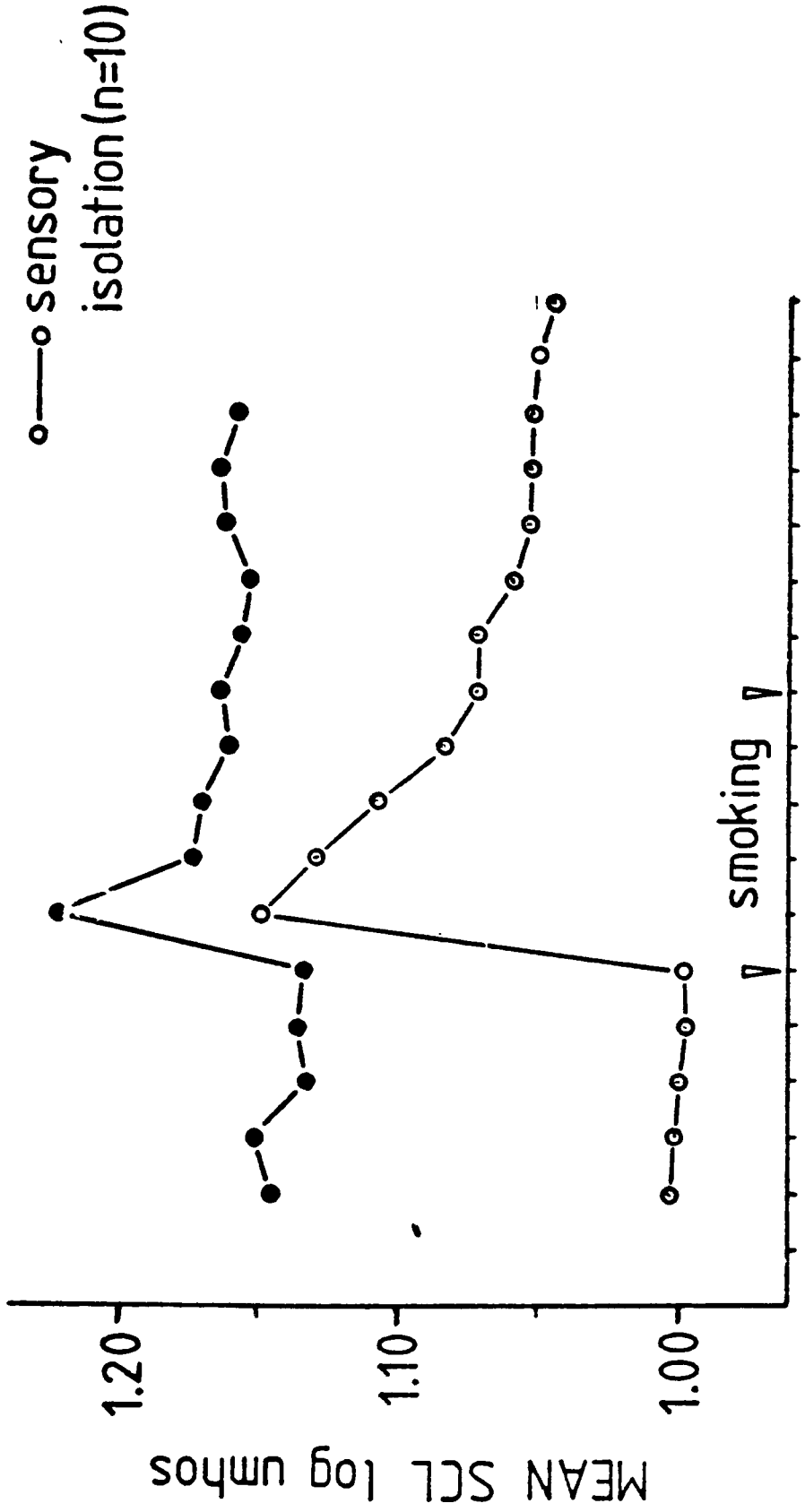


FIGURE 3 : SCLs During Stress and Sensory Isolation Conditions

Table 8 Wilcoxon matched-pairs signed-ranks test on changes in BASELINE (PRE-SMOKING, mins. 1-5) SCL between Stress and Sensory Isolation Conditions.

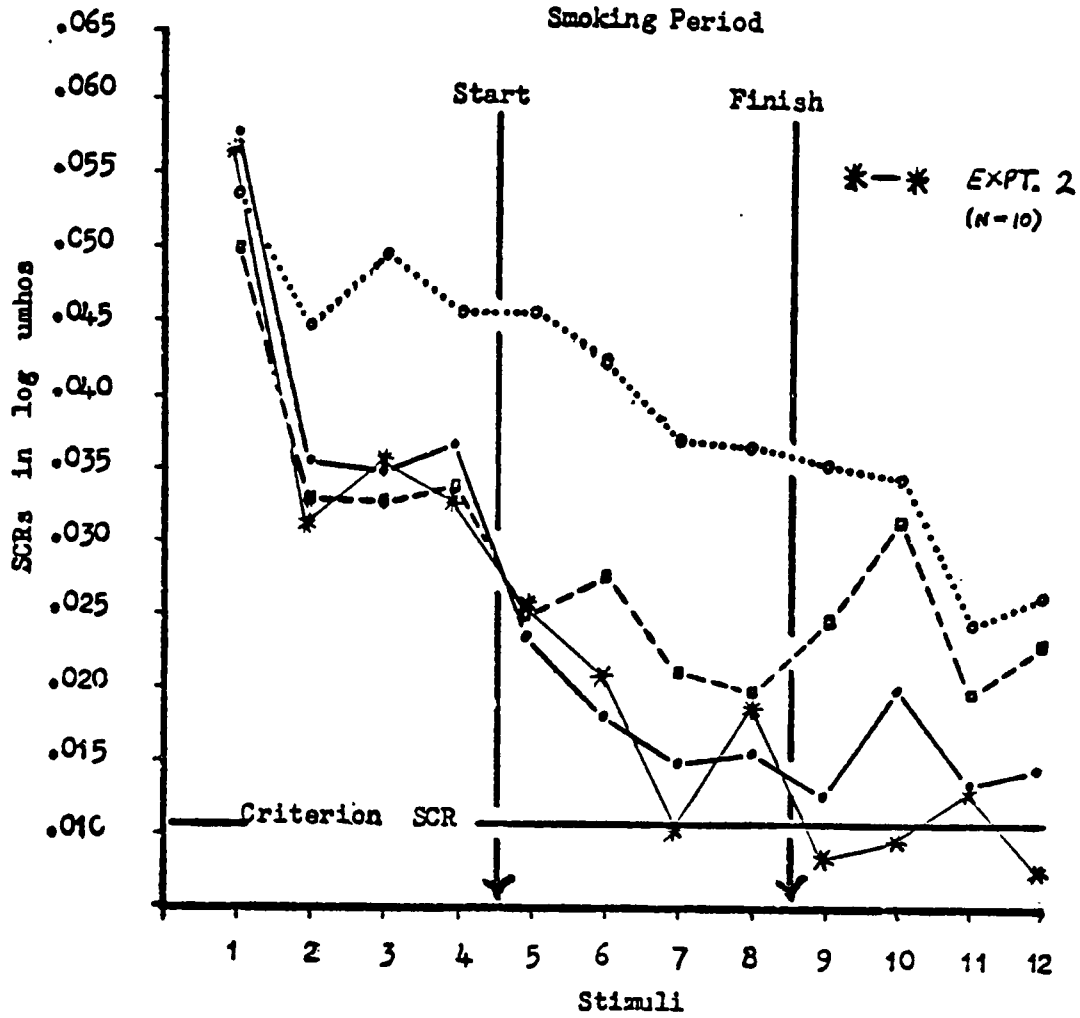
n	BASELINE SCLs (log_{10} µmhos)				CHANGE in Baseline SCL (log_{10} µmhos) between conditions. Δ = (Stress - Sensory Isolation		P 1-tailed on difference between mean baseline SCLs
	STRESS		SENSORY ISOLATION				
	m	SD	m	SD	m	SD	
10	1.141	0.262	0.999	0.451	+0.142	0.027	0.025

Table 9 Mean SCLs for Pre-Smoking (mins. 1-5), Smoking (mins. 6-10) and Post-Smoking (mins. 11-15) periods during Sensory Isolation and Stress Conditions.

Condition	n	Skin Conductance Level $\log_{10}$ µmhos					
		PRE -SMOKING		SMOKING		POST-SMOKING	
		m	SD	m	SD	m	SD
Sensory Isolation	10	0.999	0.451	1.109	0.349	1.060	0.456
Stress	10	1.141	0.262	1.175	0.263	1.160	0.288

Table 10 Wilcoxon matched-pairs signed-rankstest on changes (rise) from pre-smoking baseline SCL during smoking and post-smoking for Stress and Sensory isolation conditions.

Condition	n	Mean change in SCL $\log_{10}$ µmhos	P 1-tailed	Mean change in SCL $\log_{10}$ µmhos	P 1-tailed
		SMOKING - PRE		POST - PRE	
Sensory Isolation	10	+0.110	0.01	+0.061	0.005
Stress	10	+0.034	NS	+0.029	NS



SCRs to aversive stimuli for real smoking (●—●) sham-smoking (□--□) and situation control (○·····○) groups.

FIGURE 4 : SCR Results Superimposed for Comparison Purposes on Results Obtained in Experiment 1

Table 11 Mean SCRs to "N bursts (change in $\log_{10}$ µmhos) during Stress for Experiment 2 and comparative data from Experiment 1.

Expt.	Group	n	MEAN SCRs : change in $\log_{10}$ µmhos					
			PRE-SMOKING		SMOKING		POST-SMOKING	
			Stimuli 1-7		Stimuli 8-15		Stimuli 16-23	
			m	SD	m	SD	m	SD
2	Real	10	.0346	.0215	.0168	.0121	.0099	.0079
1	Real	8	.0421	.0212	.0215	.0145	.0142	.0101
1	Sham	8	.0330	.0090	.0250	.0101	.0243	.0136
1	Control	8	.0514	.0125	.0411	.0092	.0317	.0107

Table 12 Change in Mean SCRs by period (SMOKING-PRE, POST-PRE) for Experiment 2 with comparative data from Experiment 1.

Experiment	Group	n	SCR diff. SMOKING-PRE	P Sign test 1-tailed	SCR. diff. POST-PRE	P Sign test 1-tailed
2	Real	10	-0.0178	0.001	-0.0247	0.001
1	Real	8	-0.0206	0.004	-0.0279	0.004
1	Sham	8	-0.0080	0.035	-0.0087	0.035
1	Control	8	-0.0103	NS	-0.0177	0.004

or perhaps in terms of the Law of Initial Values (ceiling effect) since the baseline SCL is elevated during stress.

Skin Conductance Response (SCR)

SCRs to white noise burst during the baseline period (PRE-SMOKING, minutes 1-5) for this sample of subjects, as compared to real, sham or control groups in Experiment 1 during the pre-smoking baseline, were not significantly different from the real smoking group of Experiment 1 during smoking and post-smoking periods. See Tables 11 and 12 and Figure 4 for comparisons between Experiments 1 and 2.

EEG 'α'

EEG 'α' results are shown graphically as a function of time (Figure 5) and as means and SDs in Table 13. Two records were rejected from the Stress Condition because of artefact.

Since these EEG 'α' scores are based upon a single criterion value for each subject generated from the 'eyes-closed' calibration period prior to both conditions it is possible to compare baseline (pre-smoking minutes 1-5) EEG 'α' between stress and sensory isolation conditions. (This was not possible in Experiment 1 since EEG 'α' was based upon a scoring procedure involving calibration during the 'eyes-open' baseline period prior to each condition and expressing the values for EEG 'α' as deviation [+ or −] from baseline .) EEG 'α' was significantly greater during the sensory isolation versus stress pre-smoking periods (Table 14), only one subject showing more alpha during stress.

In spite of the different scoring procedures for Experiment 2, EEG 'α' results were closely similar to those observed in Experiment 1 for the 'real-smoking' group (for comparison cf. Experiment 1, Figures 8 and 9). EEG 'α' elevated from baseline during and, to some extent, after smoking in the sensory isolation condition, this effect reversing in the

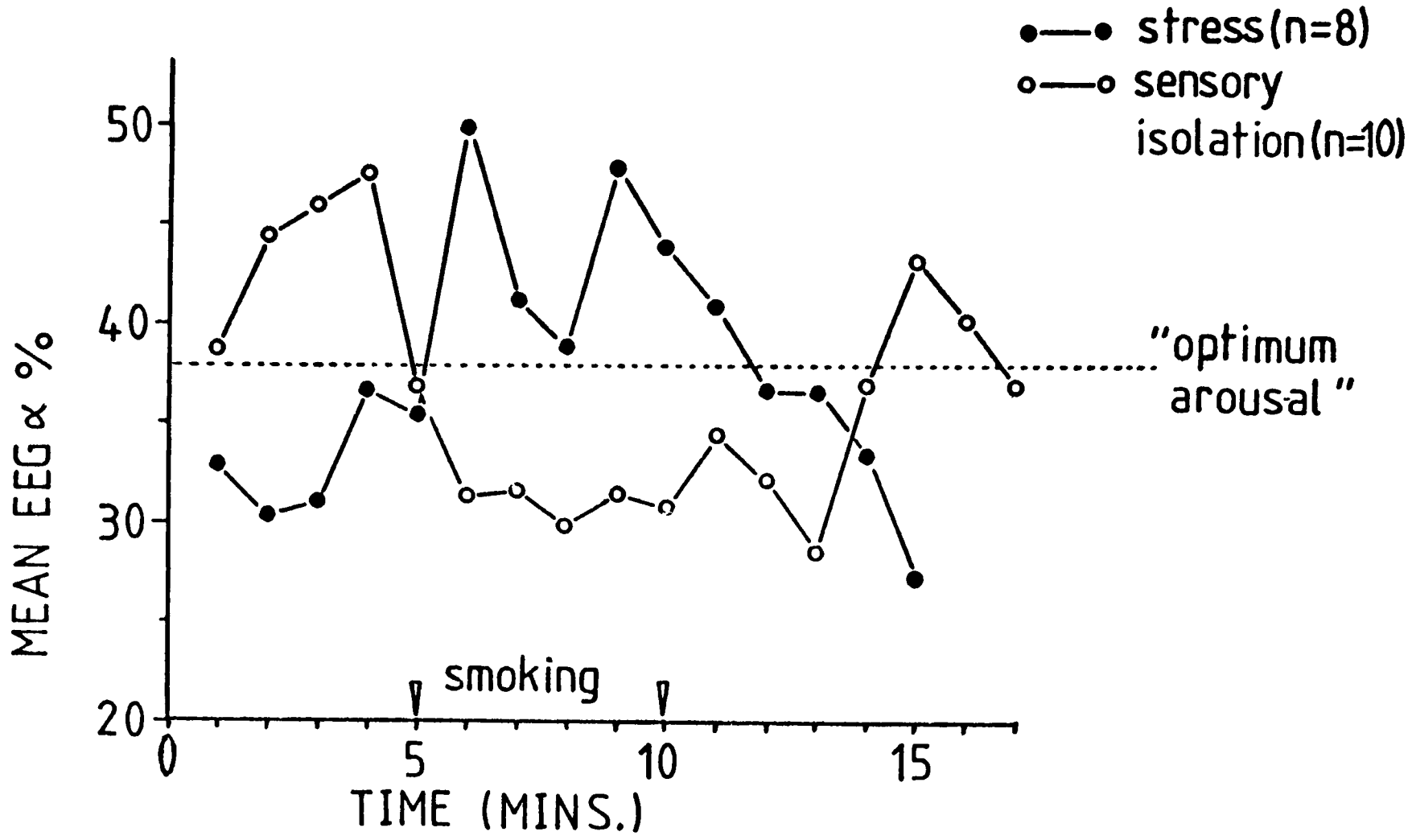


FIGURE 5 : EEG 'α' During Stress and Sensory Isolation Conditions

Table 13 Means & SDs for EEG "α" scores for Stress and Sensory Isolation Conditions by Period PRE (mins.1-5) SMOKING (mins.6-10), POST (mins. 11-15).

Condition	n	E E G "α" Scores					
		PRE-SMOKING		SMOKING		POST-SMOKING	
		m	SD	m	SD	m	SD
Stress	8	33.45	24.47	44.45	23.07	35.08	24.73
Sensory Isolation	10	42.76	17.50	31.16	14.50	35.20	20.41

Table 14 EEG "α" baseline PRE-SMOKING comparisons between Stress and Sensory Isolation.

(nb. Sign test is based on the 8 subjects for whom both ST and SI EEG records were available.)

S T R E S S (n = 8)		SENSORY ISOLATION (n = 10)		P sign-test 1-tailed (n = 8)
m EEG "α"	SD	m EEG "α"	SD	
33.45	(24.47)	42.76	(17.50)	0.035

Table 15 - Mean changes in EEG "α" from baseline (Pre-Smoking, mins. 1-5), during smoking (mins.6-10) and Post-Smoking (mins. 11-16) for Stress and Sensory Isolation Conditions.

Condition	n	EEG "α" Pre-Smoking	Δ EEG "α" Smoking-Pre	P Wilcoxon matched pairs signed ranks 1-tailed	Δ EEG "α" POST-PRE	P Wilcoxon matched pairs signed ranks 1-tailed
Stress	8	33.45	+11.00	0.025	+1.63	NS
Sensory Isolation	10	42.76	-11.60	0.025	-7.56	NS

stress condition (cf. Tables 13 and 15).

It is of interest to note that an Arousal Modulation theory of smoking would predict that the arousal 'optimum' would be roughly half-way between the EEG 'α' baseline scores for the experimentally-induced arousal extremes of isolation and stress, i.e. mean = 'optimum' $\underline{\Omega}$ 38% alpha. Consideration of Figure 5 or of Table 13 reveals that the subjects 'overshot' the postulated optimum when smoking, in both sensory isolation and stress conditions. However, for the minute prior to smoking and for two or three minutes after smoking, the subjects' mean scores for the two conditions appear to cross over near this 'optimum'. (The reason for the 'anticipatory' effect in minute 4, immediately preceding smoking, is that the smoking period was rigidly timed from the ignition of the cigarette; consequently, the effect of the command to smoke and the subject manipulating the cigarette and lighter were inevitably scored in minutes 4-5 of the EEG trace.)

Given that each subject's CNS arousal as indicated by EEG 'α' appears to be constantly changing from second to second, this 'overshoot' effect as judged from EEG 'α' scores averaged over minutes leads to a view of 'arousal modulation' as an active process involving a 'hunting mechanism' analogous to many biological or mechanical homeostats, operating over both short (seconds) and long time constants (minutes). An obvious biological analogy is the different time courses involved in release of various transmitters such as ACh, GABA (fast; in milliseconds) or peptides, such as enkephalin (slow; minutes or tens of minutes).

DISCUSSION

The battery of smoking style measures, butt weight, puffs, inhalation depth and duration, smoke exposure index, examined the hypothesis that subjects were attempting to obtain more nicotine/tar from their

cigarettes during stress as opposed to sensory isolation. Although all smoking style variables showed changes in the predicted direction, i.e. towards obtaining larger (depressant) dosages of nicotine during stress, only residual butt weight showed a significant change. The implication of this observation is that puff intensity (puff negative pressure and puff duration) is the crucial variable by means of which smokers are regulating their nicotine intake, at least as regards the variations in smoking style observed with changes in situation-induced arousal.

The effects of smoking single cigarettes on psychophysiological measures during the stress and sensory isolation conditions were similar to those found in Experiment 1. Thus, heart rate elevated significantly during smoking and post-smoking for both conditions. SCL showed a significant elevation during smoking and post-smoking for the sensory isolation condition but not significantly so during stress.

SCR results were not significantly different from the real smoking group in Experiment 1 (no internal comparison in Experiment 2 for SCR was possible, owing to the design). Respiration rates did not change significantly either to condition or to cigarette smoking.

EEG 'α' showed significant elevations and drops to cigarette smoking during stress and sensory isolation conditions respectively.

These results (apart from HR elevation to cigarette smoking during stress) either directly support (EEG 'α' results during stress and sensory isolation, SCL results during sensory isolation, HR results during sensory isolation) or at least do not contradict (SCL results during stress, RESP RATE results during stress and sensory isolation) the view that cigarette smoking is relaxing the smoker during stress and conversely stimulating the smoker during sensory isolation. Experiment 1 would

indicate that these effects are in part due to the effects of nicotine and in part due to the physical activity involved in smoking. The major value of these psychophysiological results is in replicating the results for Experiment 1 with the sample of heavier smokers studied in the present experiment.

E X P E R I M E N T 3

Additional observations on the effects of cigarette smoking during conditions of stress and sensory isolation: the use of plumbed cigarette holders and EMG.

RATIONALE

The purpose of replicating the experimental paradigm of Experiments 1 and 2 was threefold:

(a) to test the hypothesis, generated from Experiment 2, that strength of puffing (puff pressure and/or duration) rather than number of puffs is the critical smoking style variable by which smokers increase nicotine extraction from cigarettes during stress to obtain larger, depressant, doses (depth of inhalation beyond normal respiratory cycle not being important cf. Experiment 2)

(b) to examine muscle activity in relation to cigarette smoking during stress. (Various reports suggest that nicotine and cigarette smoking reduces EMG reactions to stimuli [Domino, 1973; Hutchinson and Emley, 1973], although increases in tonic EMG activity have been reported [Fagerström and Götestam, 1977]. Animal work suggests that this may be due to biphasic stimulant and depressant effects of nicotine at neuro-muscular, spinal and central sites, cf. Introduction.)

(c) to assess the robustness of the psychophysiological measures of Experiments 1 and 2 in the face of variations in electrode placement.

DESIGN

Eighteen subjects were randomly allocated to either real smoking (n = 12) or sham smoking (n = 6) groups. Experimental procedures were the same as in Experiments 1 and 2, with the following differences:

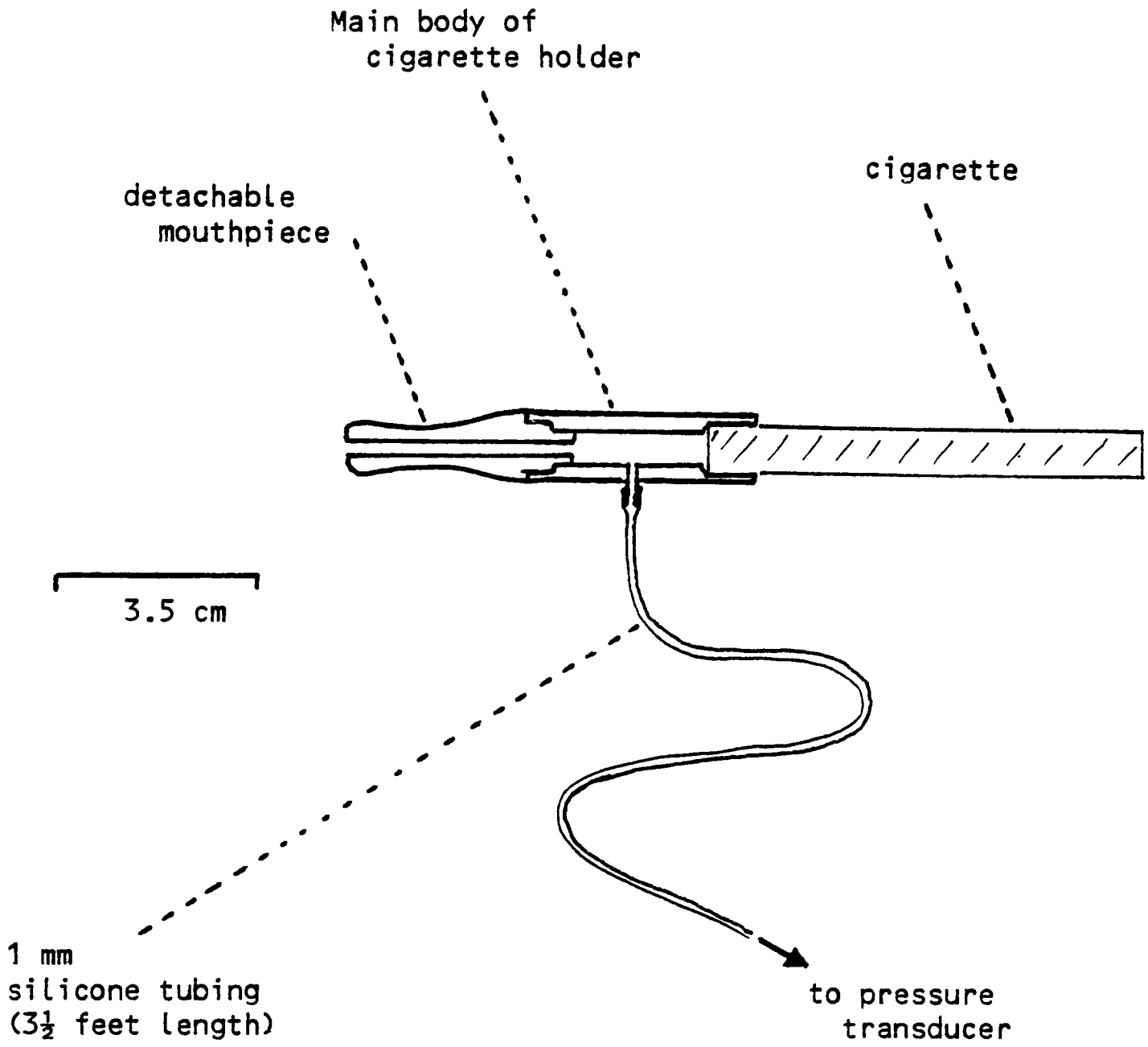
Smoking Style

1) Plumbed cigarette holder.

Subjects smoked or sham-smoked their cigarettes through a plumbed cigarette holder (cf. diagram : Figure 1)

Thin flexible silicone tubing connected the internal space of the holder to a Devices L221 Pressure Transducer. This pressure gauge outputted to one channel of the M19 Physiograph. The resulting trace enabled puff pressure drop and puff duration to be scored (cf. Figure 1).

Subjects were habituated to smoking through the cigarette holder by requesting them to smoke all their cigarettes for two days prior to the experiment through a holder identical to the experimental one, apart from the absence of plumbed-in flexible tubing. (A crude check on this was carried out by examining the inside of the holder for tar and nicotine deposits.) To further ensure familiarity with the cigarette holder used during the present experiment, the particular mouthpiece, used by each subject during the two days prior to the experiment, was detached and inserted into the plumbed experimental holder. This was carried out in the presence of the subject during the 'wiring-up' procedure. Subjects were also requested, as in Experiments 1 and 2, to practise prior to the experiment inhaling all the smoke of each puff.



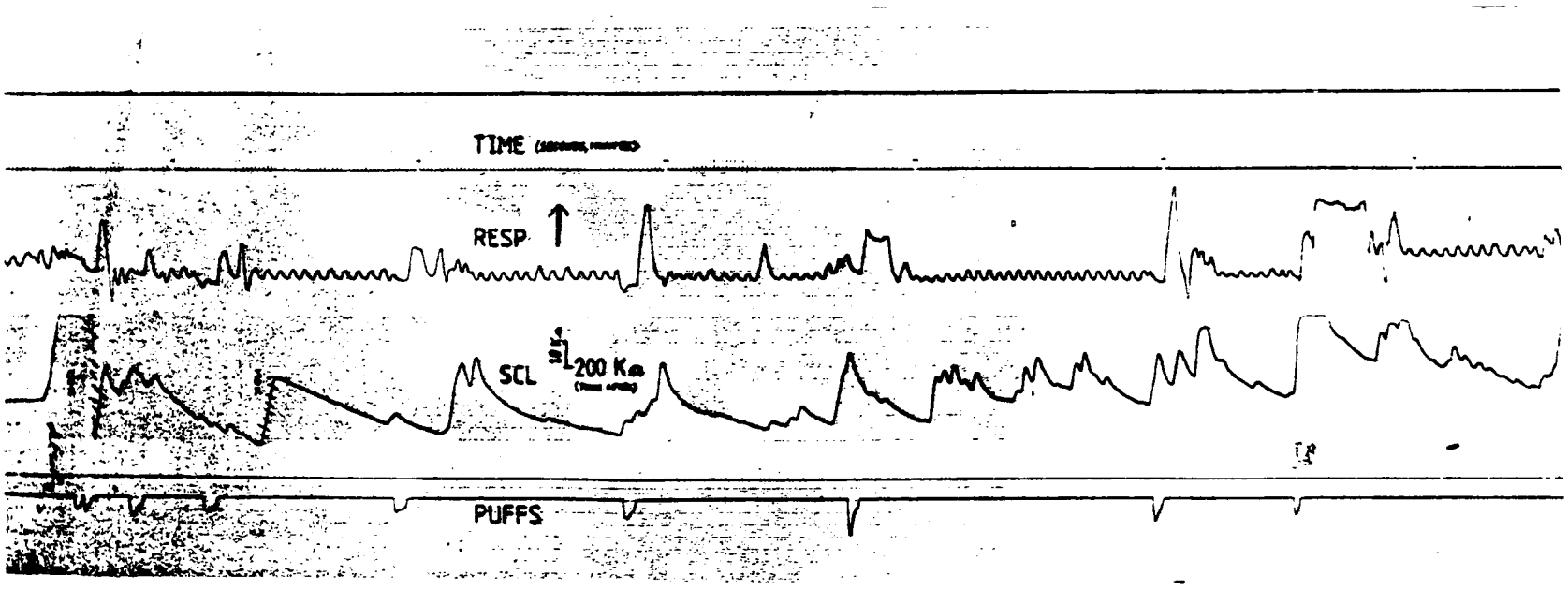


FIGURE 1 : Plumbed cigarette holder. Specimen output during smoking is shown in the photograph above. Note the inhalations immediately following each puff. Note also SC peaks associated both with the puff and also with the subsequent inhalation.

"↑" : direction of inhalation

2) Burnt Tobacco Weight.

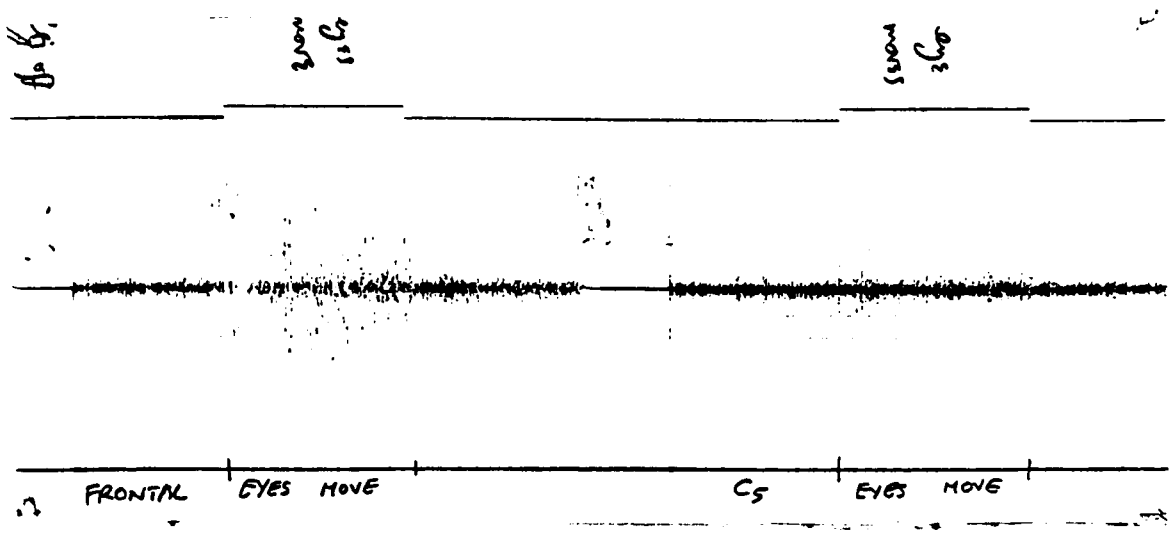
The differences for cigarette smoking between stress and sensory isolation conditions in residual butt weight observed in Experiment 2, although significant, were small. A more accurate measure was utilised for the present experiment. This measure compensated for variations in cigarette weight due to the manufacturing tolerance of cigarettes and due to the water content of cigarettes. Cigarettes taken fresh from the packet were tapped down to compact the (distal) ends and sealed in small individual glass containers with air-tight seals. Cigarettes were weighed immediately prior to the experiment. After smoking the residual butt plus charred tobacco (but not cigarette ash) was collected and re-sealed in the container. The residual buttwas then weighed after the completion of the experiment. Weight before - Weight after smoking (gram) provided the index of tobacco burnt: Burnt Tobacco Weight (over the fixed 5 minute smoking period).

Changes in electrode positions

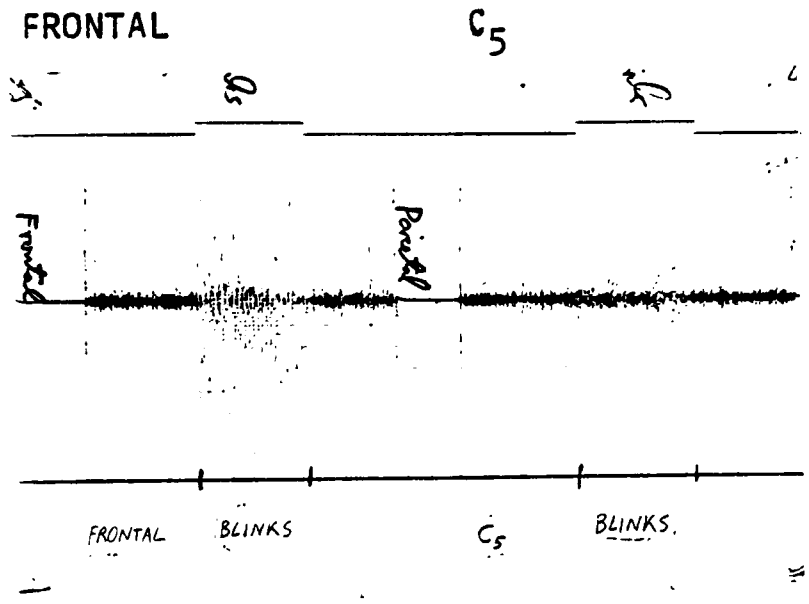
1) EEG : Indifferent electrode placement at C_5.

The frontal positioning of the indifferent electrode can lead to excessive eye-related EEG artefact. This artefact, which was evident especially during the smoking period, was identified and deleted for scoring purposes, using the criteria detailed earlier (cf. Methodology, Experiment 1). Placement of the indifferent electrode at C_5, or C_6 for left-handers, ('Ten-twenty' numbering system; Jasper, 1958) has two advantages. Firstly, eye-related artefact is virtually eliminated (cf. Figure 2). Secondly, the hemisphere showing greatest EEG reactivity is recorded from (Ornstein, 1977). This is no doubt because of the partial localisation of language functions in the left hemisphere (N.B. C_6 -

A



B



C

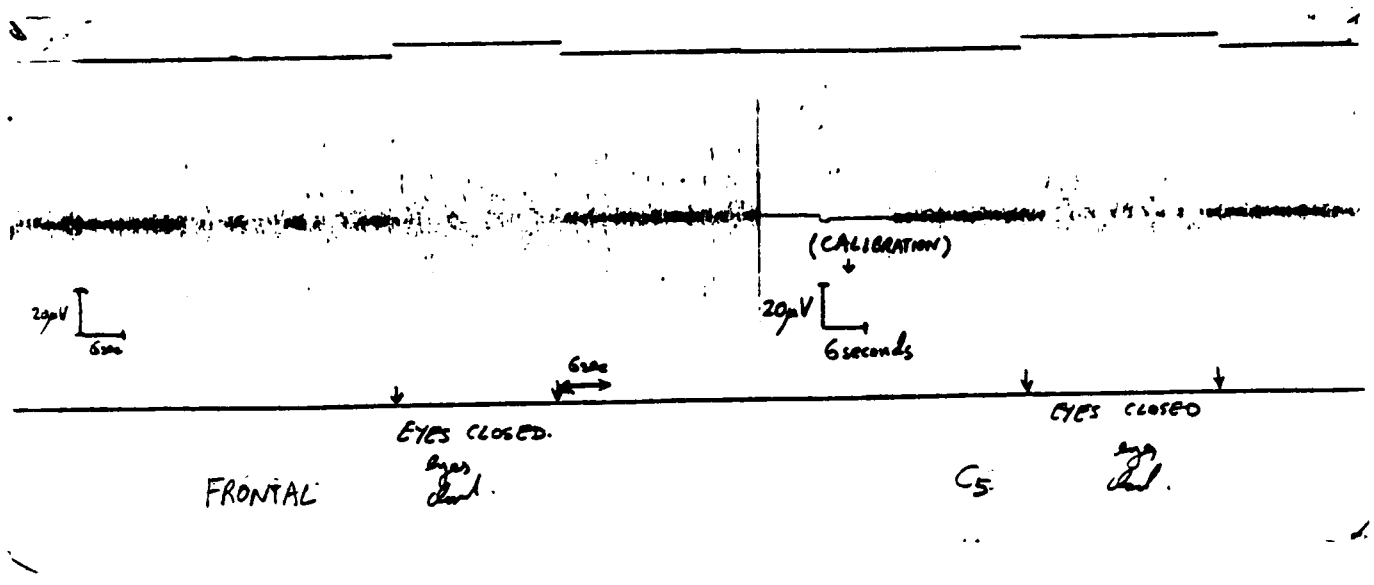


FIGURE 2 : Sample EEG traces employing indifferent electrode sites at Frontal (cf. left hand of figures) or C_5 (cf. right hand of figures). Active = Occipital, Earth = Mastoid, in all cases. Note that C_5 as opposed to Frontal sites reduce various eye-related artefacts A) "Eyes Move" B) "Eye Blinks" but do not significantly reduce C) Alpha bursts to "Eyes Closed".

Right hemisphere - was used for left-handers). In practice it was noted, from pilot studies carried out using two EEG amplifiers to simultaneously record Right and Left hemispheres, that the latter postulated advantage appeared minimal as regards EEG and effects of cigarette smoking. However, detectable Right versus Left differential EEG desynchronisation was discernible using spatial tasks (e.g. visual imagery) and verbal logical tasks (e.g. silent prose recitation or mental arithmetic), during eyes closed conditions. It is thus possible that if task demand (e.g. mental arithmetic with verbal goading by the experimenter) were used as the stressor, as has been used often in the study of the effects of tranquillisers on stress, Right or Left EEG electrode placement could well be crucial.

SC : 1) First and second fingertip placements; 2) larger electrodes; 3) SFs.

1) The two SC electrodes were attached to the whorls of the fingertips of the first and second fingers of the non-dominant hand. In Experiments 1 and 2, the first and third fingertips were used. Although some difference in electrodermal responding may be predicted on the basis of the distribution of sympathetic innervation of the hand (i.e. different dermatomes; Cambier, Masson and Dehen, 1978), a pilot study revealed no observable differences in electrodermal responding between first and third versus first and second fingers.

2) The SLE miniature Ag/AgCl electrodes were attached to the fingertips by colloidon glue, as opposed to double sided adhesive disks. This method of electrode attachment has the advantage of being more robust. The effective electrode size is increased leading to higher baseline SCL in the present experiments (see SCL results for Experiment 1, 2 versus 3). This slight change in electrode procedure does not, of

course, produce any differences between experiments in observed SCL changes within the experiment; i.e. rise in SCL due to stress, cigarette smoking or SCR's to white noise stimuli. This is because any change in SCL due to absolute differences in effective electrode area, cancel out when within subjects SCL comparisons are made.

3) Spontaneous Fluctuations (SFs) $\geq$ .5K Ω were scored during the sensory isolation condition. Two four thirty second samples from both minutes 1 - 4 and minutes 12 - 15 constituted SF scores PRE and POST smoking for each subject. The choice of these time periods obviated any confounding effects from the physical activity of manipulating the cigarette and especially from respiratory reflex. Any SF immediately following the peak inspiration of a 'large' breath (i.e. > 3 x normal respiratory depth) was deleted as breathing reflex artefact.

EMG

EMG was recorded from forearm extensor of the non-dominant arm (n = 12), rectus abdominus (n = 6) sites. Data for rectus abdominus EMG are not presented since tonic and phasic activity in this group of muscles was not sufficient to make any meaningful observations on the effects of cigarette smoking (cf. Results: 'EMG - phasic reactions to white noise bursts').

Equipment and methodology

Sites are located and marked with felt pen (cf. Venables and Martin, 1967). EMG sites were cleaned with 10% alcohol and the skin abraded until inter-electrode resistances of $\leq$ 3 K were achieved (as measured from a psychogalvanometer). In practise, this involved puncturing the skin. Standard Ag-AgCl cup electrodes in contact with electrolytic jelly (SNP Limited), were attached with colloidon glue. EMG was recorded

using a Devices AC high gain amplifier, feeding through an EMG integrater unit (Devices 3520), output from which marked one chart paper channel of Devices M19 Recording System. A high frequency cut-off of 500 kHz was used, with time constant of .03 seconds on the AC high gain amplifier. The EMG integrater unit was set to 'Long' Time constant (2 seconds nominal time constant). Use of a 'smoothing' long time constant on the EMG integrater made accurate scoring more reliable (cf. Epstein and Webster, 1975).

Scoring procedure

Tonic EMG: the EMG trace was sampled every 5 seconds, the mean of 12 such samples producing a minute block. Two 15 minute blocks were scored for stress and sensory isolation conditions for each subject.

Phasic EMG: EMG response to a white noise burst during stress was scored as the maximum rise in EMG from the tonic level of EMG expressed one second prior to stimulus onset. This value was converted to percentage of the maximum EMG response observed for each particular subject. The large individual differences in absolute magnitude of phasic EMG response made such a procedure necessary, in order not to bias analysis of results in favour of particularly (EMG) reactive individuals.

Subject position

All subjects lay prone on a comfortable bed, the head and non-dominant arm (from which EMG and SC were recorded) being supported by soft pillows. This is a slight modification from Experiments 1 and 2, where subjects sat upright for the stress conditions.

Heart rate

In order to reduce the burden of electrodes on the subject, heart rate was not recorded in this experiment. Sufficient heart rate data

for a stress/sensory isolation paradigm was judged to have been obtained in Experiments 1 and 2.

RESP

RESP was recorded as a check for adequate inhalation of smoke (cf. chart record; Figure 1) but not presented as data in their own right since Experiments 1 and 2 demonstrated that respiration rate and irregularity are not useful as measures for the effects of stress or for the effects of real versus sham smoking.

R E S U L T S

PERSONALITY AND SMOKING HABITS DATA

Personality, age range and smoking habits data for the subject sample are given as means and standard deviations in Table 1 (see Table 1). These scores are similar to those of the subjects in Experiments 1 and 2 (for comparisons with normative data see later, Chapter 4[1]). As regards comparison between the real and sham smoking sub-groups in this experiment, sub -groups are virtually identical on all scores apart from 'E'. The sham-smoking group is significantly more introvert (mean E = 8.50) than the real-smoking group (mean E = 14.50) when tested by non-parametric Mann-Whitney U test (n_1, n_2 = 6, 12; $\bar{z}$ = 2.2478, p = .0122, 1-Tailed). However, while matched groups of subjects are desirable, the significant difference of 'E' scores between sham and real groups does not lead to any significant difference between groups for baseline physiological responding.

SMOKING STYLE

As is evidenced from Table 2 (see Table 2) in which smoking style variables are detailed for real smoking (combined extensor and stomach EMG sub-groups) and sham smoking groups, subjects varied their smoking

---

[1] "Smoking, Personality and Physiology - Interactions"

GROUP	n	Age Range (Years)	Cigarette Consumption (Cigs./Day) M	SD	P M	SD	E M	SD	N M	SD	L M	SD
Real Smoking	12	18-25	16.33	(7.35)	7.17	(3.81)	14.50	(5.04)	12.50	(5.27)	3.33	(3.34)
Sham Smoking	6	18-25	15.83	(5.85)	8.33	(2.94)	8.50	(5.21)	11.00	(4.15)	1.50	(1.38)
Combined	18	18-25	16.17	(6.71)	7.55	(3.50)	12.50	(5.73)	12.00	(4.85)	2.72	(2.93)

TABLE 1

Personality (Eysenck EPQ [1975]) and smoking habit scores for real and sham smoking groups

Group	n	Variable	Stress (ST) m	Stress (ST) SD	Sensory Isolation (SI) m	Sensory Isolation (SI) SD	Δ ST-SI	P sign test 1-tailed	Correlation of variable between ST and SI Spearmans r_s	P
REAL SMOKING	12	Puffs (number)	15.75	4.88	13.75	4.86	+2.00	NS	+.81	< .01
	12	Puff Pressure Drop (mm/merc.)	10.59	4.28	7.72	3.67	+2.87	.001	+.81	< .01
	12	Puff Duration (sec.)	2.19	0.62	2.07	0.46	+0.12	NS	+.50	≈ .05
	12	Tobacco Burnt (g.)	0.605	0.110	0.548	0.118	+0.057	.019	+.88	< .01
SHAM SMOKING	6	Puffs (number)	18.71	13.31	14.70	10.39	+4.00	NS (.109)	+.94	< .05
	6	Puff Pressure Drop (mm/merc)	12.44	6.72	8.90	4.67	+3.54	.016	+.46	NS
	6	Puff Duration (sec.)	2.32	1.03	2.42	1.00	-0.10	NS	+.94	< .05
	6	Tobacco Burnt (g.)	-	-	-	-	-	-	-	-

TABLE 2a

Smoking Style Variables (Puffs, Puff Pressure Drop, Puff Duration, Tobacco Weight Burnt)

as means and standard deviations for real and sham smoking groups during stress and sensory isolation

Variable	STRESS					SENSORY ISOLATION				
	Real Smoking (n=12)		Sham Smoking (n=6)		z^1	P^1 Real v. Sham	Real Smoking (n=12)		Sham Smoking (n=6)		z^1	P^1 Real v. Sham
	m	S.D.	m	S.D.			m	S.D.	m	S.D.		
Puffs (number)	15.75	4.88	18.71	13.31	.281	N.S.	13.75	4.86	14.70	10.39	.094	N.S.
Puff Pressure Drop (mm/merc.)	10.59	4.28	12.44	6.72	.281	N.S.	7.72	3.67	8.90	4.67	.562	N.S.
Puff Duration (sec)	2.19	0.62	2.32	1.03	.094	N.S.	2.07	0.46	2.42	1.00	.562	N.S.
Tobacco Burnt[2] (g)	Red.		Red.		Red.	Red.	Red.		Red.		Red.	Red.

[1] Mann-Whitney U Test; n = 12, 6; 1-tailed

[2] Comparisons real v. sham are redundant for Tobacco Burnt

TABLE 2b: Comparison of Real versus Sham Smoking Style during Stress and Sensory Isolation Conditions

style in the predicted direction: to obtain more (i.e. depressant dose)[1] nicotine/tar from their cigarettes during stress as opposed to sensory isolation conditions.

Differences between stress and sensory isolation conditions in number of puffs and puff duration are not significant. However, subjects puffed more strongly (pressure drop stress > sensory isolation: $p = .001$) and burnt more tobacco over the 5 min. smoking period (Tobacco burnt stress > sensory isolation: $p = .019$) (cf. Table 2). Thus the prediction, from Experiments 1 and 2, that puff intensity is the crucial smoking style variable, i.e. the means by which smokers regulate their nicotine intake to obtain larger (depressant)[1] doses during stress, was strongly supported. The results for the sham smoking group also support this hypothesis. Puff pressure was significantly greater ($p = .016$ during stress as opposed to sensory isolation, whereas puff number or duration did not change significantly (cf. Table 2).

As observed in Experiment 1 and 2, individual differences in smoking style appear to be marked. The correlations between stress and sensory isolation conditions, for the various smoking style measures, are all positive and significant, except for puff pressure during sham smoking which, while showing a positive correlation between conditions, is non-significant ($r_s = .46$, non-significant sham smoking, cf. Table 2). The fact that Burnt Tobacco Weight correlated significantly ($r_s = +.88$, $p < .01$) between conditions in this experiment, but that the equivalent measure, Residual Butt Weight, did not correlate in Experiment 2 ($r_s = +.27$, non-significant, see Experiment 2, Table 2) probably reflects the greater accuracy of the methods employed for assessing tobacco weight in the present experiment. While Residual Butt Weight of a cigarette smoked over a fixed time interval may be a sufficiently accurate measure to significantly

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[1] Smoking style results suggest that the subjects absorbed more nicotine during stress and it is postulated that larger nicotine dosages are more likely to be depressant.

discriminate changes in smoking style between stress and sensory isolation (see Experiment 2; Smoking Style), the errors inherent in manufacturing tolerances of cigarettes, together with possible effects of humidity changes on tobacco weight, are arguably the reason for the non-significant Butt Weight correlation between conditions in Experiment 2.

Consideration of Figure 3 reveals that the rate at which the smoker puffs, the duration of the puff and puff pressure, all progressively decline over the five minute smoking period for both stress and sensory isolation conditions. This decline is significant for puffing rates and duration and marginally significant for pressure when rates for minutes 1-2 and 4-5 do real smoking are compared by non-parametric sign test for puffing rate (Stress, $p < .001$; Sensory Isolation, p .001), puff duration (Stress, $p < .003$; Sensory Isolation, $p < .001$), puff pressure (Stress, $p < .073$; Sensory Isolation, $p < .194$). The smoking style profiles for the sham smoking group are highly similar (not significantly different) to the real smoking group for both stress and sensory isolation conditions. This gradual decline in the vigour of cigarette smoking over the five minute smoking period has also been previously noted, for puffing rates, in Experiments 1 and 2.

The most plausible explanation[1] is that, given the extreme rapidity with which nicotine reaches its presumed target receptors in the C.N.S. (approximately 8 seconds after tobacco smoke inhalation, Russell, 1976), the optimum level of nicotine in the C.N.S. has been achieved by the smoker soon after lighting the cigarette and that the subsequent period of cigarette smoking represents a 'topping-up' process to replace nicotine as it leaves the C.N.S. (N.B., C.N.S. nicotine clearance is probably rapid, brain half-lives for nicotine are of the order of minutes for small mammals although human data is unavailable, cf. Stalhandshake, 1970).

[1] An alternative explanation is that, since tar/nicotine accumulates towards the butt throughout the time-course of smoking, each successive puff of equivalent vigour will be "stronger" i.e. produce more tar/nicotine per puff: hence the "tailing-off" of smoking vigour towards the end of smoking a cigarette.

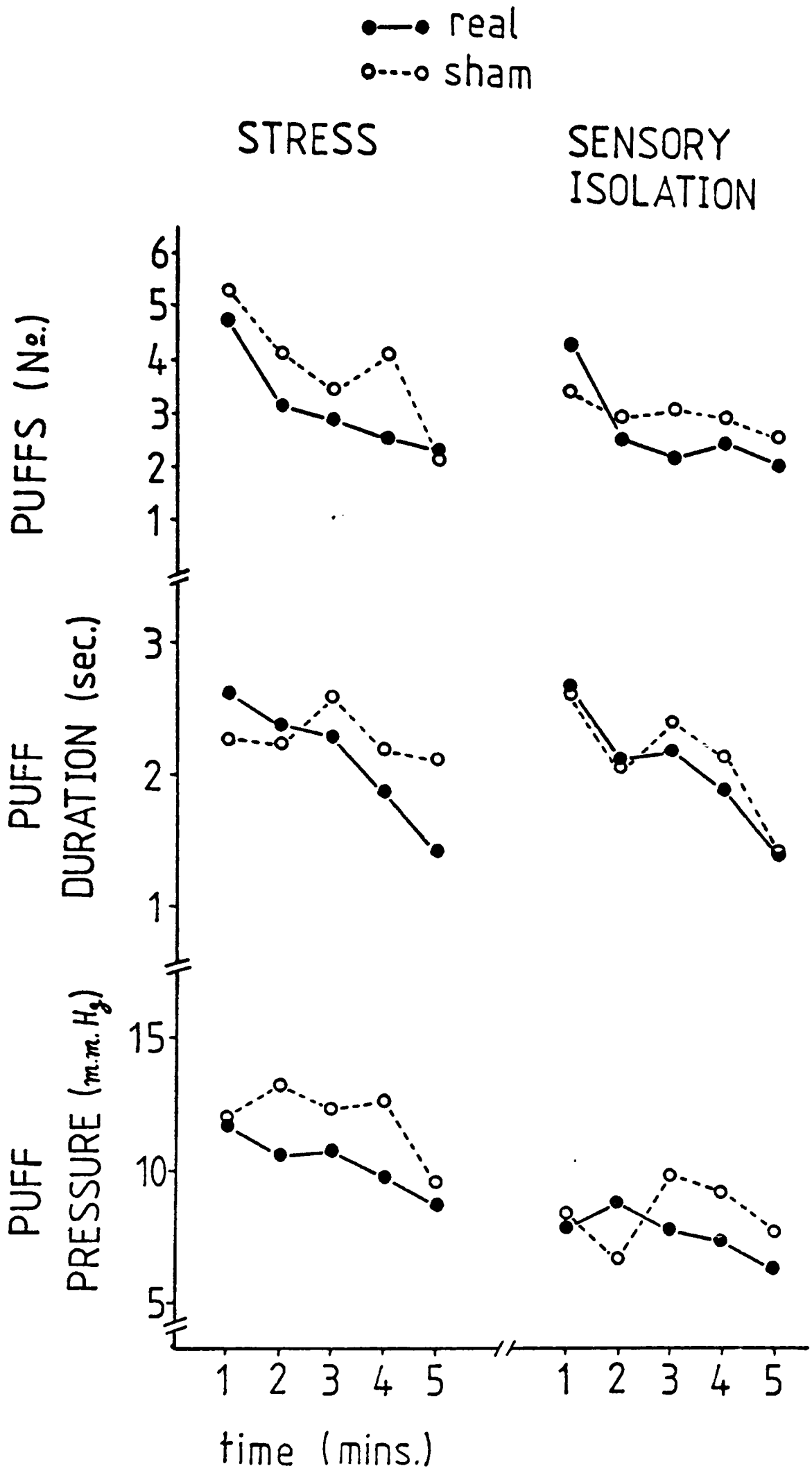


FIGURE 3 : Smoking style for Stress and Sensory Isolation conditions: Puffing rate, Puff duration and Puff pressure.

Analogous declines are observed in the rate of eating and drinking as satiety is achieved. The assumption inherent in the above argument is that puffing rates, puff duration and puff pressure provide an index of the amount of nicotine absorbed. This is a reasonable assumption for this experiment since subjects were instructed and observed to inhale all the cigarette smoke. Once inhaled, the nicotine from the smoke is efficiently absorbed into the arterial blood (Russell, 1976). (N.B. There is reason to believe that variations in depth of inhalation, beyond a certain minimal depth [i.e. normal respiratory cycle depth], probably do not significantly affect the efficiency of absorption of nicotine. Rawbone has recently retracted his suggestion [Rawbone, 1978] that depth of inhalation is a critical variable in the absorption of CO and by implication also for nicotine [B.A.T. Informal one day conference on CO absorption, March 1980]).

However, in the real world, this progressive decline in smoking vigour (puff rate, duration, pressure) over the course of smoking one cigarette is no doubt masked to some extent. The smoker may simply blow the smoke out of his mouth or nose without even minimal inhalation. (Analogously people do not normally spit out food or drink and so satiety mechanisms for hunger and thirst are easier to observe.) In spite of this possible confounding variable, similar declines have also been noted by surreptitious observation outside the laboratory (Schulz and Seehofer, 1978).

Skin Conductance Level (SCL)

SCL data are presented graphically (Figure 4) and as means and standard deviations, by period, activity and condition in Table 3.

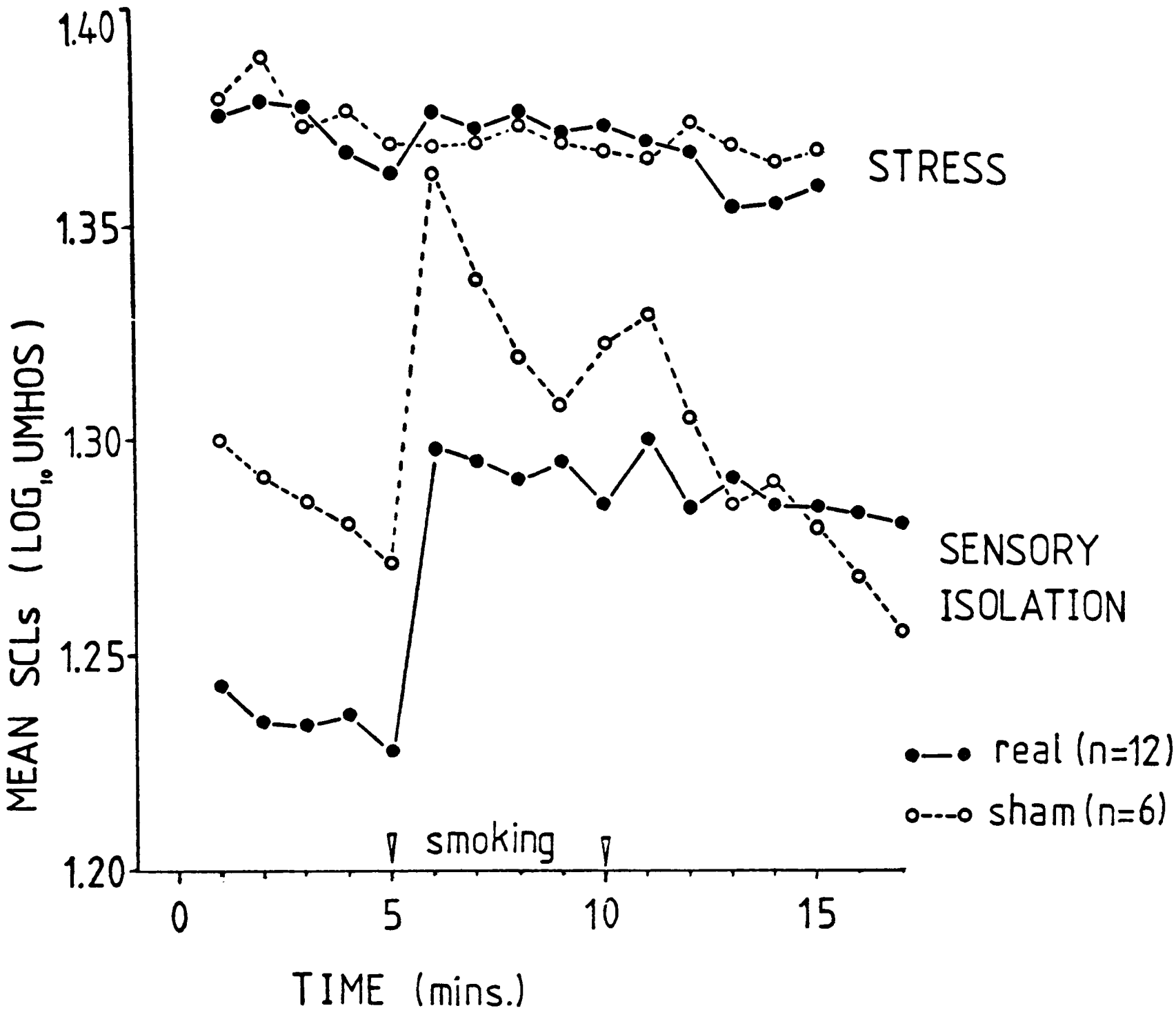


FIGURE 4 : Mean SCL (log_{10} µmhos) for real and sham smoking groups during stress and sensory isolation conditions.

TABLE 3

Mean SCLs $\log_{10}$ µmhos (±S.D.s) by period (pre, smoking, post), activity (real and sham-smoking) and condition (stress, sensory isolation)

			TIME PERIOD		
ACTIVITY	CONDITION	N	PRE-SMOKING Mins. 1 - 5	SMOKING Mins. 6 - 10	POST-SMOKING Mins. 11 - 15
REAL SMOKING	Stress	12	1.371 (.310)	1.374 (.334)	1.361 (.325)
	Sensory Isolation	12	1.235 (.209)	1.294 (.225)	1.290 (.225)
SHAM SMOKING	Stress	6	1.378 (.316)	1.370 (.320)	1.368 (.325)
	Sensory Isolation	6	1.287 (.267)	1.330 (.263)	1.299 (.259)

Predictably SCL was sensitive to the effects of stress. Pre-smoking baseline SCL was significantly elevated by stress compared to sensory isolation conditions for both real and sham smoking groups. However, three subjects in the real smoking group showed small drops in SCL for stress versus sensory isolation, reducing the significance level of stress-induced SCL elevation for this (real smoking) group (cf. Table 4). It could be hypothesised that this is explicable in terms of personality differences. The real smoking group is more extraverted than the sham smoking group, and thus may be less sensitive to stress (Gray, 1971). However, any such explanation must be tentative since the mean stress-induced rise in SCL for the more extraverted real-smoking group is greater than that of the (introverted) sham smoking group (cf. Table 4 and Figure 4). This difference in SCL between groups is non-significant. Thus a more parsomonious explanation is that these differences are sampling artefacts due to relatively small groups (n = 12, 6)

Having established that the pre-smoking SCL baselines for real and sham smoking groups are not significantly different as regards the effects of stress versus sensory isolation, comparisons of the effects of real or sham smoking can be made. As in Experiments 1 and 2, it would appear that the effect of real and sham smoking during sensory isolation is to elevate SCL. This effect achieves significance, post-smoking, for the real-smoking group but not for the sham-smoking group (cf. Table 5, Figure 4). The relatively transient rise in SCL for the sham-smoking group presumably reflects the absence of nicotine which would be required to maintain SCL elevation post-smoking. As also noted in Experiment 2, this smoking-induced SCL elevation does not occur during the stress condition for real or sham-smoking (cf. Table 5). While an explanation for this

TABLE 4

Significance of stress-induced rise in mean pre-smoking SCL for real and sham smoking groups

ACTIVITY	N	BASELINE SCL log μmhos STRESS m	STRESS SD	SENSORY ISOLATION m	SENSORY ISOLATION SD	Δ * ST-SI	P on ST-SI WILCOXON MATCHED-PAIRS 1-TAILED
Real Smoking	12	1.371	.310	1.235	.209	+0.136	.025
Sham Smoking	6	1.378	.316	1.287	.267	+0.091	.005

* Mann-Whitney rank-sum test $n_1 = 12$; $n_2 = 6$; $z = 0.000$; p = N.S.

on Δ_{ST-SI} Real versus Sham:

stress-induced SCL rise

CONDITION	ACTIVITY	N	CHANGE IN SCL log µmhos SMOKING-PRE	P WILCOXON 1-TAILED	CHANGE IN SCL Log µmhos POST-PRE	P WILCOXON 1-TAILED
Sensory Isolation	REAL	12	+.059	.025	+.055	.025
	SHAM	6	+.043	.005	+.012	NS
Stress	REAL	12	+.003	NS	-.010	NS
	SHAM	6	-.008	NS	-.010	NS

TABLE 5

SIGNIFICANCE OF RISES IN SCL FOLLOWING REAL AND SHAM SMOKING:

Smoking (mins 6-10) - Pre (mins 1-5), Post (mins 11-15) - Pre (mins 1-5); for stress and sensory isolation conditions.

difference in smoking effects between stress and sensory isolation conditions may be couched in terms of the Law of Initial Values (see SCL Results, Experiment 2), the lack of any significant cigarette-induced SCL rise during stress is also compatible with an Arousal Modulation Model of smoking.

Of some interest is the observation that 3 subjects in the real-smoking group showed small drops in SCL during and post-smoking. This leads to the lower significance for real versus sham smoking effects shown in Table 5, in spite of the fact that the mean smoking-induced SCL elevation is greater for real smoking. While this may simply reflect the occasional 'aberrant' responses of subjects often observed in psychophysiology, it is possible that some degree of internal consistency is evidenced for these outliers. Thus two out of three deviant subjects are also members of the sub-group who were mentioned earlier as showing small drops in SCL to white noise stress. To focus more sharply on these two subjects (P.C., M.C.) it is noteworthy that subject P.C. had an Eysenck (1975) 'N' score of 21 (the highest amongst the 18 subjects) while subject MC recorded 'P' score of 15 (the highest amongst the 18 subjects). Unfortunately, there is no statistical method for assessing the probability of simultaneous outlier observations (on different measures) for such small number of observations (cf. later discussion: 'Post-hoc analysis of deviant responders').

Skin Conductance Responses to White Noise Bursts (SCR)

SCRs to white noise bursts in the stress conditions are presented graphically (Figure 5) and as means, by period and activity (see Table 6). As in Experiments 1 and 2, the major effect is habituation of the SCR to white noise stimuli (this effect is significant by simple sign test).

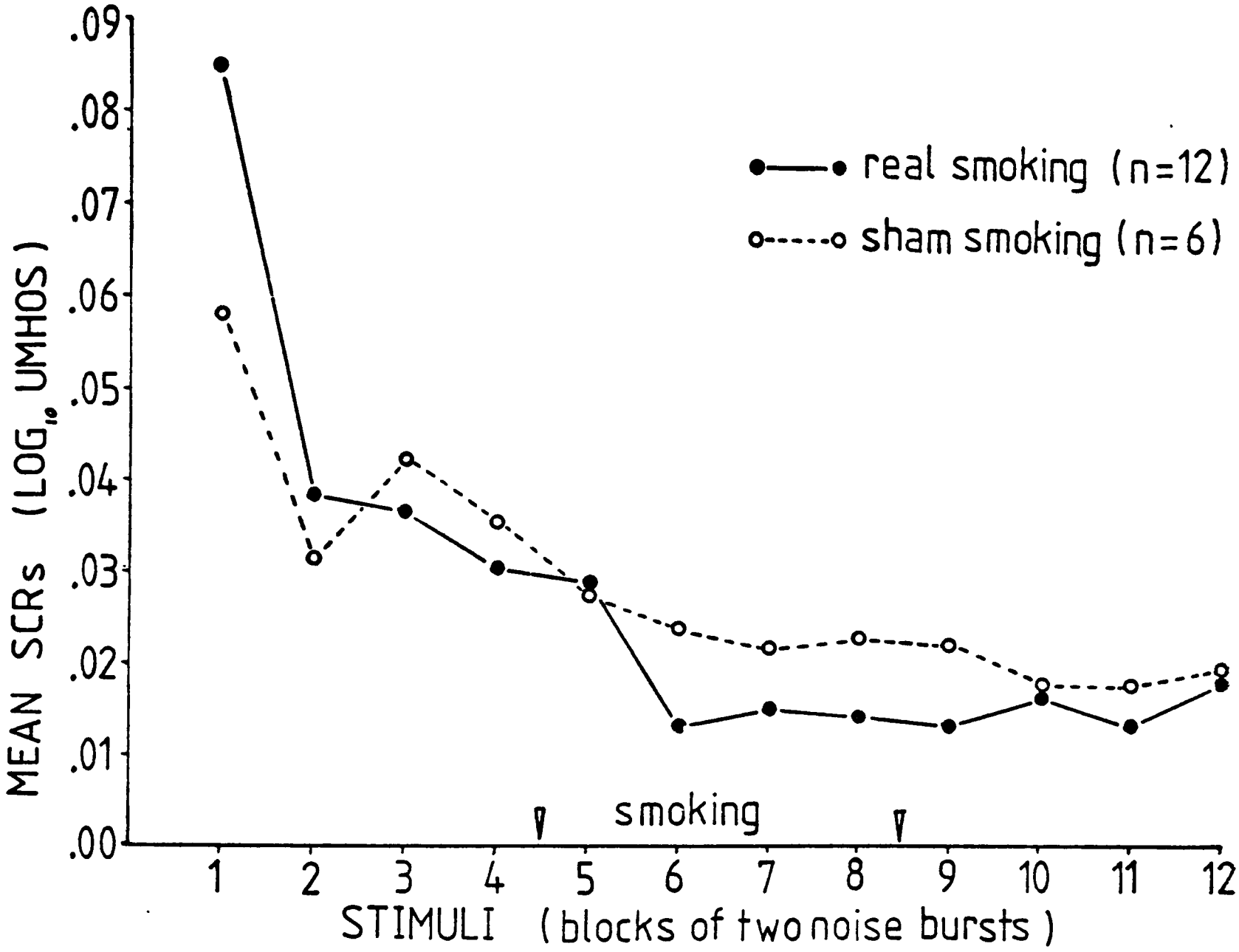


FIGURE 5 : SCRs (change $\log_{10}$ µmhos) for real and sham smoking groups to white noise bursts during stress. Stimulus number (x axis) represents blocks of two white noise bursts except for Stimulus 1 which is the initial white noise burst (i.e. initial amplitude for SCR).

TABLE 6

Mean SCRs ($\pm$ S.D.) to white noise bursts by period (PRE-SMOKING, SMOKING, POST-SMOKING) and activity (REAL and SHAM-SMOKING).

		SCRs (change in $\log_{10}$ µmhos)					
ACTIVITY	N	PRE-SMOKING STIMULI 1 - 7		SMOKING STIMULI 8 - 15		POST-SMOKING STIMULI 16 - 23	
		m	SD	m	SD	m	SD
Real Smoking	12	.0429	(.0276)	.0188	(.0181)	.0157	(.0159)
Sham Smoking	6	.0399	(.0116)	.0247	(.0084)	.0192	(.0098)

TABLE 7

Comparison of drops in SCR from baseline

(SMOKING-PRE) and (POST-PRE)

for real and sham smoking groups

Time Period Comparisons		Smoking - Pre		Post - Pre	
Group		Real Smoking	Sham Smoking	Real Smoking	Sham Smoking
N		12	6	12	6
Mean (±SD) Drop In SCR		-.0241 (±.0180)	-.0152 (±.0068)	-.0272 (±.0188)	-.0207 (±.0060)
Significance of Comparison between Real and Sham Smoking Mann-Whitney Test	z	.5620		.2810	
	P	N.S.		N.S.	

Also of interest is the relative effect of smoking versus sham-smoking on the rate of habituation of the SCR. Table 7 below compares rates of habituation of the SCR between real and sham-smoking groups for smoking and post-smoking periods as against the pre-smoking baseline SCR.

As can be seen from Table 7 and from Figure 5, while the real-smoking group habituates (SCRs) more quickly to the aversive white noise bursts than the sham-smoking group, this effect is non-significant. This result conflicts with previous reports that cigarette smoking produces a significant increase in habituation rate to tone stimuli α-blocking (Friedman et al. 1974), SCR (Mangan and Golding, Experiment 2, 1978). However, this may reflect the strength of sham-smoking as a control. Consideration of Table 17 and Figure 8 in Experiment 1 suggests that the differences between sham and real smoking are relatively small compared to control (doing nothing in the equivalent time period to real or sham smoking).

Spontaneous Fluctuations (SFs) during sensory isolation

SF data are presented in Table 8 below, and as a scattergram of pre-smoking versus post-pre smoking (see Figure 6).

Although the real-smoking group showed more SFs pre-smoking than the sham-smoking group (9.75 v. 6.00 respectively, Table 8) this difference is not significant (Mann-Whitney; n = 12,6; $\bar{z}$ = .3746; p = non-significant). Of more interest are the relative effects of real or sham smoking on SFs, as indicated by POST versus PRE comparisons. As can be seen from Table 8, SFs do not change significantly for real or sham smoking. This negative result contrasts with the previously reported significant decreases in SF rate after real smoking versus control (Mangan and Golding, 1978). It is possible that the reason for these contradictory results is a difference

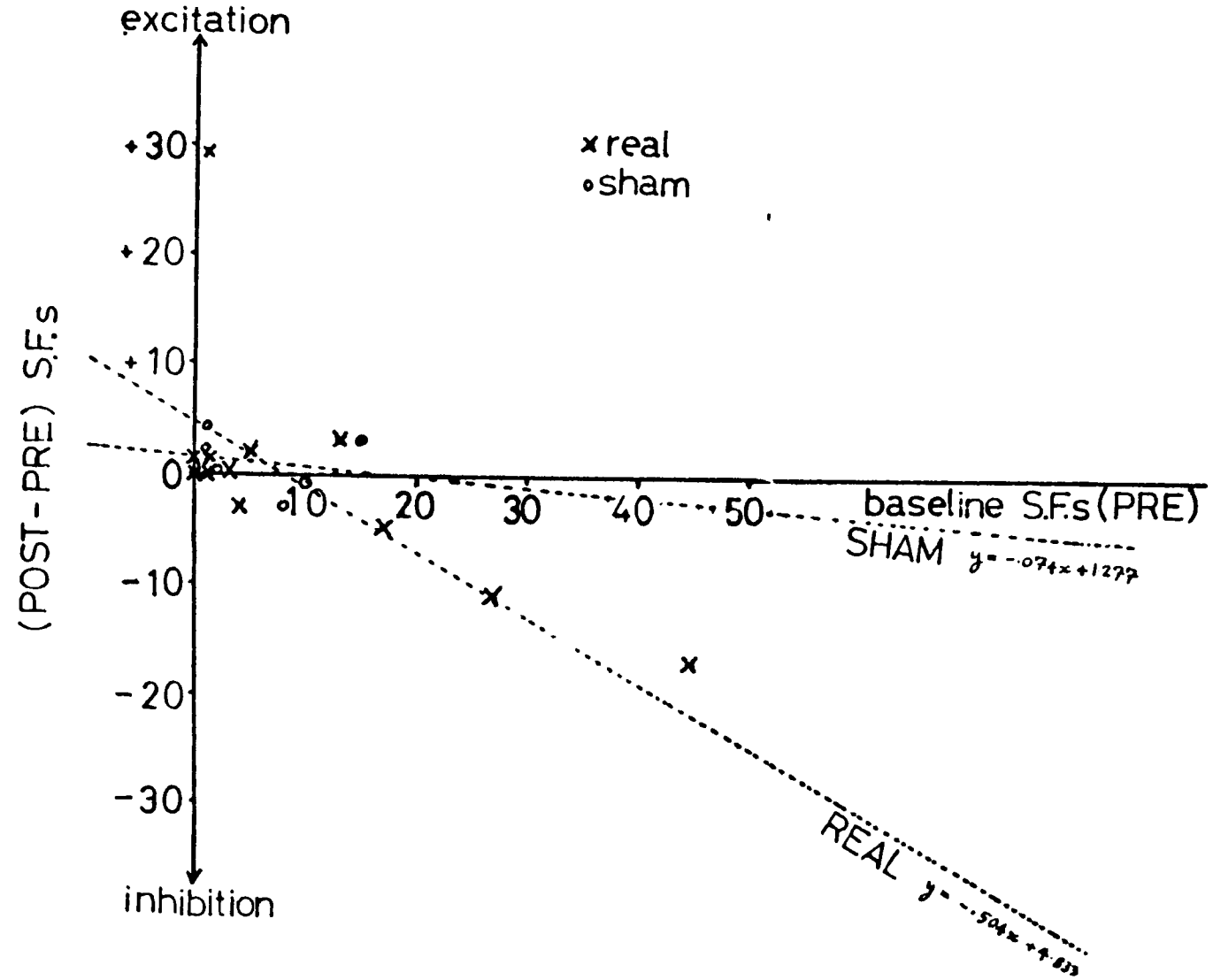


FIGURE 6 : Scattergram of PRE-smoking baseline S.F.s versus change (POST-PRE) smoking S.F.s for real (n = 12) and sham (n = 6) smoking groups during sensory isolation. Dotted lines are regression lines for SHAM and REAL.

Activity	N	SFs during sample time			P	Correlation
		PRE (mins 1-4) m (SD)	POST (mins 12-14) m (SD)	Δ POST - PRE m (SD)	Sign Test	r_p Pre X (Post-Pre)
Real Smoking	12	9.75 (±13.90)	9.67 (±10.79)	-.083 (±10.87)	N.S.	- .645 (*)
Sham Smoking	6	6.00 (± 5,93)	6.83 (± 6.08)	+.833 (± 2.64)	N.S.	- .166 (N.S.)

(r_p : * = $p < .05$)

TABLE 8

SFs (>.5K Ω) sampled during minutes 1-4 and 12-15

- PRE and POST - smoking (4 x 30sec. samples in each case) during sensory isolation

in the physiological starting state of the subject. Thus subjects in a low-arousal situation (sensory isolation) may tend to obtain stimulant rather than depressant effects from cigarette-smoking, whereas in neutral or high arousal situations (the former being true for the Mangan and Golding, 1978 study), depressant effects of cigarette smoking may predominate. This hypothesis, which is in many ways a restatement of the 'Arousal Modulation Model' of cigarette smoking, is testable. Thus, analysing the natural variation in starting state (SFs, Pre-Smoking) of subjects, it should be possible to demonstrate that smokers with very low levels of arousal (low SF rate), tend to obtain stimulant (i.e. increase in SF rate, POST-PRE) effects from smoking. Examination of PRE x (POST-PRE) correlations for SFs and the scattergram (see Table 8, Figure 6) reveals that this is the case for real, but not for sham smoking. Although consideration of Figure 6 suggests that this (significant) result is based on a skewed distribution, the result is convincing for several reasons. Firstly, re-analysis of Mangan and Golding's (1978) SF data revealed the same picture. Secondly, this result is confirmed in subsequent experiments in this thesis. Thirdly, the direction of outcome (excitation or inhibition) of many drugs usually regarded as stimulant or depressant (e.g. amphetamine, alcohol, cannabis, nitrazepram etc.) on both animals and humans is known to be strongly influenced by the pre-drug starting state of the organism (e.g. see reviews in: Domino, 1973; Gilbert, 1979; Ashton, Golding, Marsh, Millman, Rawlins, Stepney and Thompson, 1980, in press).

In the light of the evidence quoted above, it would seem reasonable to suggest that both the absence of any significant smoking-induced reduction in SF rate and the significant outcome of the 'starting state' analysis of SF rate support an Arousal Modulation Model of cigarette smoking.

EEG 'α'

EEG 'α' results are tabulated by activity, condition and time period in Table 9 and presented graphically in Figure 7a,b, and 8, for both stress, sensory isolation and combined conditions.

As expected, the effect of stress versus sensory isolation was to produce a significant reduction of alpha activity for real and sham smoking groups during the pre-smoking baseline period (cf. Table 10). Two subjects in the real smoking group showed 'paradoxical' increases in alpha activity to stress. These two aberrant responders account for the small differences in pre-smoking EEG α observed between real and sham smoking groups. These baseline EEG differences between groups are not significant when tested by Mann-Whitney U test (cf. Table 11).

Of greater interest are the effect of real and sham smoking on EEG 'α' during the stress and sensory isolation conditions. The EEG results only partially replicate those of the preceding Experiments 1 and 2. Thus, although, as in Experiments 1 and 2, real and, to a lesser extent, sham smoking caused alpha blocking, which was most conspicuous during the actual smoking period, unlike Experiments 1 and 2, there was no significant smoking-induced elevation of EEG 'α' during the stress condition (cf. Table 12 and Figure 7a).

The failure to demonstrate significant depressant effects of cigarette smoking on EEG 'α' in this experiment may be due to several factors which differed in this experiment compared to Experiments 1 and 2 - different scalp electrode placements, a large number of 'deviant' responders in the subject sample (on SCL measures), the use of a cigarette holder during smoking, subjects lying prone instead of sitting up during stress, heart rate electrodes absent. While the importance of the last

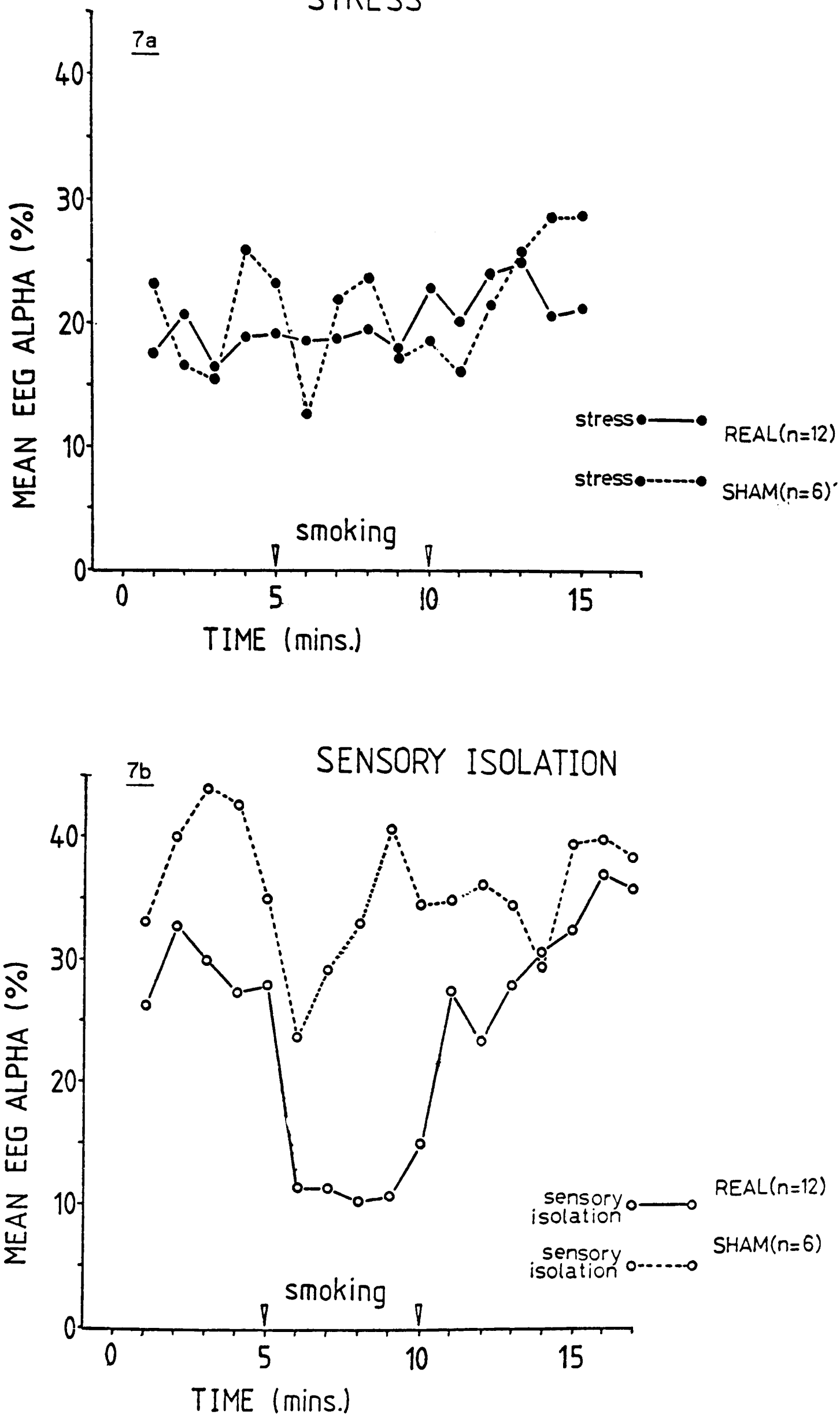


FIGURE 7a, b: Mean EEG 'α' for real smoking and sham smoking groups during (a) Stress (b) Sensory Isolation.

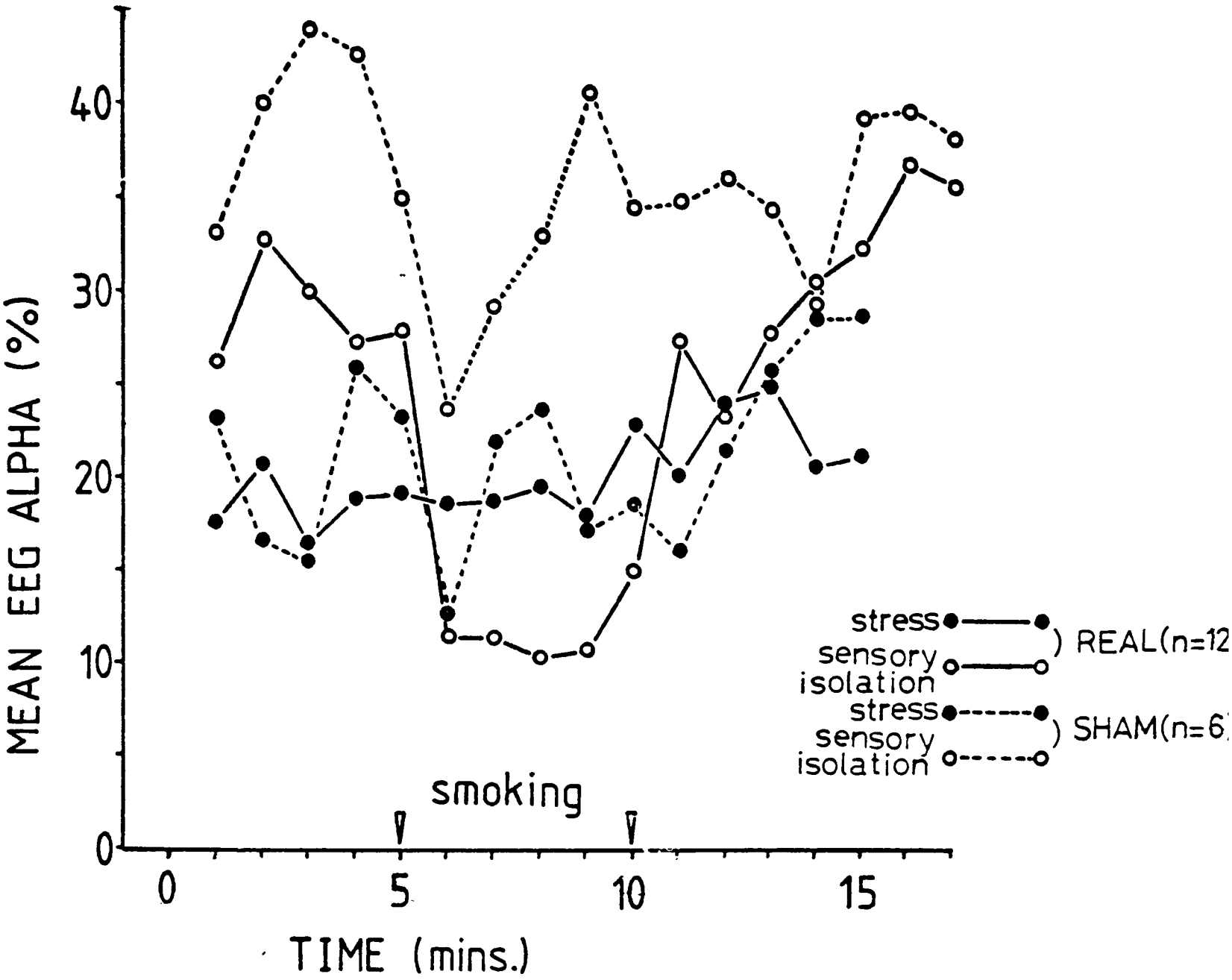


FIGURE 8 : Mean EEG 'α' for Real and Sham smoking groups during Stress and Sensory Isolation conditions (Figures 7a, 7b, superimposed)

TABLE 9

Mean EEG 'α' % by group (real smoking, sham smoking), condition (stress, sensory isolation) and time period (pre-smoking, smoking, post-smoking).

			EEG 'α' % by time period		
Group	Condition	N	Pre mins 1-5	Smoking mins 6-10	Post mins 11-15
Real Smoking	Stress	12	18.55 (12.35)	19.63 (18.58)	22.32 (24.52)
	Sensory Isolation	12	28.80 (19.78)	11.87 (6.61)	28.60 (24.97)
Sham Smoking	Stress	6	20.43 (15.48)	18.90 (16.48)	24.43 (22.52)
	Sensory Isolation	6	39.06 (27.78)	32.37 (32.10)	35.07 (26.68)

TABLE 10

Sign tests on reduction of EEG 'α' during baseline (Pre-Smoking, mins 1-5) Stress versus Sensory Isolation for Real and Sham Smoking Groups

Group	N	EEG 'α' During Baseline				Δ ST-SI	P Sign Test 1-tailed
		STRESS		SENSORY ISOLATION			
		m	SD	m	SD		
Real	12	18.55	(12.35)	28.80	(19.78)	-10.25	.019
Sham	6	20.43	(15.48)	39.06	(27.78)	-18.63	.016

TABLE 11

Mann-Whitney U for differences between

Real (n=12) and Sham (n=6) smoking groups for

EEG 'α' baselines during stress or sensory isolation in Table 10

Condition	Sham n_1 , Real n_2	$\bar{z}$	P 1-Tailed
Stress	6 , 12	0.28098	NS
Sensory Isolation	6 , 12	0.84292	NS
Δ ST-SI	6 , 12	0.65560	NS

TABLE 12

Sign Tests on Differences from Pre-Smoking Baseline in EEG 'α': Smoking-Pre, Post-Pre, by group (real smoking, sham smoking) and condition (stress, sensory isolation).

Group	Condition	N	EEG 'α' Smoking-Pre	P Sign Test 1-Tailed	EEG 'α' Post-Pre	P Sign Test 1-Tailed
Real Smoking	Stress	12	+ 1.08	N.S.	+ 3.77	N.S.
	Sensory Isolation	12	- 16.93	.019	- 0.20	N.S.
Sham Smoking	Stress	6	- 1.53	N.S.	+ 4.00	N.S.
	Sensory Isolation	6	- 6.79	N.S. (.109)	- 3.99	N.S.

three factors (cigarette holder, subject body position, absence of heart rate electrodes) cannot be completely excluded, they are arguably less critical than the first two listed above - electrode placement and the presence of deviant (SCL) responders.

Subjects were habituated to the cigarette holders for several days prior to testing, and it is difficult to believe that lying prone as opposed to sitting upright, or the absence of heart rate electrodes significantly depreciates the stressful effects of white noise, or prevents the depressant actions of cigarette smoking. In any case, should these latter factors be crucial, it would be debatable whether results obtained for cigarette smoking in the laboratory bear any relevance to the effects obtained by cigarette smoking in the real world - some people smoke through cigarette holders, often while standing up, and no cigarette smoker normally smokes with electrodes attached to his/her body. Returning to the first two possibilities, electrode position and 'deviant' subjects, both seem plausible explanations for the failure to replicate the significant smoking-induced elevations of EEG 'α' observed in Experiments 1 and 2.

Electrode position: It is possible that part of the cigarette-induced EEG 'α' elevation observed during stress for Experiments 1 and 2 could be accounted for in terms of slow eye-movement artefacts associated with the act of smoking. Since the indifferent electrode placements in Experiments 1 and 2 were frontal, it is probable that in spite of the rigorous scoring procedures carried out on the EEG records with the prime objective of eliminating any such source of error (see Methodology sections for Experiments 1 and 2), some eye-related electrical activity in the 8-13 Hz level lasting for longer than 0.5 sec. and not 'spikey', was produced by subjects and that this was scored as alpha. Such activity was probably

not scored as alpha in the present experiment, since the indifferent electrode position was further away from the eyes (see methodology section for this experiment). Provided that this source of artefact is roughly constant for cigarette smoking during both stress and sensory isolation (N.B. puffing rates are similar for both conditions) we can regard it as a constant source of error during the smoking period (mins 6-10). With this suggestion in mind, it is informative to compare the results for cigarette-induced changes in EEG 'α' during the smoking period in Experiments 2 and 3 for real-smoking groups.

Table 13 shows the net differences for changes in EEG 'α' for real-smoking during stress and sensory isolation conditions in Experiments 2 and 3. As can be seen, the effect of cigarette smoking on EEG 'α' is significantly different ($p \leqslant .001$ in each case) between conditions. Of more interest is the fact that the net differences between conditions are highly similar (they are not significantly different): 22.60 and 18.01, % alpha. Assuming that there is a constant eye-related alpha artefact due to the activity of cigarette smoking during both stress and sensory isolation conditions, we can assign it an approximate value[1] (N.B. puffing rates are very similar between conditions and experiments). This value is between_stress: {11.00 - 1.08 = 9.92} and sensory isolation: {-11.60 + 16.93 = 5.33} i.e., activity-related eye artefact alpha % ≏ + 8.0 (the higher value for stress may be due in part to the non-significant stress-induced elevation of puffing rates). Having roughly quantified an estimate of smoking-induced EEG 'α' artefact it is logical to test this value (artefact ≏ + 8% alpha for smoking) against some predictions inherent in the original calculations. The obvious example is sham-smoking. Although sham-smoking no doubt contributes some of the observed smoking-induced EEG 'α' effect by virtue of its postulated secondary reinforcing nature (e.g.

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[1] 'α' artefact value based on comparisons between Experiments 2 and 3, cf. Table 13.

TABLE 13

Comparison of cigarette smoking effects on EEG 'α' for stress and sensory isolation conditions, Experiments 2 and 3.

Experiment	N	Mean cigarette-induced changes in EEG 'α' % (Smoking-Pre)		Δ ST-SI Net difference	P Sign Test
		Stress (ST)	Sensory Isolation (SI)		
2	10	+ 11.00	- 11.60	22.60	= .001
3	12	+ 1.08	- 16.93	18.01	< .001

Hauser et al. 1958 or see Introduction) , it is perhaps more than coincidence that the value for sham-smoking induced EEG 'α' elevation during stress for Experiment 1 was +7.41 % alpha, smoke-pre (cf. Experiment 1, Table 22). although the scoring criteria for EEG 'α' were slightly different (cf. Experiment 1, Methodology), this value of +7.41 is close to the calculated artefact error: + 8% alpha. By contrast, consideration of the post-smoking period for EEG 'α' reveals little or no difference between Experiments 1, 2 and 3. This is predictable if it is assumed that eye-related alpha artefact is predominantly present during activity (i.e. raising the cigarette to the mouth, puffing, flicking ash).

It is, however, important to put this finding into perspective. Thus, there is no evidence that cigarette smoking further augments EEG arousal during *stress* , and although the present result does not show positive depressant EEG effects of cigarette smoking during stress (for 7 subjects out of 12, an increase of EEG 'α' was observed while real-smoking during stress), comparison between stress and sensory isolation conditions of cigarette smoking effects reveals a highly significant difference ($p < .001$, Table 13).

EMG: Tonic Activity. Tonic EMG data are presented graphically (Figure 9) and in Table 14 for both real and sham smoking groups during stress and sensory isolation conditions by time period. Only data for forearm extensor muscle are presented, since rectus abdominus tonic EMG activity was too low to make reliable observations of the effects of cigarette smoking.

White noise stress produces an elevation in forearm extensor muscle activity. However, this stress induced elevation of EMG activity is only significant for the real-smoking group (cf. Table 15).

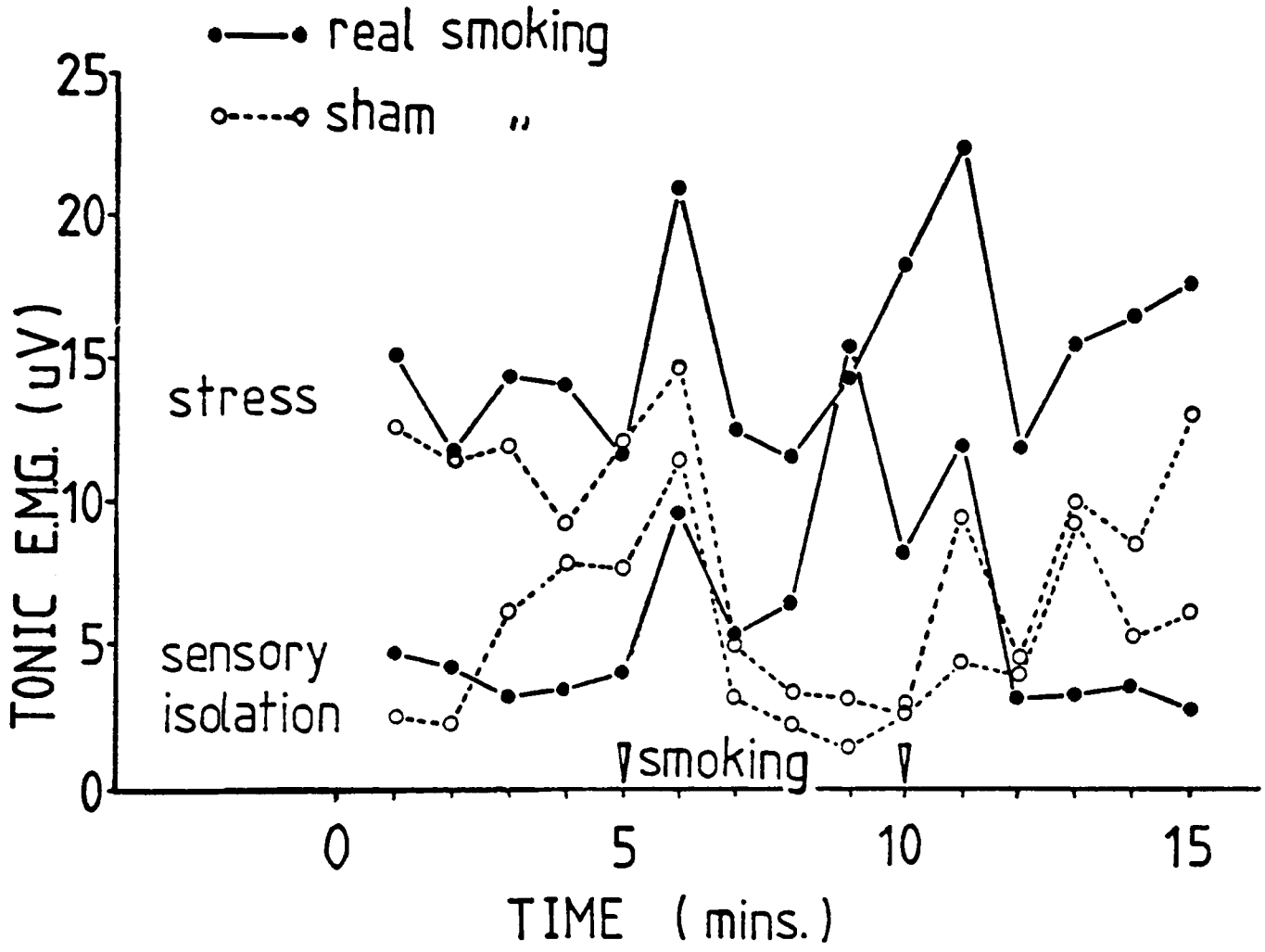


FIGURE 9 : Tonic EMG (forearm extensor muscle) for Real smoking (n = 6) and Sham smoking (n = 6) groups during Stress and Sensory Isolation conditions.

TABLE 14

Mean tonic forearm extensor muscle EMG activity (μV)
for real and sham smoking groups during
stress and sensory isolation conditions by time period

			EMG (μV) Forearm Extensor					
Group	Condition	N	Pre mins 1-5 m	(SD)	Smoking mins 6-10 m	(SD)	Post mins 11-15 m	(SD)
Real Smoking	Stress	6	13.55	(7.22)	15.80	(16.33)	17.04	(20.50)
	Sensory Isolation	6	4.04	(2.91)	9.08	(11.88)	4.98	(3.24)
Sham Smoking	Stress	6	11.61	(14.26)	5.93	(6.53)	9.32	(13.12)
	Sensory Isolation	6	5.23	(5.62)	4.32	(3.14)	5.86	(7.34)

TABLE 15

Stress-induced elevation of baseline tonic EMG activity

Group	N	Baseline tonic EMG (μV) (mins 1-5)		Δ ST-SI	P 1-Tailed Sign Test
		STRESS m (SD)	SENSORY ISOLATION m (SD)		
Real Smoking	6	13.55 (7.22)	4.04 (2.91)	+ 9.51	.016
Sham Smoking	6	11.61 (14.26)	5.23 (5.62)	+ 6.38	N.S.

Comparison of baseline tonic EMG between real and sham smoking groups reveals no significant difference (Mann-Whitney U test; n_1, n_2 = 6,6; p = non-significant). Thus the differences in tonic EMG between real and sham smoking groups is probably a random sampling effect due to small group sizes (n_1, n_2 = 6,6). An alternative explanation for the (non-significant) greater stress-induced tonic EMG of the real smoking group may be that the real-smoking group was more extraverted (cf. 'Personality and Smoking Habits' section), and could be predicted to respond differentially to stress in the EMG system as opposed to autonomic nervous system.[2] The effects of real and sham smoking are presented in Table 16.

Although it would appear that real-smoking as opposed to sham-smoking elevates tonic EMG irrespective of condition (cf. Table 16), none of the comparisons are statistically significant (Mann-Whitney U tests on sham versus real comparisons are non-significant also). This is perhaps due to the small sizes of groups (n_1, n_2 = 6,6) and the great individual differences in tonic EMG (response stereotypy as discussed earlier). Nevertheless, in general terms, the trend of the data supports the view that real as opposed to sham cigarette smoking increases tonic EMG and thus levels some support to Fagerström and Götestam's (1977) report that cigarette smoking elevates (trapezius) muscle (N.B. cigarette smoking during sensory isolation elevates tonic EMG to a marginally significant extent, $p < .109$, cf. Table 16). This stimulant EMG effect, although non-significant, is all the more convincing upon close consideration of

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[2] Barrell and Price (1977) report that subjects respond differentially to shock stress in the EMG (trapezius) as opposed to autonomic (heart rate) system depending on whether they are 'confronters' or 'avoiders' respectively on questionnaire self-report. This 'confronter-avoider' personality dimension is similar conceptually to a 'flight-flight' dimension thought to underly (Gray, 1971) 'extraversion-introversion' (N.B. While the more extraverted real-smoking group was more reactive to stress on tonic EMG it was less reactive to stress than the introverted sham-smoking group on tonic SCL, an autonomic measure [cf. SCL results]).

Group	N	Condition	EMG (μV) Pre (mins 1-5)	EMG Δ Smoke (mins 6-10) − Pre (mins 1-5)	P Sign Test 1-Tailed	EMG Δ Post (mins 11-15) − Pre (mins 1-5)	P Sign Test 1-Tailed
Real Smoking	6	Stress	13.55	+ 1.25	N.S.	+ 3.49	N.S.
	6	Sensory Isolation	4.04	+ 5.04	N.S.(.109)	+ 0.94	N.S.(.109)
Sham Smoking	6	Stress	11.61	- 5.68	N.S.	- 1.29	N.S.
	6	Sensory Isolation	5.23	- 0.91	N.S.	+ .63	N.S.

TABLE 16

Effects of real and sham smoking on tonic EMG (forearm extensor) during stress and sensory isolation conditions

of Figure 9. Note that the initiation of both real and sham smoking produces bursts of irrelevant muscle activity (min. 6, Figure 9). Hence, given that the physical activity of smoking produces some irrelevant EMG activity, and that the puffing rate (although not puff pressure) is higher for sham as opposed to real smoking (cf. Smoking Style Results) it is possible that the physical activity of smoking is obscuring to some extent any differences between real and shal smoking due to nicotine. Against this it is of course necessary to balance the earlier observation that the real-smoking group appears to be (non-significantly) more reactive in the EMG system.

EMG - phasic reactions to white noise bursts

Phasic EMG responses to white noise bursts are presented graphically (Figure 10) and as means by activity and time period (Table 17). Only forearm extensor muscle EMGs are presented. (N.B. Habituation of EMG responses recorded from Rectus Abdominus [lower stomach] electrodes sites, to white noise stimuli, was extremely rapid, mean response being 10% of maximum EMG response by stimulus number 5, all subjects showing complete habituation after stimulus number 10. Two subjects out of these six showed a small return of EMG responding at the Rectus Abdominus site for stimuli 18-23.)

Consideration of Figure 10 and Table 17 reveals that habituation, of the forearm extensor EMG response to successive stimuli, occurs. The habituation of the EMG response shows a similar profile to that for the habituation of SCR (cf. Figure 5); an initial rapid decline after stimulus number one followed by a slower phase of habituation for stimuli 2-23. However, considerable individual differences obviate any simple relationship between SCR and phasic EMG responses to white noise stimuli. While some individuals show a parallel habituation of SCR and phasic EMG

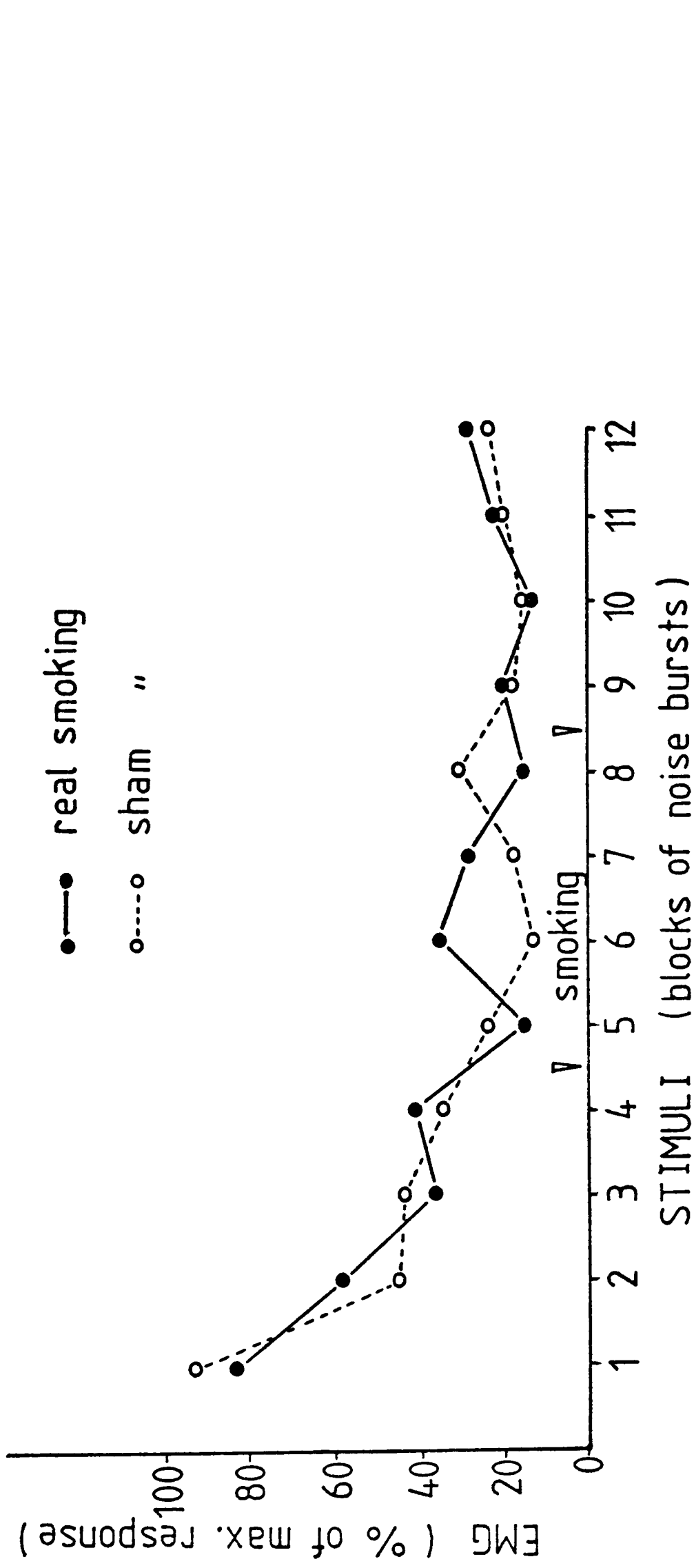


FIGURE 10 : Phasic EMG responses (forearm extensor muscle) to blocks of white noise stimuli, for Real (n = 6) and Sham (n = 6) groups.

Group	N	Forearm Extensor EMG response to stimuli (% maximum)			P Sign Test 1-Tailed	
		PRE Stimuli 1-7	SMOKING Stimuli 8-15	POST Stimuli 16-23	Smoking - Pre	Post - Pre
		m SD	m SD	m SD		
Real Smoking	6	54.57 (29.14)	27.75 (29.06)	20.08 (18.10)	.016	.016
Sham Smoking	6	49.18 (21.17)	20.32 (29.67)	19.53 (29.07)	NS (.109)	NS(.109)

TABLE 17

Mean Phasic EMG responses (% of maximum EMG response) to white noise stimuli for real and sham smoking groups by time period

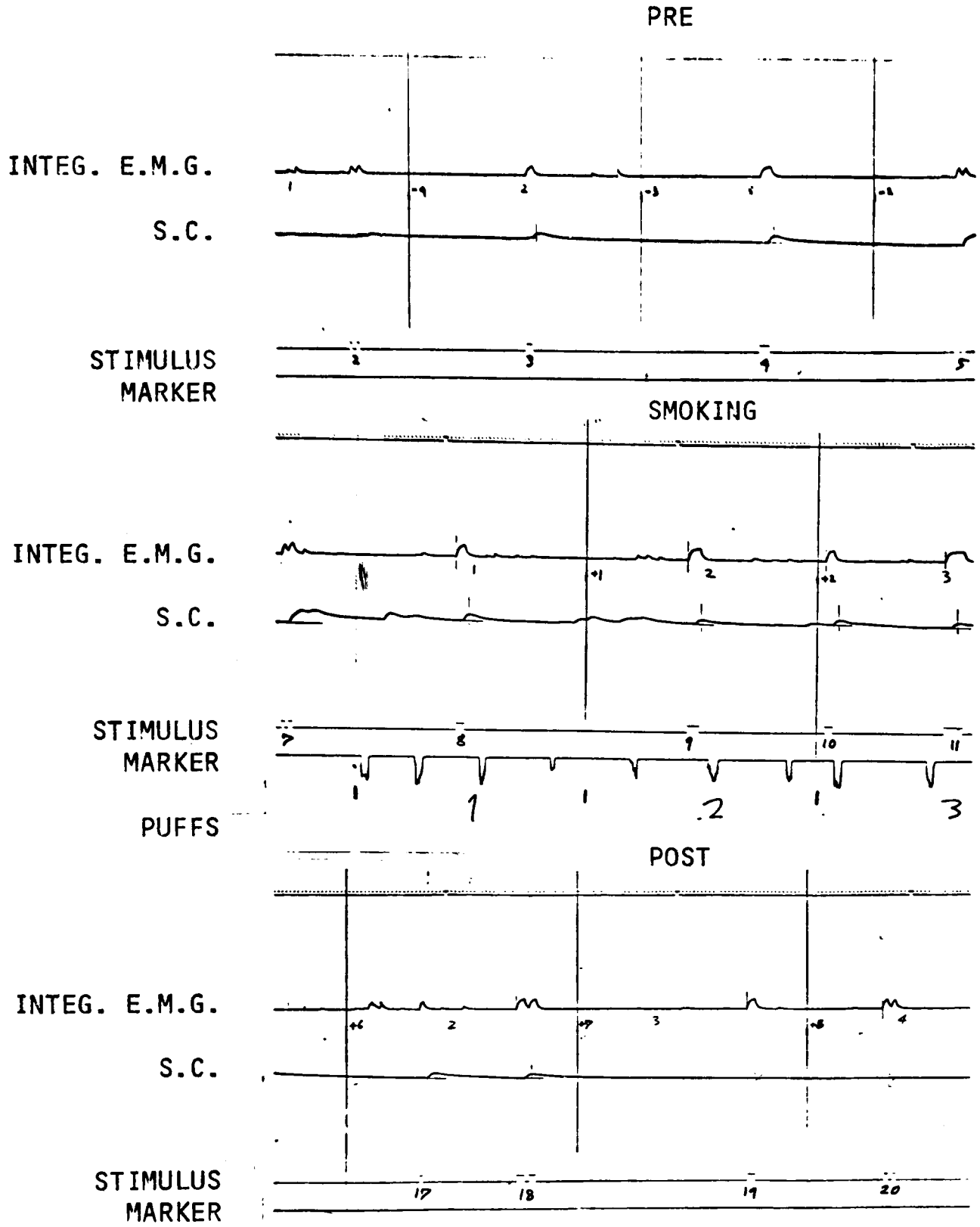


FIGURE 11 : Subject TP sham smoked during stress condition. Response modalities and time period are shown. Note that after noise stimulus number 18 SCR has habituated completely but phasic EMG reactions to noise stimulus continue undiminished. This is an example of response stereotypy, and unusual in that EMG habituates more rapidly than SCR in most subjects.

responding, other subjects respond differentially in these two systems (cf. later Discussion section & Figure 11).

Real cigarette smoking as opposed to sham-smoking does not lead to a significantly faster rate of EMG habituation (Mann-Whitney U test, Real versus Sham EMG, n_1, n_2 = 6,6; p = non significant for Smoking-Pre and Post-Pre comparisons). However, consideration of Table 17, in which the real and sham groups are analysed separately, reveals that the drop (Smoking-Pre, Post-Pre) in EMG responding is significant for the real smoking group (p = .016) but only of marginal significance for the sham smoking group (p = .109). To this extent, the EMG data are congruent with studies on other muscle groups that nicotine and real cigarette smoking, as opposed to placebo and herbal cigarette smoking, produce significant reductions in patellar reflex and stress-induced massetter muscle contractions (Domino, 1973; Hutchinson and Emley, 1973).

A POST-HOC ANALYSIS OF DEVIANT RESPONDERS

As mentioned in the SCL results section there appears to be some consistency amongst deviant responders; subjects aberrant on one response also tended to be aberrant on other responses. In attempting to systematise this observation for both SCL and EEG results, the following distinctions were made.

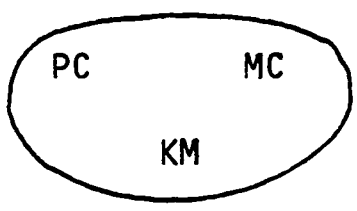
(i) 'Deviants' are defined as subjects who showed physiological responses to experimental manipulations (i.e. the effects of stress versus sensory isolation or of real and sham smoking) against the 'expected direction'.

(ii) The 'expected direction' is defined as the direction (increase or decrease) of movement of the physiological variable in response to the experimental manipulation which has achieved significance

in Experiments 1, and 2. Thus SFs and EMG are excluded (not scored in Experiments 1 and 2); as are SCRs since for each subject SCRs move in only one direction i.e. habituate to a greater or less degree. Similarly, excluded on the basis of failing to achieve significance in Experiments 1 and 2 are respiration rate changes to condition (stress versus sensory isolation) or smoking (real or sham); heart rate was not recorded.

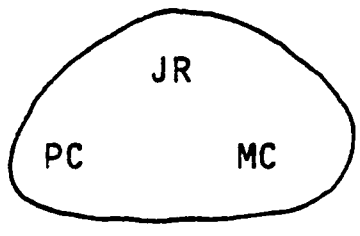
In the following diagrams the results of selecting out deviants on the above criteria are shown. Subjects are represented by their initials. Both real (n = 12) and sham (n = 6) smoking groups are included. Subjects from the sham smoking group have their initials following by an asterisk.

STEP 1 The set of subjects who showed <u>drops</u> in baseline SCL to stress cf. sensory isolation.



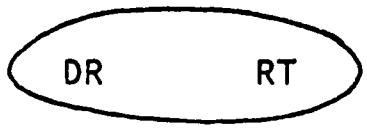
deviant n = 3
residual n = 15

STEP 2 The set of subjects who showed <u>drops</u> in SCL during the real or sham smoking period for the sensory isolation condition.



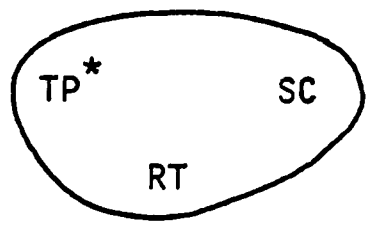
deviant n = 3
residual n = 15

STEP 3 The set of subjects who showed <u>increases</u> in baseline EEG 'α' during stress versus sensory isolation.



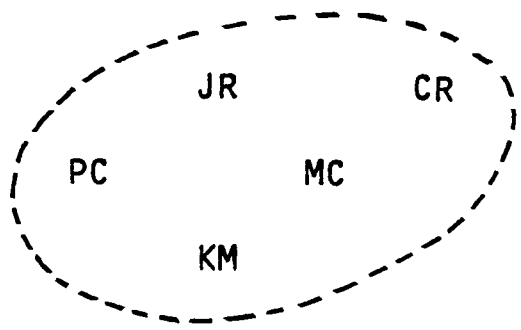
deviant n = 2
residual n = 16

STEP 4 The set of subjects who showed <u>increases</u> in EEG 'α' during the real or sham smoking period for the sensory isolation period.



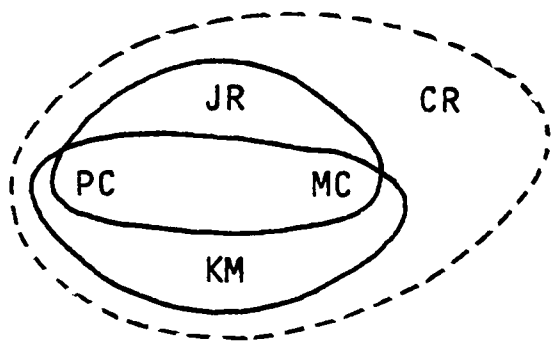
deviant n = 3
residual n = 15

STEP 5 The set of subjects who *show* <u>decreases</u> in EEG 'α' during the real-smoking period for the stress condition. (N.B. the sham smoking group is not included since the effects of sham smoking were not significant on this result for Experiment 1).



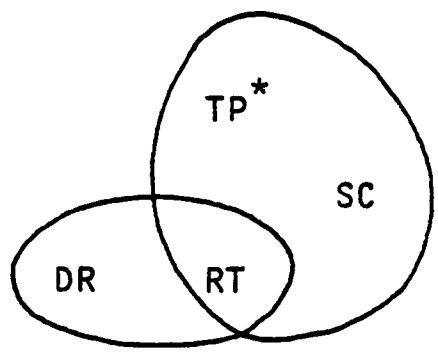
deviant n = 5
residual n = 7 (real group)
residual n = 13 (all)

STEP 6 Superimposed sets 1-5 with residue subjects.



(sham)	(real)
SJ*	MH
MS*	MO
WM*	AO
RC*	MJ
SL*	

deviant n = 9
residual n = 9



The superimposed sets demonstrate several properties:

i) More deviants appear to be present in the real smoking group (see Step 6), even allowing for the fact that the real smoking group is twice the size of the sham smoking group (n = 12, 6), and for the fact that Step 5 is applicable to real smokers only (Step 5 only adds one more deviant: subject CR). A personality theorist might be tempted to explain this result on the basis that the sham smoking group was significantly more introverted (Eysenck [1975] "E") than the real smoking

group (see Personality and Smoking Habits Results[3]). There is evidence (e.g. Eysenck, 1977) that introverts are more susceptible to the arousing properties of external stimuli, which in this case are white noise bursts during the stress condition and real or sham smoking. Consequently it might be argued that, since all deviants (apart from CR, see Step 5) in this analysis are defined in terms of their showing depressant responses to external stimulation, which apply to both real and sham groups (i.e. increases of baseline EEG 'α' to stress, increases of EEG 'α' from baseline to real or sham smoking during sensory isolation, decreases of baseline SCL to stress, decreases of SCL from baseline to real or sham smoking; Steps 1 - 4) one might reasonably expect deviants to be more extraverted. Thus extraverts, being less sensitive than introverts to the arousing effects of stress or real and sham smoking during sensory isolation, are more likely to show deviant responses. Since the real smoking group is significantly more extraverted than the sham smoking group it might be predicted that more deviants will appear in the real smoking group - as observed. (N.B. Although at first sight this argument seems convincing, a closer look at the extraversion data contradicts the hypothesis that deviant responding is associated with high extraversion scores. Table 18 gives the mean extraversion scores for 'deviants' [on any response - Step 6] and 'normals'. Thus deviants are not more extraverted than normals - the reverse is more *true*). However, the EPQ scores of deviants reveal that they are 'odd' in a special sense, namely, that, while appearing no different from normals on any particular personality score, they appear to contain many extreme scores (this was also noted in Experiment 2) (e.g. JR, N = 21; SC, E = 21; MC, P = 15, etc.). The implication of

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[3] The only self-report measure on which the sham versus real smoking group differed significantly was extraversion (E = 14.50 (±5.04) REAL, 8.50 (±5.21) SHAM; p = .0122).

this in terms of Eysenck's personality theory is unclear.

ii) There seems to be some evidence that EEG 'α' deviants (lower group, Step 6) form a group independent of SCL deviants (upper group, Step 6). This is congruent with the notion that EEG and electrodermal response systems are, to a degree, independent (see Experiment 1: 'Intercorrelations between Electrodermal and EEG Measures').

iii) Despite such independence the set of five deviants who showed decreases in EEG 'α' during the real-smoking period for the stress condition (Step 5) includes all four SCL deviants (upper group, Step 6). Given the earlier evidence that EEG and electrodermal systems are only partially linked this finding is curious. It might be expected that these five deviants would include the set of EEG deviants (lower group, Step 6) rather than electrodermal deviants (upper group, Step 6). However, it is also clear that these five subjects who showed decreases in EEG 'α' to smoking during stress (i.e. smoking causing a further increase in EEG arousal during the highly [EEG] arousing stress condition) are significantly less aroused (SCL) by stress versus sensory isolation or cigarette smoking during sensory isolation, whether compared to the remaining seven members of the real smoking group, or all other subjects (n = 13) (see Table 19).

Thus, the subjects who tended to show (significant) paradoxical decreases in SCL arousal[4] to the effects of stimulation, appeared more aroused (EEG 'α') by cigarette smoking during stress. This significant result on deviant SCL responders in part accounts for the negative result in this experiment as regards the postulated relaxing (EEG 'α') effects of cigarette smoking during stress. The alternative explanation

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[4] One EEG deviant subject - CR - showed normal SCL responses, see Step 6.

TABLE 18

GROUP	N	Extraversion	
		m	SD
Deviants (any response)	9	11.77	(5.33)
Normals	9	13.22	(6.34)

TABLE 19

Comparison of deviant and non-deviant EEG responders to real cigarette smoking during stress for baseline (pre-smoking) SCL changes to stress versus sensory isolation (Δ_{ST-SI}) and to changes in SCL to real or sham cigarette smoking during sensory isolation ($\Delta_{Smoking-Pre}$)

	DEVIANTS		NON-DEVIANTS			
	Real-Smokers		Real-Smokers		Sham-Smokers	
N	5		7		6	
	m	SD	m	SD	m	SD
Δ SCL ST-SI log µmhos	+.031	(.124)	+.199	(.181)	+.091	(.073)
Δ SCL Smoke-Pre log µmhos	+.002	(.069)	+.101	(.066)	+.043	(.034)

MANN-WHITNEY TEST	DEVIANTS versus NON-DEVIANTS					
	Real Smokers versus Real Smokers			Real Smokers versus All		
	n	z	P	n	z	P
Δ SCL ST-SI log µmhos	5, 7	2.030	.0212	5, 13	1.922	.0274
Δ SCL Smoke-Pre log µmhos	5, 7	2.030	.0212	5, 13	1.922	.0274

as mentioned earlier is, of course, that the scalp electrode placements differed in this experiment compared to Experiments 1 and 2.

General Discussion

The battery of smoking style measures (tobacco burnt, puff rate, puff duration and puff pressure) supported the view that subjects were attempting to obtain more nicotine/tar from their cigarettes during stress as opposed to sensory isolation. As predicted from Experiments 1 and 2, the critical smoking style variable, by which subjects obtained larger (i.e. hypothesised to be depressant) doses of nicotine during stress, was puff pressure as opposed to puff rate and puff duration. It may be speculated that manipulation of puff rate and puff duration by the smoker would be an inefficient means of obtaining large (depressant) doses of nicotine during stress. Thus simply increasing puff rate, while no doubt leading to increased nicotine extraction from the cigarette and consequently higher blood nicotine levels,may not lead to depressant action of nicotine. This is because nicotine arrives at the brain in the form of a series of nicotine-rich blood 'boli ' for inhalation-style smoking (Russell, 1976). A large number of low-nicotine boli (i.e. from increasing puff rate) while in absolute terms being equivalent to a small number of high-nicotine boli (i.e. from increasing puff pressure) may not produce depressant CNS effects since brain nicotine as opposed to blood nicotine levels achieved may be too low, due to pharmacokinetics (cf. Stalhandshake, 1970). This view is supported by the observation that when the same total dose of nicotine is injected into rats over the same time period, the effects are stimulant or depressant (as measured by cortical activity and ACh release) depending on whether the nicotine is presented as a large number of small doses or as a few large doses, respectively (Armitage et al., 1968).

It is more difficult to explain why increase in puff duration should not be a satisfactory means by which smokers could obtain depressant doses of nicotine. It may be simply that a short intense puff is a more efficient means of extracting a high dose of nicotine from a cigarette than a long low pressure puff. The extra volume of smoke necessary to produce the same quantity of nicotine for a single puff may be unacceptably large by the latter means. The temperature of the burning core of tobacco to produce efficient volatilisation of nicotine and the condensation rate along the tobacco rod may be important factors here; there is evidence that the concentration of nicotine and the ratio of nicotine to other smoke constituents is greater for higher puff pressure (Thornton, British American Tobacco Group Research and Development, Southampton, personal communication).

The extent to which these laboratory observations are generalisable to smoking in the real world is debatable. Factors such as total time spent smoking a cigarette and inhalation of all the smoke from each puff, which were controlled in the present studies, may be of importance. So too may be the relative artificiality of the laboratory environment; small but significant elevations of puffing rate in laboratory smoking compared with surreptitiously observed smoking, outside the laboratory environment, have been noted (Comer and Creighton, 1978). However, it may be noted, at least in general terms, that the absolute puffing rate, puff duration and the decline in smoking vigour (as indexed by minute by minute analysis of puff rate, duration, pressure) over the course of smoking a single cigarette, bear a close resemblance to those observed surreptitiously (Comer and Creighton, 1978; Schulz and Seehofer, 1978). This would seem to imply that laboratory smoking is a fair approximation of smoking in the real world. This is perhaps unsurprising given the

extreme 'robustness' of smoking behaviour as reflected in the highly significant and positive correlations between stress and sensory isolation conditions for individuals' real and sham smoking styles, and indeed by the close similarity between real and sham smoking style overall (cf. Figure 3 , Table 2).

There are two possible sorts of explanations for the highly idiosyncratic manner in which an individual smokes a cigarette. Both of these explanations may be correct. Firstly, individual differences in sensitivity to nicotine (i.e. receptor sensitivity, metabolic rate, body weight, etc.) together with differences in characteristic arousal state (i.e. trait anxiety, extraversion, etc.) may impose fairly narrow limits on the type of smoking behaviour which would lead to the deposition of an 'optimal' dose of nicotine in an individual smoker's CNS. There is indeed some evidence for this suggestion (Ashton et al., 1974). Secondly, it is possible that idiosyncracies in smoking style are produced by chance reinforcement, i.e. they are non-functional in the analogous sense, for eating behaviour, that one individual may prefer to eat his food with a fork, another with a spoon and yet another might insist on chop-sticks. Similarly, one person may gobble his food, another may eat in a leisurely fashion. This type of non-functional idiosyncratic behaviour, often called - 'superstitious behaviour' - is also observed in the operant conditioning of animals. Idiosyncratic ways of pressing a lever for reward may be accidentally reinforced by the experimenter. For example, a rat may become 'convinced' after only a few trials, that it is necessary to circle around and press only with the left paw to obtain reward, whereas the only necessary operant response, to obtain reward, is any lever press.

In the present case - cigarette smoking behaviour - where the presumed reinforcer is the arrival of nicotine at CNS receptors, the only

necessary response for nicotine reinforcement is some degree of smoke inhalation. To prove definitely that the idiosyncracies of smoking behaviour are functional, it would be neccessary to force subjects to adopt different smoking styles on the same nicotine delivery cigarettes and observe whether or not these new patterns of behaviour become fixed. The evidence from studies (e.g. Russell, Sutton, Feyerabend and Cole, 1978) in which cigarette nicotine delivery is varied, or nicotine is provided by some other route, would suggest that some degree of self-titration for nicotine occurs, as reflected in compensatory variations in smoking behaviour. However, it should be noted that this type of evidence only lends inferential support to the view that the idiosyncracies of smoking style are functional in terms of providing an 'optimal' dose of nicotine for a particular individual.

The psychophysiological effects of cigarette smoking in the present experiment appear to be broadly compatible to those observed in Experiments 1 and 2. Cigarette smoking and to a lesser extent sham-smoking produced stimulant effects during sensory isolation as indicated by rise in SCL and decrease in EEG alpha activity. Similarly, two other measures, SFs and tonic EMG, not included in Experiments 1 and 2 indicated that cigarette smoking produced stimulant effects during sensory isolation. By contrast, cigarette smoking during stress did not produce significant stimulant effects on SCL, tonic EMG, or EEG alpha whether compared to pre-smoking baselines or sham smoking. However, cigarette smoking, compared to sham smoking, did not significantly increase the rate of habituation of SCR and phasic EMG response to white noise stimuli. Thus the evidence that cigarette smoking produces depressant effects for tonic and phasic responding during stress is less clear-cut than in Experiments 1 and 2. This may have been due, in part, to the inclusion of a number

of 'aberrant' responders in the subject sample (as discussed earlier). These aberrant subjects appeared to respond paradoxically to the effects of stress by reducing autonomic and EEG arousal.

In summary, cigarette smoking produced stimulant effects during sensory isolation and mixed depressant and stimulant effects during stress. There was some evidence that individual differences in starting state arousal determined the direction of cigarette smoking effect during both sensory isolation and stress conditions. These starting state effects are compatible with an Arousal Modulation Model of cigarette smoking and suggest that individual differences may provide a profitable avenue of investigation.

Boredom, bōr'dum, n. the domain of bores, who weary one.

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E X P E R I M E N T 4

CIGARETTE SMOKING DURING 'MILD BOREDOM'

Rationale

The aims of this experiment were threefold:

I Firstly to study the effects of cigarette smoking in a range of arousal intermediate between that of 'Stress' and 'Mild Sensory Isolation'.

II Secondly to assess the reliability of the behavioural and psycho-physiological measures by experimental repetition with the same subjects.

III Thirdly to improve controls by separately examining the psycho-physiological effects of inhalation per se.

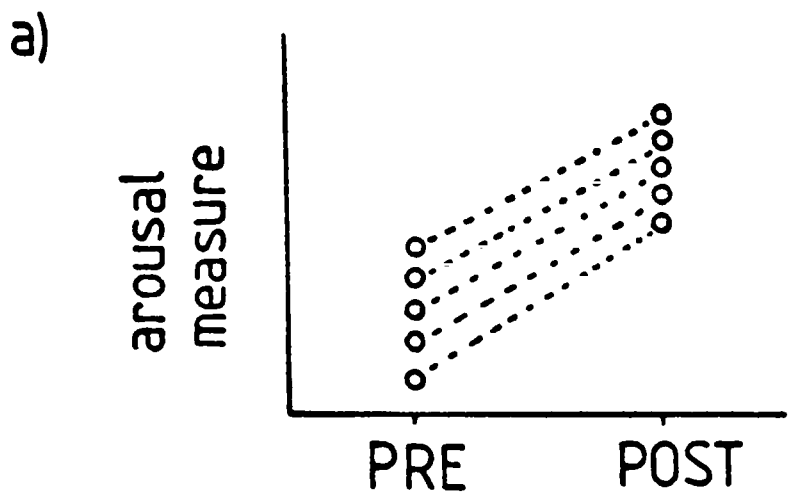
I In Experiments 1, 2 and 3, two arousal extremes were used - 'Mild Sensory Isolation' and "White Noise' situations of underarousal/ drowsiness and aversive overarousal respectively. However, the majority of situation in which cigarette smoking occurs are more commonly in intermediate arousal states. One such example corresponds to the real life situations of mild boredom. The situation, in other words, during which people smoke because they have nothing better to do, e.g., sitting in a station waiting room, waiting for a bus, standing in a dole queue, listening to a tiresome speaker, etc. Of course, once an alternative activity is presented the situation of boredom no longer exists, e.g.,

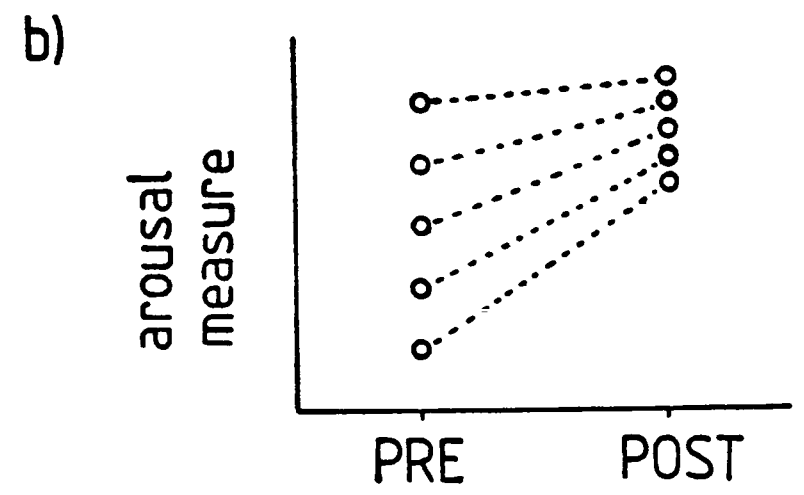
investigating or complaining about the non-arrival of transport, conversing *with* fellow passengers, reading a novel or newspaper, day dreaming or simply falling asleep. Perhaps cigarette smoking represents a convenient way of alleviating boredom with minimal effort on the part of the smoker.

In this "intermediate arousal" situation it was hypothesised that the starting states of subjects would be normally distributed, reflecting a distribution of arousal states both <u>below</u> a hypothetical optimum, i.e., verging towards drowsiness and <u>above</u> a hypothetical 'optimum', i.e., verging towards anxiety or irritability. It was hypothesised that cigarette smoking in such a situation would be reinforcing by virtue of its ability to lower the arousal of individuals who were slightly overaroused (i.e., calming the anxious or irritable smoker) and conversely to raise the arousal of under-aroused individuals (i.e., stimulating the drowsy smoker). This is analogous to the postulated reinforcing nature of smoking in Experiments 1, 2 and 3: the extremes of under and over-arousal, produced by the experimental conditions of sensory isolation and white noise respectively, corresponding to the natural variation of arousal between individuals in a 'neutral' experimental condition.

Several possible outcomes for the effects of cigarette smoking in this situation may be envisaged (cf. Figure 1). Assuming that cigarette smoking does have a significant effect, possible outcomes are listed below (with respect to Figure 1).

a) The simplest outcome; cigarette smoking significantly raises (or lowers) physiological responding irrespective of the pre-smoking baselines. Sign test is significant, Post x (Post-Pre) correlations and F ratio are





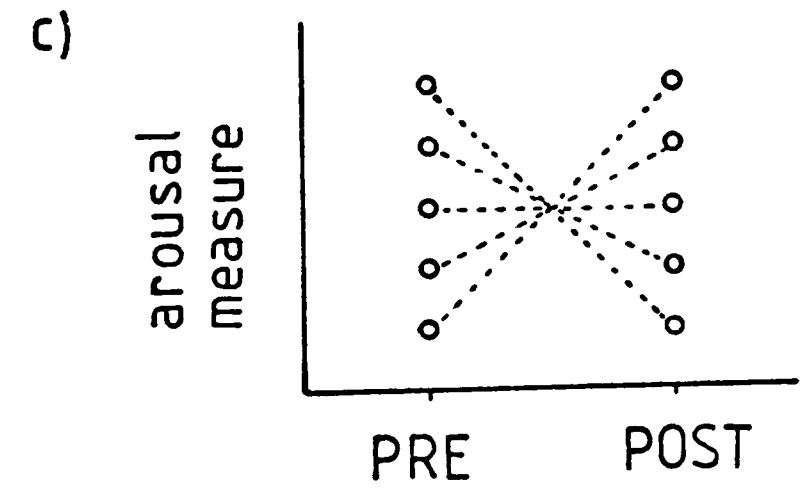


FIGURE 1 : Possible types of effects of cigarette smoking on a measure of physiological arousal. Individuals' arousal levels are shown as circles PRE and POST smoking, joined by dotted lines. For details see text.

not significant.

b) Cigarette smoking may or may not significantly raise (or lower) physiological responding depending on the level of the pre-smoking baselines. This is analogous to the 'Law of Initial Values'. Sign test may or may not be significant, Post x (Post-Pre) correlations and F ratio are significant.

c) Cigarette smoking does not significantly effect either the mean or variance of the physiological response measure. However, the magnitude and direction of smoking effect is determined by the pre-smoking baseline. Post x (Post-Pre) correlations are significant and negative.

In addition to the three main possible outcomes listed above, 'mixed' outcomes are possible, e.g., one could envisage an outcome where cigarette smoking produces no change in variance but significant negative Pre x (Post-Pre) correlations and significant sign tests. This would be a combination of examples (a) and (c) above.

Further complications of analysis may be caused by other factors such as interactions of drug effect with personality, previous drug usage, self-titration for the drug by the user, etc. (Ashton et al. 1980 in press). Selected examples of this type of effect are given later (see 'Starting State Effects').

II In order to assess the reliability of the physiological starting state of subjects in the laboratory situation, the experiment was repeated twice for each subject. Pre-smoking baselines were examined in two ways: (i) within sessions, i.e., pre sham-smoking versus pre real-smoking (ii) between sessions, i.e., pre real-smoking (first session) versus pre real-smoking (second session), and pre sham-smoking (first

session) versus pre sham-smoking (second session).

Three types of comparison were carried out. Sign test and F ratio to determine if the means and variance of the pre-smoking baselines had changed significantly. Correlations to determine if the pre-smoking baselines had remained significantly unchanged. While the two former comparisons are negative proofs of baseline stability, the latter comparison is a positive proof of baseline reliability.

Similarly the reliability of smoking effect was assessed by means of (post-Pre) x (Post-Pre) correlations. These were carried out both within sessions $real_1$ x $sham_1$, $real_2$ x $sham_2$ and also between sessions for $real_1$ x $real_2$, $sham_1$ x $sham_2$, smoking effects (subscripts refer to $first\ session_1$, and $second\ session_2$, respectively). The outcome of these results may be predicted.

If the pre-smoking baseline x pre-smoking baseline correlations are small, one may predict that the correlations of smoking effect should also be small. Provided that pre-smoking baseline correlations are large i.e., baseline arousal is reliable, it would seem reasonable to predict that real x real correlations of smoking effect should be greater than real x sham or sham x sham correlations of smoking effect. This is inherent in the arousal modulation model of cigarette smoking outlined earlier. Subjects are hypothesised to smoke in order to obtain stimulant effects when under-aroused and depressant effects when over-aroused. Sham smoking may produce some effect but this will be smaller and less reliable than a real smoking effect since the putative reinforcer, nicotine, is absent. Consequently, arousal modulation is less reliable with sham than with real cigarette smoking where the

smoker may titrate him or herself with the 'optimum' dose of a biphasic drug, nicotine.

III It is well known that deep inhalation and exhalation produces transient tachycardia followed by bradycardia and SCR by virtue of the reflex relationships between respiration and the autonomic nervous system (cf. Venables and Martin, 1967). This reflex relationship between a voluntary response - respiration - and autonomic responding, which is much less susceptible to voluntary control, has been exploited systematically by various Eastern disciplines (e.g., Hatha Yoga) as a means of arousal control. Therefore, it is of interest to determine to what extent respiration, in the manner of smoking inhalation, contributes to the sham-smoking effects on EEG 'α' and SCL which were observed in the previous experiments.

METHODOLOGY

Materials and equipment

Devices M19 and associated recording equipment was used as detailed in Experiments 1, 2 and 3. Plumbed cigarette holders were not used. Cigarettes smoked (or sham smoked) were 1.3 mg. nicotine delivery.

Self-report measures

Subjects reported average cigarette consumption per day for 1.3 mg cigarettes smoked in between recruitment and first experimental session, and also completed an EPQ (Eysenck, 1975). Subjects marked their subjective mood rating on a simple unidimensional analogue scale shown below. This was completed before and after (real) smoking a cigarette.

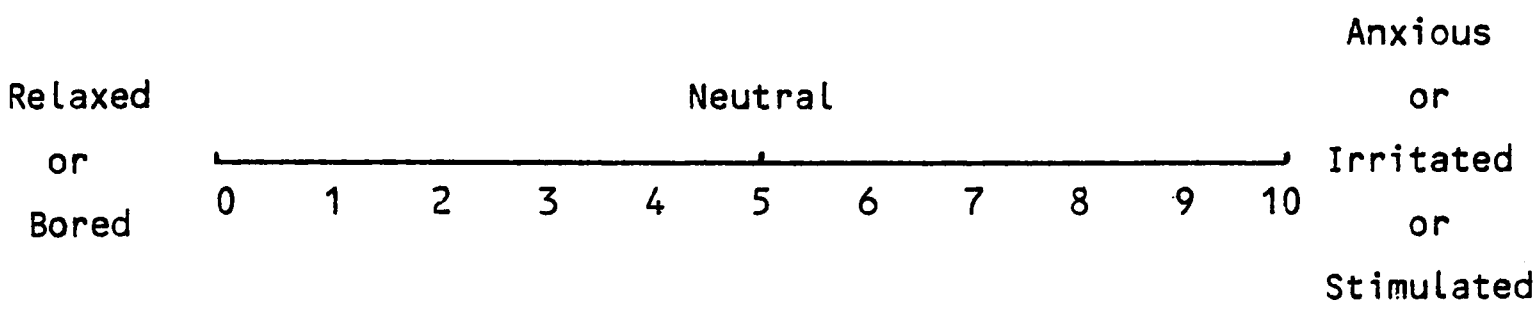
Do you feel anxious/irritated/stimulated or relaxed/bored.

Please indicate on the scale where:

0 is most relaxed or bored

5 is neutral

10 is most anxious/irritated/stimulated



Recording procedures

Depth of inhalation, and EEG 'α' were recorded as detailed in Experiment 3. Respiration rate and heart rate were recorded as detailed in Experiments 1 and 2. SC was recorded as detailed in Experiment 3 except that smaller electrodes (SLE miniature Ag/AgCl) were used (cf. Experiments 1 and 2 versus 3, SC methodology) and the skin was not abraded although of course cleaned with 10% ethanol in water. Abrasion was not carried out on the assumption that this technique, although having some merit in terms of goodness of electrical contact, might be a confounding variable for between session reliability estimates of pre-smoking baseline SCL. (N.B. this produces slightly lower basal SCL levels compared to Experiments 1 and 2 during sensory isolation.)

Scoring procedures

SCL, SFs and EEG 'α' were scored as detailed in Experiment 3. Respiration rate and heart rate were scored as detailed in Experiments 1 and 2. Puffing rate was scored as in Experiment 1 (plumbed cigarette holders

were not used).

Subject procedures

Ten habitual smokers were recruited by word of mouth, Subject Panel and advertisement. Each subject was shown the test room and familiarised with electrode attachment procedures a few days prior to the experiment and informed that the purpose of the experiment was to measure their physiological responses to cigarettes in a neutral, rather boring environment. After each experiment they would each receive standard payment for time and travelling costs. This prior habituation was felt essential to reduce any novelty inherent in the experimental situation which would be especially strong in the first session and thus reduce the intersession reliability.

In addition, each Subject was asked to refrain from alcohol and other drugs for the day prior to the experiment, and cigarettes, tea and coffee for two hours prior to the experiment. All Subjects smoked 1.3 mg. cigarettes for at least three days prior to the first session and in between the two sessions of the experiment. In fact this was the usual delivery strength of cigarettes smoked by the Subjects. Each Subject was tested on two sessions, one week apart at the same time of day (to minimise any day of the week and diurnal rythm effects).

Each session consisted of a real smoking, sham smoking and breathing control randomised between Subjects but not between sessions, since this would bias reliability estimates.

Before the experiment began the room was studied with the Subjects and any object of interest was habituated, e.g., a seemingly minor facet of the test room, the number of screw holes in the wall was found to be of some minimal interest for some Subjects and so these holes were counted

to their satisfaction. The experimenter in his conversation limited himself to such neutral topics as the weather, etc.

Subjects were seated in a comfortable arm chair. Their shoes were removed and their feet rested on a block of foam rubber. Physical comfort was deemed to be essential owing to the relatively long duration of the experimental periods (real, sham, breathing control; approximately 35-40 mins each). Subjects faced a blank white wall uniformly lit and were asked not to indulge in any excessive eye movements. Subject's watches were removed. Subjects sat without activity for 15 mins prior to an intercom instruction. Subjects were instructed to start smoking only 5-10 mins after a signal had been given via intercom, or at such time if this occurred later, when they felt they were very bored and wanted something to do (on the basis that a pleasure postponed is a pleasure increased). By this strategem it was hoped to intensify some-what their desire for a cigarette, producing larger measureable responses. Subjects were instructed to cease smoking after 5 minutes.

An important consequence vis_a_vis this control of when to start smoking by the Subject rather than by the experimenter is that it reduces the command effect due to the experimenter's signals. To this extent the experiment was more 'naturalistic' than Experiments 1, 2 and 3. Sham and real smoking instructions to Subjects prior to the experiment were as detailed in Experiment 1. Prior to each period the Subject went through a quick "dummy run" to check the lighter, cigarette and ash-tray were conveniently placed and that he fully understood what he was to do.

For the breathing control, the Subject was asked to take twelve breaths, of similar depth, duration and temporal spacing corresponding to the inhalations during natural smoking. Twelve was chose as a number

approximating the number of smoke inhalations observed for the average smoker. The required depth of inhalation approximately an 'average' puff inhalation was demonstrated by verbal feedback via an intercom to the Subject during a short dummy run prior to the breathing control sections of the two experimental sessions. This depth approximated as closely as possible the average inhalation observed from the respiration channel of the physiograph during smoking for each particular Subject.

RESULTS

Results are presented in four sections:

A Main effects of real and sham smoking and deep breaths: means, S.D.s and sign tests.

(i) Personality and cigarette consumption

(ii) Mood

(iii) Heart rate

(iv) Respiration rate

(v) SCL

(vi) SFs

(vii) EEG 'α'

(viii) Smoking Style

B Between and within session reliabilities of pre-smoking baselines.

C Between and within session reliabilities of real and sham smoking effects.

D Determination of real and sham smoking effects by pre-smoking baselines: PRE x (POST-PRE) correlations.

A (i) Personality and cigarette consumption

Personality data (Eysenck, 1975, EPQ) and cigarette consumption (number per day) for the ten Subjects are given below (cf. Table 1). The Subject sample is by and large similar, on these indicators, to the samples of Experiments 1, 2 and 3. The only feature of note is a slightly high mean 'P' scores (cf. comparison norms.: Eysenck, 1975). However, high 'P' scores have also been noted in the previous experiments (see later chapter on personality).

A (ii) Mood

The mean pre-smoking mood ratings indicate that Subjects assessed themselves as being fairly relaxed/bored prior to smoking (0 = relaxed/bored, 5 = neutral, 10 = anxious/irritated/stimulated). The effect of cigarette smoking was to raise the mean mood scores to just below 'Neutral' (= 5). However, this effect was not significant on a 2-tailed Sign Test (cf. Table 2), some Subjects reporting that the cigarette stimulated them, others that it relaxed them. No significant changes in variance PRE versus POST occurred (F ratio).

A (iii) Heart Rate

Consideration of Table 3 reveals the expected result, real smoking, but not sham smoking, nor deep breaths, elevates heart rate. These heart rate elevations, due without doubt to nicotine, are similar in magnitude to the effects of real smoking during stress and sensory isolation in Experiments 1, 2 and 3.

Regarding the effects of deep breaths it is noteworthy that the non-significant POST-PRE rise in heart rate declines from +4.00 (bpm) in the first sessions to +.20 (bpm) in the second session. This relatively small change is surprisingly significant ($p = .022$, $N = 10$,

TABLE 1

EPQ and cigarette consumption (n = 10)

Variable	Mean	SD
P	8.1	2.96
E	13.9	4.58
N	10.6	2.76
L	4.1	2.60
Cigarettes/day	16.1	7.98
Age range (yrs)	18-28	

TABLE 2

Mean Mood Ratings, Pre and Post Real-Smoking

ACTIVITY	SESSION	N	M O O D						P Sign Test 2-Tailed
			PRE		POST		Δ PRE-POST		
			m	SD	m	SD			
Real Smoking	First	10	3.30	1.77	4.80	2.25	+ 1.50		NS
	Second	10	3.20	2.04	4.90	2.69	+ 1.70		NS

ACTIVITY	SESSION	N	HEART RATE (b.p.m.) PRE m	PRE SD	POST m	POST SD	Δ PRE-POST	P Sign Test 1-Tailed
Real Smoking	First	10	74.30	11.18	87.80	12.31	+ 13.50	.001
Real Smoking	Second	10	74.00	10.65	87.40	10.64	+ 13.40	.001
Sham Smoking	First	10	78.60	10.71	78.60	9.38	0.00	NS
Sham Smoking	Second	10	76.00	12.47	75.60	12.14	- 0.40	NS
Deep Breaths	First	10	76.50	10.98	80.50	10.63	+ 4.00	NS
Deep Breaths	Second	10	75.10	11.45	75.30	8.17	+ 0.20	NS

TABLE 3

Mean Heart Rate (b.p.m.) by time period for real and sham smoking and deep breaths

x = 1, 2-Tailed Sign Test) and perhaps indicates that the small heart rate elevation due to deep breaths observed in the first session is a consequence of some novelty in the procedure which has habituated by the second session. Habituation of the phasic aspects of the respiratory-cardiovascular reflex has been reported (Venables and Martin, 1967) and this result indicates that habituation to the slower, tonic, aspects of the effects of deep breaths on the cardiovascular system also occurs.

No significant changes in variance PRE versus POST occurred (F ratio).

A (iv) Respiration Rate

Consideration of Table 4 reveals that cigarette smoking, whether real or sham, had no significant overall effect on respiration rate. This is consistent with the uniformly negative findings as regards cigarette smoking and PRE versus POST smoking respiration rates in Experiments 1, 2 and 3. No significant changes in variance PRE versus POST occured (F ratio).

A (v) SCL

SCL results are presented by period, activity and session (cf. Table 5) and graphically (cf. Figures 2 and 3). Note that the baseline SCLs are lower than those observed during sensory isolation in Experiments 1, 2 and 3. This does not indicate that the Subjects are less aroused, but is due to a slightly different SCL electrode procedure (cf. 'Recording Procedures' earlier).

Real cigarette smoking, but not sham smoking nor deep breaths, significantly elevated SCL during and after smoking (cf. Table 5). This result is consistent with those observed in Experiments 1, 2 and 3 for the effects of cigarette smoking during sensory isolation.

ACTIVITY	SESSION	N	RESPIRATION RATE (b.p.m.) PRE m	PRE SD	POST m	POST SD	Δ PRE-POST	P Sign Test 2-Tailed
Real Smoking	First	10	16.30	2.45	17.10	3.73	+ 0.80	NS
	Second	10	15.80	2.62	16.10	3.31	+ 0.30	NS
Sham Smoking	First	10	15.30	3.06	15.90	3.07	+ 0.60	NS
	Second	10	15.80	2.66	14.60	2.95	- 1.20	NS

TABLE 4

Mean Respiration Rates (b.p.m.) PRE and POST real or sham smoking

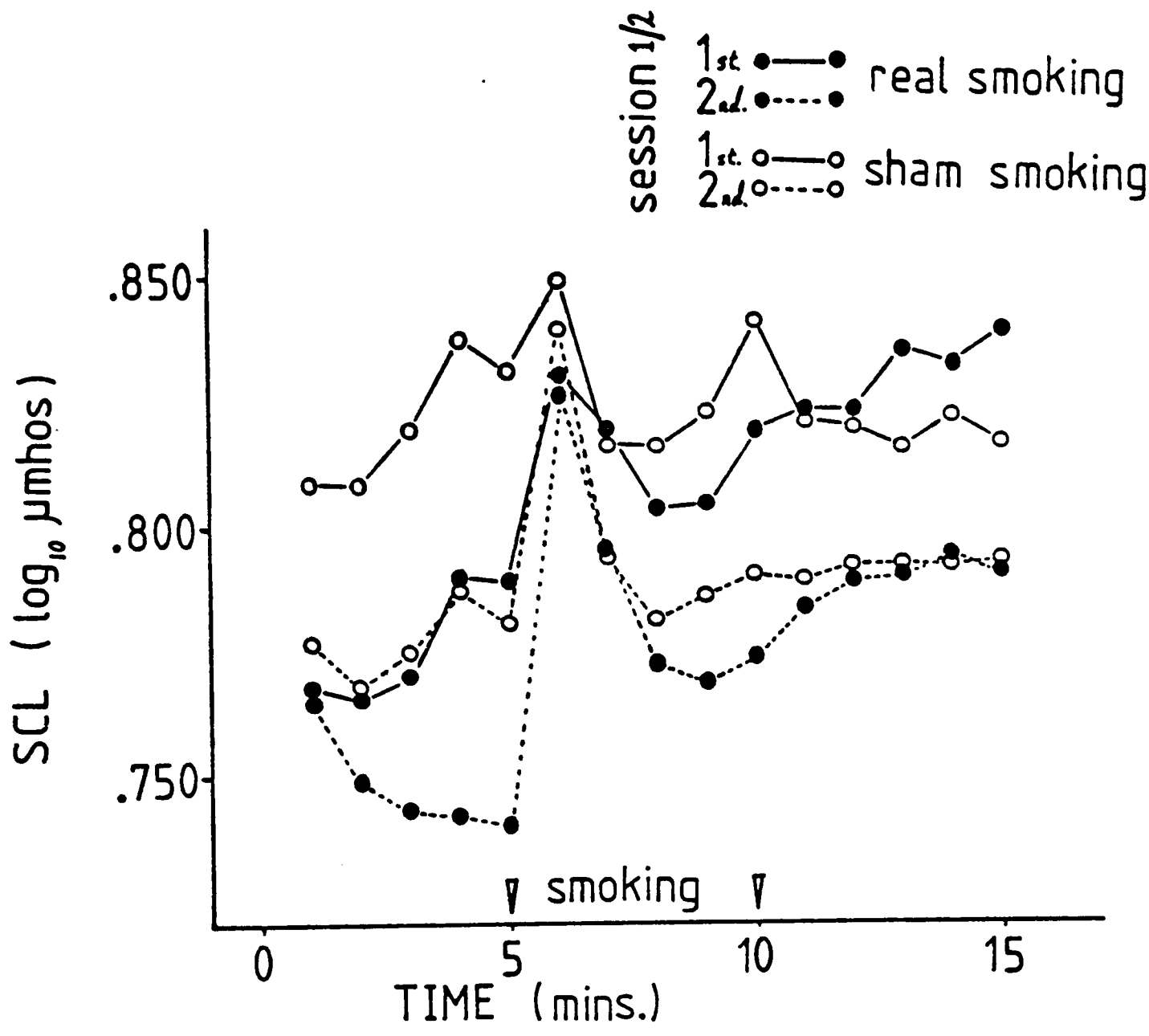


FIGURE 2 : SCL for real and sham smoking (n = 10,10) during boredom, first and second sessions.

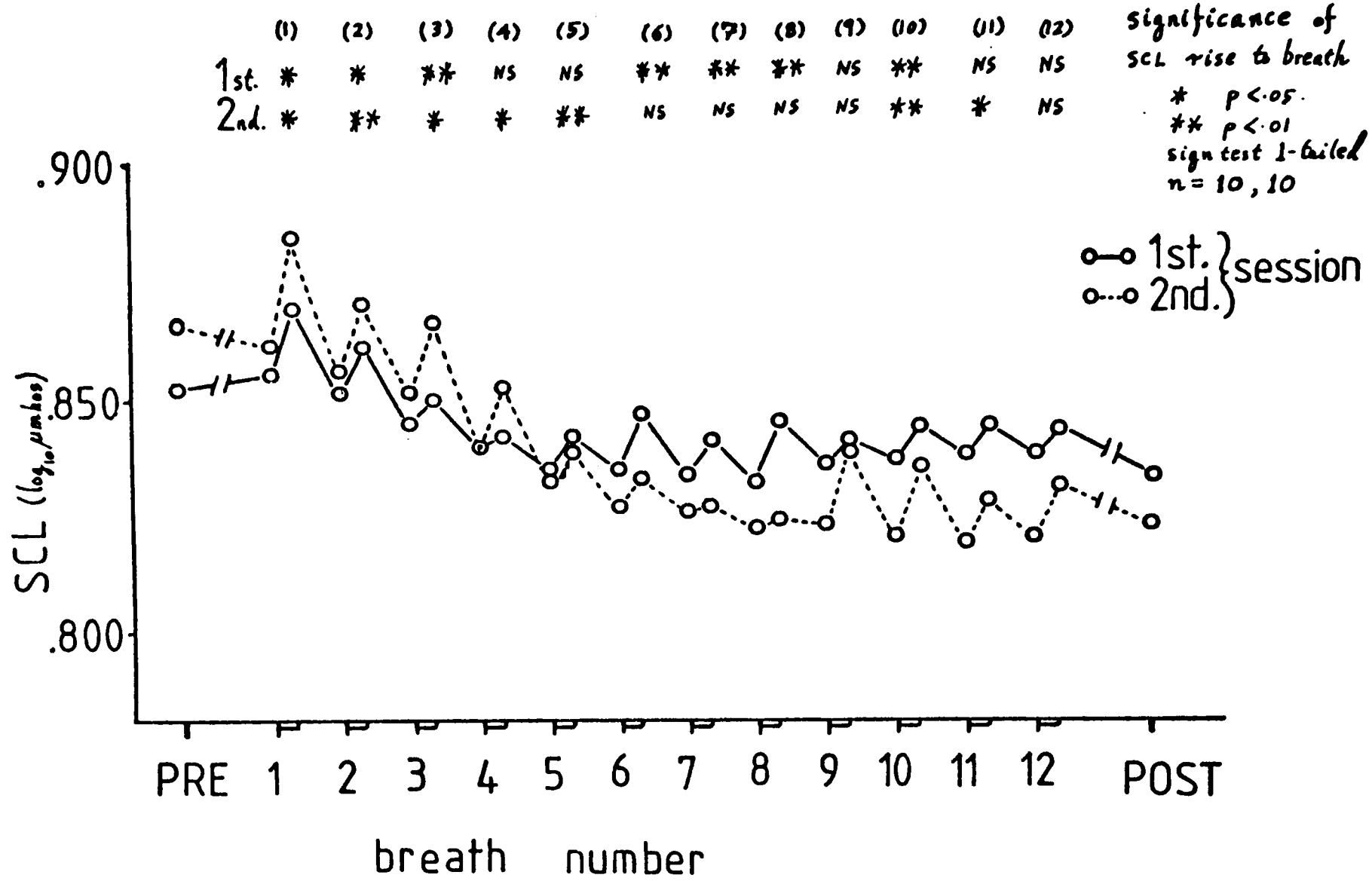


FIGURE 3 : Skin Conductance reflex responding to Deep Breaths control, breaths number 1-12, first and second sessions. Significance of SC rise is given above.

			SCL (log µmhos)						
ACTIVITY	SESSION	N	PRE (mins 1-5) m	SD	SMOKE (mins 6-10) m	SD	POST (mins 11-15) m	SD	Δ SMOKE-PRE	P Sign Test 1-Tailed	Δ POST-PRE	P Sign Test 1-Tailed
Real Smoking	First	10	.775	.199	.816	.223	.831	.248	+ .041	.011	+ .056	.055
Real Smoking	Second	10	.748	.172	.787	.172	.790	.199	+ .039	.011	+ .042	.011
Sham Smoking	First	10	.821	.227	.830	.220	.820	.222	+ .009	NS	- .001	NS
Sham Smoking	Second	10	.778	.193	.799	.189	.793	.200	+ .021	NS	+ .015	NS
Deep Breaths	First	10	.852	.250	.843	.260	.832	.259	- .009	NS	- .020	NS
Deep Breaths	Second	10	.866	.181	.838	.191	.822	.204	- .028	NS	- .044	NS

TABLE 5a

Mean SCL (log µmhos) by time period for real and sham smoking and deep breaths

COMPARISON	N	SCL △ SMOKE - PRE Log μmhos		P[1]	SCL △ POST - PRE Log μmhos		P[1]
		REAL (m)	SHAM (m)		REAL (m)	SHAM (m)	
REAL VERSUS SHAM SMOKING EFFECT : FIRST SESSION	10	+.041	+.009	N.S.	+.056	-.001	N.S. (.055)
REAL VERSUS SHAM SMOKING EFFECT : SECOND SESSION	10	+.039	+.021	N.S.	+.042	+.015	N.S. (.055)

[1]Sign Test , 1-Tailed ,N = 10, Real versus Sham .

(N.B. Deep breaths control - effects are not significantly different from those of sham smoking)

TABLE 5b : Comparison of Real versus Sham smoking effects on SCL (Log μmhos), First and Second sessions.

As in previous experiments, the characteristic pattern of a rapid elevation of SCL upon the start of smoking is observed. This elevation is transient for sham smoking but continues into the post-smoking period for real smoking, no doubt because of the effects of nicotine (cf. Figure 2). The initial SCL elevation is probably due to the motor activity involved in the onset of real or sham smoking. The contribution of inhalation would appear to be relatively minor as revealed by comparison of Figure 2 and 3.

The relatively unstable (with time) pre-smoking SCL baselines during boredom (cf. Figure 2) by comparison to the smooth SCL baselines observed during sensory isolation in the previous experiments perhaps indicate that Subjects were anticipating the onset of activity. (Subjects initiated activity - real or sham smoking - under their own control, although smoking was terminated exactly 5 minutes after starting smoking by experimental command via intercom, cf. Subject procedures.) However, the definitive assignation of this effect as being due to 'anticipatory' arousal is difficult given that it does not appear to occur prior to real-smoking, second session (cf. Figure 2). All changes in variance PRE versus POST are non significant (F ratio).

Although contributing little to the overall effects of real smoking on the SCL, the effects of a series of deep breaths on SCL are interesting in their own right. Consideration of Figure 3 reveals an irregular pattern of habituation of the electrodermal reflex to deep breaths, this irregular habituation appearing to be slightly more rapid in the second session. This irregular pattern of reflex SC responding to inhalation is the reason why SF data are not presented for the actual smoking period (mins. 6-10) in the experiments carried out in this thesis.

A (vi) SFs

SF data is presented (cf. Table 6) by session (first and second), activity (real and sham smoking) and time (Pre and Post smoking). There was no evidence that real or sham smoking significantly reduced SFs. This is consistent with the effects of cigarette smoking on SFs noted in Experiment 3 for sensory isolation condition. Although cigarette smoking has been reported to significantly reduce SFs (Mangan and Golding, 1978), the critical determining variable appears to be Subjects' starting state, as previously discussed in Experiment 3 (cf. later section 'D', PRE x (POST-PRE) correlations).

There are no significant PRE versus POST changes in variance (F ratio).

A (vii) EEG 'α'

EEG 'α' (%) data is presented (cf. Table 7) by session (first and second), activity (real and sham smoking, deep breaths) and time period (pre, smoking, post) and also graphically (cf. Figure 4). While in the first session real smoking significantly reduces EEG 'α' activity, sham smoking marginally so and deep breaths not at all, this effect is attenuated in the second session. Note that sign tests are set to 1-tailed to better illustrate the order of effect: real > sham > breaths, for 2-tailed simply double "p" (cf. Table 7). It is interesting that the EEG 'α' blocking effects of cigarette smoking during boredom are less pronounced than observed during sensory isolation but greater than during stress (cf. Experiments 1, 2 and 3). This result supports the view that the effects of smoking - stimulant or depressant - 'tonic' cortical activity depend to some extent on the pre-smoking level of arousal: the level of arousal in the present experiment being roughly in between those of sensory isolation and stress.

TABLE 6

Mean Spontaneous Fluctuations (SFs)

PRE and POST real and sham cigarette smoking

ACTIVITY	SESSION	N	SFs PRE m	SFs PRE SD	SFs POST m	SFs POST SD	Δ POST-PRE	P Sign Test 2-Tailed
Real Smoking	First	10	13.90	9.49	12.90	7.74	- 1.00	NS
	Second	10	15.50	8.78	14.00	5.40	- 1.50	NS
Sham Smoking	First	10	11.70	8.23	11.10	9.01	- 0.60	NS
	Second	10	16.60	9.41	14.00	8.43	- 2.60	NS

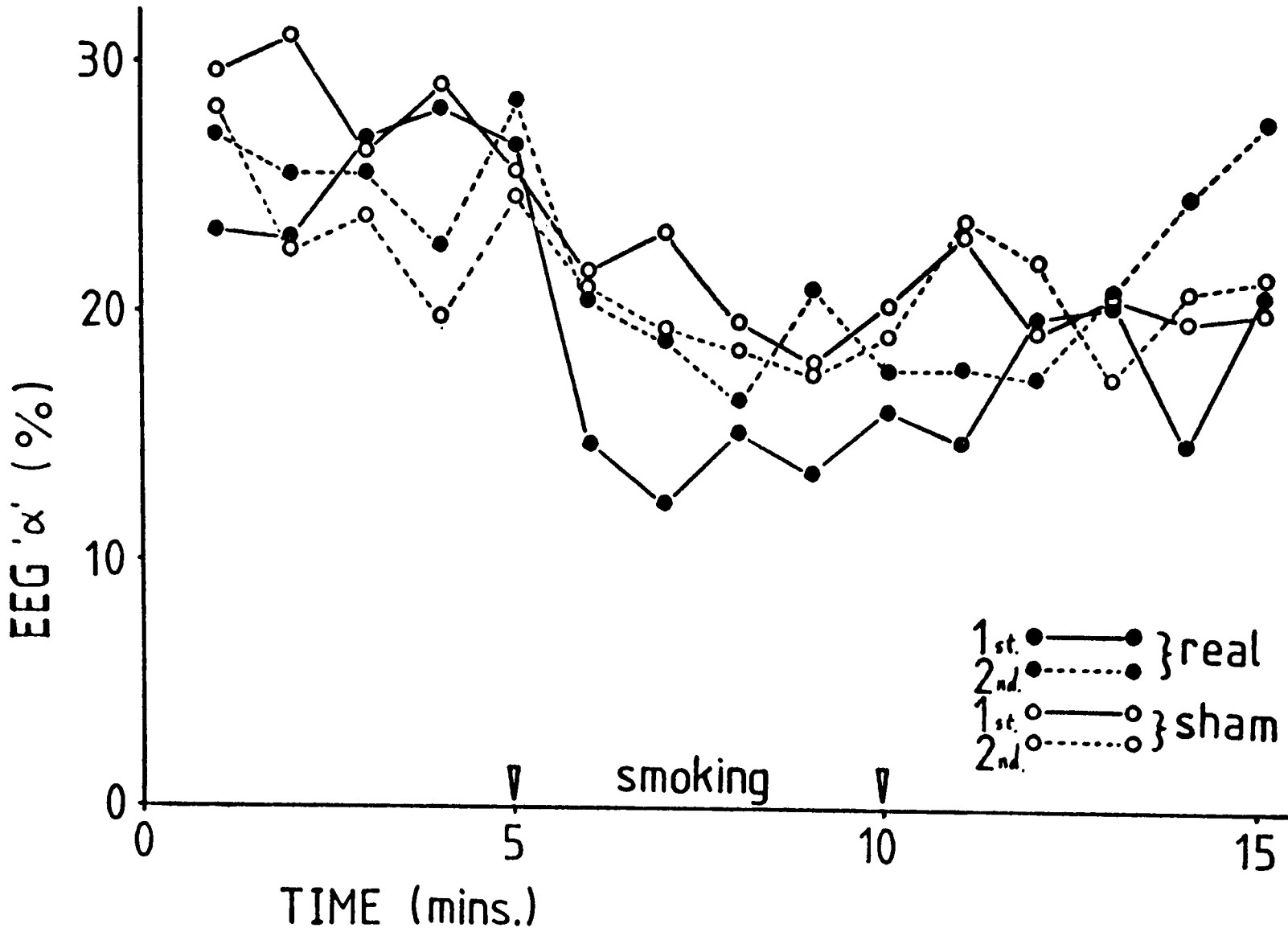


FIGURE 4 : EEG 'α' for real and sham smoking groups during boredom (n = 10,10), first and second sessions.

			EEG 'α' (%)						
ACTIVITY	SESSION	N	PRE (mins 1-5) m SD	SMOKE (mins 6-10) m SD	POST (mins 11-15) m SD	Δ SMOKE-PRE	P Sign Test 1-Tailed	Δ POST-PRE	P Sign Test 1-Tailed
Real Smoking	First	10	25.70 (14.30)	14.40 (11.08)	18.04 (11.93)	- 11.30	.001	- 7.66	.055
Real Smoking	Second	10	25.88 (19.87)	18.94 (18.89)	21.66 (15.38)	- 6.94	NS	- 4.22	NS
Sham Smoking	First	10	28.44 (15.52)	20.62 (11.01)	20.52 (11.38)	- 7.82	.055	- 7.92	NS
Sham Smoking	Second	10	23.80 (15.40)	19.12 (11.08)	21.06 (8.28)	- 4.68	NS	- 2.74	NS
Deep Breaths	First	10	25.79 (15.10)	24.20 (15.60)	24.90 (15.50)	- 1.59	NS	- 0.89	NS
Deep Breaths	Second	10	24.84 (16.20)	20.30 (13.06)	22.57 (14.45)	- 4.54	NS	- 2.27	NS

TABLE 7

Mean EEG 'α' (% time > criterion) by time period for real and sham smoking and deep breaths

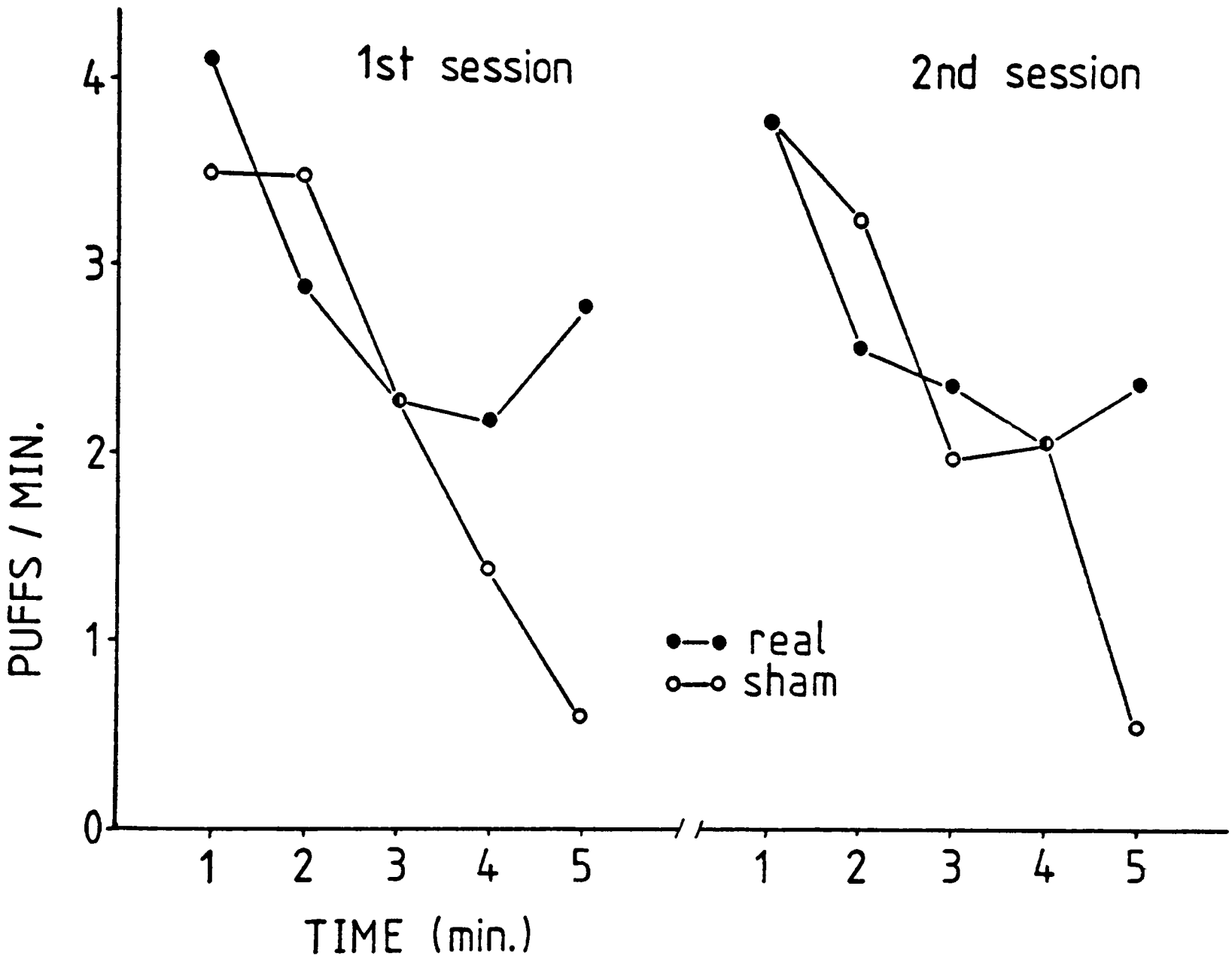


FIGURE 5 : Puffing rates for real and sham smoking during boredom (n = 10,10), first and second sessions.

TABLE 8

Mean number of puffs for

1st and 2nd sessions real and sham smoking

SESSION	N	Number of puffs			
		REAL		SHAM	
		m	SD	m	SD
First	10	14.0	4.6	11.6	2.6
Second	10	13.5	4.2	11.4	1.8

TABLE 9

Between and within session correlations for number of puffs

Comparison	Pearson r_p	P
$Real_1$ x $Real_2$	+ .87	***
$Sham_1$ x $Sham_2$	+ .70	*
$Real_1$ x $Sham_1$	+ .70	*
$Real_2$ x $Sham_2$	+ .61	NS

* p < .05
** p < .01
*** p < .001

DF = 8

There is a trend for the variances of mean pre-smoking EEG 'α' scores to be reduced during the smoking period and post-smoking for real and sham smoking, but not for deep breaths (cf. Table 7). This trend of variance reduction achieves significance for post sham-smoking period in the second session (POST versus PRE; F = 3.46; DF = 9, 9; p = .05). This variance reduction may reflect a 'ceiling' or 'Law of Initial Values' effect of real and sham smoking on EEG 'α' when the overall trend of smoking on electrocortical activity is stimulant. This point is more fully discussed in the subsequent experiment (cf. Experiment 5: Results section, 'Main effects of cigarette smoking on psychophysiological measures irrespective of nicotine strength').

A (viii) Smoking Style

Puffing rates are presented by session and activity (cf. Table 8) and graphically as puffing rate minute by minute (cf. Figure 5). Although Subjects overall took more puffs when real smoking than sham smoking,this is not significant statistically (Sign test). As observed previously in Experiments 1, 2 and 3, smokers tend to show an attenuation in puffing rate over the five minute smoking period (cf. Figure 5), this being especially marked for sham smoking.

As noted in Experiments 1, 2 and 3 idiosyncracies in smoking style are marked and relatively stable. As can be seen (cf. Table 9) the number of puffs taken from a cigarette is a highly reliable measure, whether this is correlated across individually between sessions or between real and sham smoking within each session.

B Between and within session reliabilities of pre-smoking baselines

Two main effects are prominent in the pre-smoking baseline correlation (cf. Table 10). Firstly, pre-smoking baselines appear to be more reliable within as opposed to between session for Heart rate,

Respiration rate and SCL but this is perhaps not surprising. Secondly, heart rate and respiration rate appear to be relatively more reliable than SCL, SFs and EEG 'α'.

For SCL, low baseline correlations may be partly a reflection on the limits of reproducibility of electrode contact; between session baseline SCL correlations being lower than within session baseline SCL correlations (cf. Table 10). However, technical considerations cannot explain why EEG 'α' and SFs tend to show the same or even slightly higher between session rather than within session baseline correlations. The most plausible explanation for the smallness of all the baseline correlations for SFs and EEG 'α' is that these two measures are perhaps the most sensitive to small changes in arousal and thus show that pre-smoking baselines of arousal, for these measures at least, are not as consistent both within and between session as might be hoped.

It is to be expected (cf. Rationale) that low baselines correlations will predict low smoking effect correlations and vice versa. Thus, heart rate and respiration rate smoking effects should show better correlations than the remaining measures. This is examined next.

C Between and within session reliabilities of real and sham smoking effects.

As predicted in the previous section, heart rate and to a lesser extent respiration rate show the highest smoking effect correlations (cf. Table 11). The between session correlations tend to be higher than within session correlations. This is not surprising given that the former are Δ real$_1$ x Δ real$_2$, Δ sham$_1$ x Δ sham$_2$ correlations whereas the latter are Δ real$_1$ x Δ sham$_1$, Δ real$_2$ x Δ sham$_2$ correlations. The significant negative (-.72 $p < .05$, cf. Table 11) Δ sham$_1$ x Δ sham$_2$ respiration correlation is inexplicable, perhaps it occurs by chance: twenty

VARIABLE	COMPARISON	Between Session r_p Pearson corr. 1 session x 2 session	P	COMPARISON	Within Session r_p Pearson corr. real x sham	P
Mood	Real	+ .60	NS	Red.	Red.	Red.
Heart Rate	Real Sham	+ .61 + .65	NS *	First Second	+ .94 + .96	*** ***
Respiration Rate	Real Sham	+ .76 + .76	** **	First Second	+ .85 + .97	** ***
SCL	Real Sham	+ .50 + .33	NS NS	First Second	+ .95 + .75	*** *
SFs	Real Sham	+ .48 + .63	NS *	First Second	+ .35 + .53	NS NS
EEG 'α'	Real Sham	+ .59 - .02	NS NS	First Second	+ .39 + .58	NS NS

* $p < .05$
** $p < .01$
*** $p < .001$

N = 10
DF = 8

TABLE 10

Reliability of pre-smoking levels of arousal measures

between sessions (real x real, sham x sham) and within sessions (real x sham, real x sham)

VARIABLE	COMPARISON Between Sessions	r_p Pearson corr.	P	COMPARISON Within Sessions	r_p Pearson corr.	P
Mood	Δreal x Δreal	+ .87	***	-	-	-
Heart Rate	Δreal x Δreal Δsham x Δsham	+ .74 + .63	* *	Δreal x Δsham 1st Δreal x Δsham 2nd	- .51 + .06	
Respiration Rate	Δreal x Δreal Δsham x Δsham	+ .78 - .72	** *	Δreal x Δsham 1st Δreal x Δsham 2nd	+ .21 - .36	
SCL	Δreal x Δreal Δsham x Δsham	.00 + .19		Δreal x Δsham 1st Δreal x Δsham 2nd	- .49 + .80	**
SFs	Δreal x Δreal Δsham x Δsham	+ .34 + .25		Δreal x Δsham 1st Δreal x Δsham 2nd	- .30 + .20	
EEG 'α'	Δreal x Δreal Δsham x Δsham	+ .57 + .01		Δreal x Δsham 1st Δreal x Δsham 2nd	+ .19 - .34	

* p < .05
** p < .01
*** p < .001

N = 10
DF = 8

TABLE 11

Reliability of subjective and physiological smoking effects Δ = (Post-Pre): between session correlations: Δreal 1' x Δreal 2', Δsham 1' x Δsham 2', and within session correlations: Δreal x Δsham, 1' session, Δreal x Δsham, 2' session.

		REAL SMOKING		SHAM SMOKING	
VARIABLE	SESSION	r_p PEARSON CORR. PRE x (POST-PRE)	P	r_p PEARSON CORR. PRE x (POST-PRE)	P
Mood	1	- .84	**	-	-
	2	- .90	***	-	-
Heart Rate	1	- .10		- .65	*
	2	- .28		- .25	
Respiration Rate	1	+ .47		- .47	
	2	- .17		- .15	
SCL	1	+ .50		- .23	
	2	+ .11		- .12	
SFs	1	- .64	*	+ .04	
	2	- .79	**	- .45	
EEG 'α'	1	- .56		- .77	**
	2	- .64	*	- .90	***

* $p < .05$
** $p < .01$
*** $p < .001$

N = 10
DF = 8

TABLE 12

Starting State Effects on Magnitude and Direction of Smoking Effect: (PRE x (POST-PRE) Correlations

correlations will yield $\tilde{\sim}$ 1 correlation of $p < .05$ simply by chance.

D Determination of real and sham smoking effects by pre-smoking baselines: PRE x (POST-PRE) correlations

Significant negative pre x (post-pre) correlations indicate that the greater the baseline pattern of arousal the less is the stimulant effect of real or sham smoking. There would appear to be evidence that subjective Mood rating, SFs and EEG 'α' show this property, but that heart rate, respiration rate and SCL do not (cf. Table 12). These measures, SFs and EEG 'α' (apart from Mood), were observed to be the least reliable in terms of baseline correlations (cf. section B) or smoking effect correlations (cf. section C). A picture thus emerges that heart rate and respiration rate tend to show highly stable individual differences as do the effects of smoking on these measures; each smoker showing a characteristic, so-called 'Autonomic Fingerprint'. In contrast, SFs and EEG 'α' appear to be less stable measures but show strong determination of smoking effect by the pre-smoking baseline. In general terms this pattern of responding amongst the various measures is consistent with the observations made in Experiments 1, 2 and 3. In these experiments, heart rate was elevated by cigarette smoking to a similar degree, irrespective of whether the Subject was in a high arousal (stress) or low arousal (sensory isolation) situation. However, the pattern of effect of cigarette smoking on EEG 'α', SCL and SFs in Experiments 1, 2, and 3 was highly determined by situation arousal (EEG 'α', SCL) or starting state arousal (SFs; Experiment 3).

GENERAL DISCUSSION

In general terms it would appear that the overall effect of cigarette smoking during boredom was stimulant, producing significant elevations of heart rate, SCL and significant decreases of EEG 'α'.

Sham smoking produced some SCL and EEG activation but had no effect on heart rate. Deep breaths produced very little heart rate, SCL or EEG activation, indicating that the motor components of cigarette smoking account for the major part of any sham smoking effect. The stimulant nature of cigarette smoking during boredom was supported to a non-significant extent by Subject's self reports of feeling less relaxed/bored after smoking on a simple mood rating scale. Overall effects on respiration rate and SFs were non-significant. The effects of cigarette smoking during boredom thus appears to resemble the effects of cigarette smoking observed in Experiments 1, 2 and 3 during sensory isolation (although stimulant effects of cigarette smoking on SCL and EEG 'α' are less marked during boredom compared to sensory isolation). This is perhaps unsurprising since most Subjects reported themselves as being rather underaroused on the mood rating scale.

However, the most interesting results were those gained by using correlation coefficients to look for consistencies in pre-smoking levels of arousal measures, consistencies of smoking effect and the degree to which starting state predicted outcome of smoking effect. Although a large number of correlations will produce some significant correlation coefficients simply by chance, there was sufficient reason to believe that the overall picture generated from these correlation tables was valid. Both the very large numbers of significant correlations and the consistency of the pattern of their location supports the latter view.

The picture that emerged was of a relatively stable 'autonomic fingerprint' for an individual as regards both pre-smoking heart rate and respiration rate and the effect that cigarette smoking had on these two measures. SCL appeared rather unreliable between sessions but quite reliable within each session, implying that the exact reproducibility of

of electrode contact left something to be desired. By contrast technical considerations were less likely to account for the low baseline and smoking effect correlations for EEG 'α' and SFs since between as opposed to within session correlations were very similar. It seemed likely that the EEG 'α' and SF rate were the most sensitive and labile of all the measures and low correlations reflected true variation in physiological arousal of Subjects over time. Consequently, smoking effect correlations were similarly low for ΔSF rate and ΔEEG 'α'.

However, the effects of cigarette smoking on SF rate and EEG 'α' were well predicted from the pre-smoking baselines: individuals with high levels of arousal tending to show no change or depressant effects, while individuals with low levels of arousal tended to show stimulant effects. This reproduces the results found for SFs during sensory isolation in Experiment 3. In addition, although not calculated at the time, a post-hoc PRE x (POST-PRE) correlations for the EEG data during sensory isolation reveals a similar picture (Experiment 3; sensory isolation, EEG 'α' Pre x (Post-Pre) correlations: Real smoking (n = 12) r_p = -.89, Sham smoking (n = 6) r_p = -.01).

Subjects also appeared to show some degree of self awareness of this effect, those who rated themselves as being very relaxed/bored reporting themselves stimulated by smoking, those who were less relaxed/bored reporting either no change or that the cigarette had relaxed them.

However, correlations between subjectively assessed mood either pre-smoking or change, correlated poorly with objective physiological measures of arousal, seldom being above r = +.40 and for brevity are not reported. This may mean that either Subjects' introspection of their arousal state is inaccurate or that the physiological measures of arousal used (HR, RESP, SCL, SFs, EEG 'α') are only crude indicators

of what a person is feeling. It is also necessary to bear in mind that the various arousal systems themselves are only partially linked and a Subject's introspection of his state of arousal will probably represent a summation of the activity in these various systems. The association between self-report of mood and objective physiological measures is perhaps best studied using extreme arousal states as in Experiments 1, 2 and 3.

E X P E R I M E N T 5

EFFECTS OF VARIATIONS IN PREDICTED NICOTINE DELIVERY OF CIGARETTES ON PSYCHOPHYSIOLOGICAL RESPONDING AND SMOKING BEHAVIOUR

Rationale

This experiment was designed to test the hypothesis that smokers attempt some degree of self-titration towards an 'optimum' dose of nicotine (which may vary between individuals and between situations) in the face of variations of nicotine delivery of cigarettes above and below the nicotine yield of the cigarettes they normally smoke. There is mounting evidence that cigarette smokers do in fact attempt some degree of self-titration, both by changes in smoking style (number of puffs, puff duration, puff intensity and depth of inhalation) and by changes in the total number of cigarettes smoked. Evidence for this view comes from a number of studies in which nicotine delivery to the smoker has been varied by means of variations in nicotine content of tobacco, filter efficiency, smoke dilution, and length of the tobacco rod (Ashton and Watson, 1970; Cherry and Forbes, 1972; Frith, 1971; Russell, Wilson, Patel, Cole and Feyerabend, 1973, 1975; Schachter, 1977; Turner, Sillett and Ball, 1974; Russell, Sutton, Feyerabend and Cole, 1978; Ashton, Stepney and Thompson, 1978; 1979), although the literature is by no means unanimous - some authors reporting negative results (Goldfarb, Jarvik and Glick, 1970; Mangan and Golding, 1978; Friedman and Fletcher, 1976). The aim of this study was to examine how quickly (if at all) smokers can adapt to variations in nicotine delivery.

Such compensatory behaviour is predicted by both Nicotine Addiction and Arousal Modulation hypotheses. Thus the central tenet of an Arousal Modulation model of cigarette smoking is the postulate that the smoker can titrate him/herself with the appropriate dosage of a biphasic drug - nicotine - in order to obtain stimulant (low dosage) or depressant (high dosage) effects from cigarette smoking as the situation demands. Thus in a fixed situation, in this case the low to neutral arousal setting of a laboratory, subjects should be able to rapidly compensate (over the space of one or two cigarettes) for variations in nicotine delivery and thus achieve similar physiological effects (appropriate to the situation) from smoking different delivery cigarettes. Such a rapid adjustment in smoking behaviour to obtain the 'correct' i.e. most rewarding dosage of nicotine is not as crucial to the Nicotine Addiction models of smoking, although such models do necessitate the demonstration of self-titration by the smoker for nicotine in face of variations in nicotine delivery of cigarettes. In contrast whilst the Nicotine Addiction model of smoking predicts that even a low dose of nicotine would be rewarding to a nicotine deprived smoker (although a nicotine dose closer to the usual intake would be more rewarding), an Arousal Modulation model would predict that a low (stimulant) dose of nicotine would actually be aversive in a high stress condition since it would further augment arousal and conversely a high (depressant) dosage of nicotine would similarly be non-rewarding in a low-arousal situation since it would further lower arousal below the postulated 'optimum' (low nicotine x low arousal and high nicotine x high arousal would of course be predicted to be rewarding by an Arousal Modulation model).

For the purposes of the present experiment it was decided to examine the effects of varying the nicotine delivery of cigarettes in a

low arousal situation - sensory isolation - and to allow subjects to smok successively two high and also two low nicotine delivery cigarettes (varied by means of a ventilated holder) over two experimental sessions. A variety of measures of physiological arousal (EEG 'α', SCL, SFs, Heart Rate, Respiration Rate) and smoking style (puffs, inhalation, tobacco burnt weight) were used. The latter measures assess to what extent subjects varied smoking style to compensate for variations in nicotine delivery and so obtain an 'optimum' (stimulant for this low-arousal situation) dosage of nicotine. The former, physiological measures, were to assess whether or not subjects achieved the same physiological effect irrespective of nicotine delivery.

METHODOLOGY

Materials and equipment

Devices M19 and associated recording equipment was used as detailed in previous experiments.

Two types of MD4 ventilated holders were used (cf. Figure 1). A modified MD4 holder which was sealed and 'bored out' to act simply as a cigarette holder. This is referred to as a 100% holder and was also used to habituate subjects to smoking through cigarette holders prior to the experiment. This 100% holder and an unmodified 20% MD4 (filter number 4) were used to provide high and low nicotine delivery conditions. Cigarette smoked prior to the experiment were 1.3 mg, cigarettes used during the experiment were 1.8 mg (Government figures based on standardised smoking machine, laboratory of Government Chemist). On this basis smokers nominally had 1.3 mg delivery cigarettes as their 'normal' brand, 1.8 mg delivery for the high nicotine condition, and 0.36 mg delivery for the low nicotine, all in externally similar holders.

It took a long time to become a regular smoker. It needn't take anything like as long to stop.

MD4

MD4: The Progressive System.

There are only two ways to stop smoking: gradually and immediately. Very few people ever achieve the latter, but most of those who attempt to stop by cutting down also fail, because any habit is amazingly difficult to break.

Now at last, there is a successful progressive method, new to this country but well-established and indeed proven in both the United States and Switzerland. The simple principle of MD4 is to **slowly** reduce the amount of tar and nicotine absorbed from each cigarette through a series of condensation filters. It succeeds because you don't attack the habit itself until the dependence is beaten. Throughout the course, you needn't change any of your smoking habits such as your brand or your favourite cigarette of the day. All that comes later.

And best of all, the system is designed to help eliminate the usual side-effects such as irritability, nervousness and undue weight-gain. You are teaching yourself to be a non-smoker, and it can be done. It has already been done by literally thousands of people in the two countries mentioned above.

The Method.

Each of the four condensation filters is progressively more effective; and each is used for two weeks only. By gradually reducing your dependence upon cigarettes, MD4 makes the whole process as painless, and therefore as likely to succeed as possible. There is only one vital rule: you must reduce your intake of tar and nicotine progressively.

From today, do not smoke even a single cigarette without the relevant MD4 filter. Do that, and there is no more painless way to stop smoking. (Furthermore, you could of course continue smoking with the final filter should you wish to: ten such cigarettes are equivalent to just two without the filter.)

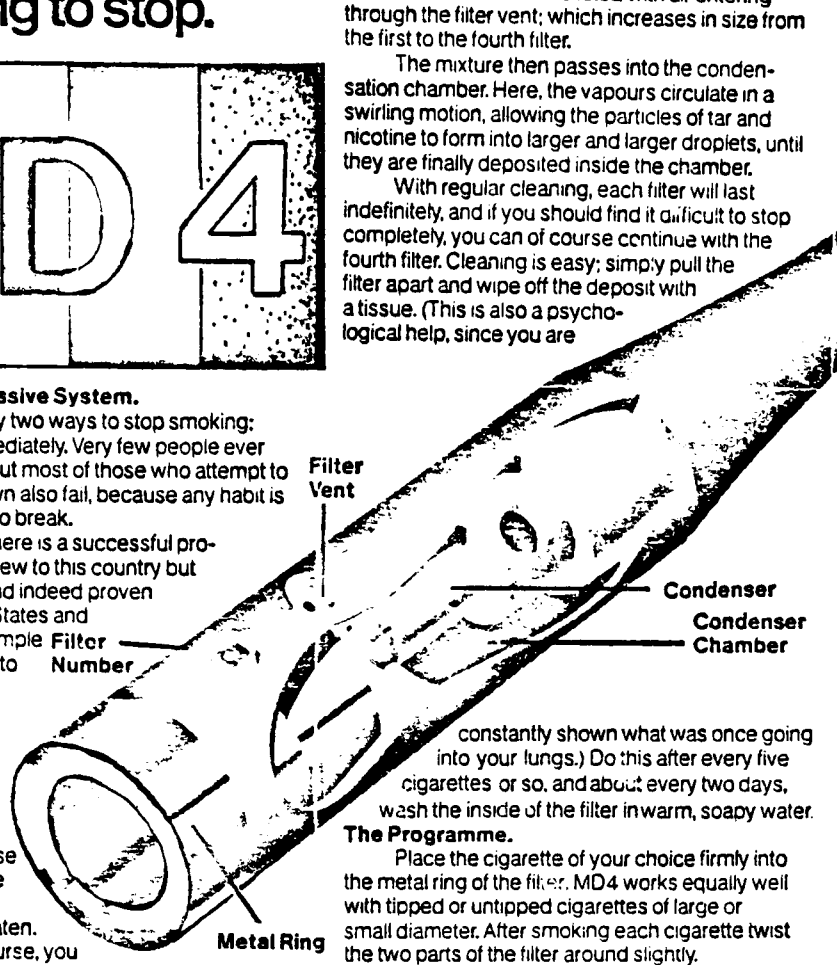
The Mechanics.

The MD4 condensation filter was developed by a group of American doctors, and like so many very good ideas, it simply hadn't been done before.

The smoke is first diluted with air entering through the filter vent; which increases in size from the first to the fourth filter.

The mixture then passes into the condensation chamber. Here, the vapours circulate in a swirling motion, allowing the particles of tar and nicotine to form into larger and larger droplets, until they are finally deposited inside the chamber.

With regular cleaning, each filter will last indefinitely, and if you should find it difficult to stop completely, you can of course continue with the fourth filter. Cleaning is easy; simply pull the filter apart and wipe off the deposit with a tissue. (This is also a psychological help, since you are constantly shown what was once going into your lungs.) Do this after every five cigarettes or so, and about every two days, wash the inside of the filter in warm, soapy water.



The Programme.

Place the cigarette of your choice firmly into the metal ring of the filter. MD4 works equally well with tipped or untipped cigarettes of large or small diameter. After smoking each cigarette twist the two parts of the filter around slightly.

Use each condensation filter for just two weeks, before moving to the next one. Filter No. 1 reduces the tar and nicotine inhaled by about 30%. Some people may find that their cigarette consumption increases slightly at first to compensate, and that is quite understandable. Indeed, you may allow yourself this slight 'relapse'; but after this, do not increase your cigarette consumption whatsoever. Equally, do not tempt failure by rushing the course or severely cutting down your daily intake.

On reaching Filter No. 2, you are sufficiently accustomed to the method to move on to a 60% tar and nicotine reduction. This allows you to maintain your smoking while making wide inroads into your tobacco habit. And you should begin to feel the first benefits, such as less coughing and breathlessness.

Filter No. 3 brings you a 70% reduction and with the fourth and final filter, a good 80% of those noxious substances will not be getting through. By the end of the eight weeks, your body is starting to free itself from its build-up of nicotine.

The fifth and final stage – actually stopping – will involve some will-power, but you couldn't be better prepared. Your body has acquired a taste for its improved health, you have suffered little from the usual side-effects and most important, you actually want to be a non-smoker. That in itself is considerably more than half the battle.

The following pertinent advice will help you to win through the final stage; do please re-read it in eight weeks time.

The Final Step.

Eight weeks have passed and you have broken the back of your tobacco habit. Many of us find it quite natural to stop at this point, with very little discomfort. But here is some guidance on how to break the problem once and for all.

Your diet is most important. Smoking numbs the tastebuds to most subtle flavours, and it is for this reason that people tend to put on weight afterwards. Not only through eating instead of smoking, but because they rediscover the taste for food.

The solution is quite straightforward: you only need become more conscious of what you eat. Follow something of a diet for a few weeks, balance fatty foods with something acidic such as lemon. Eat mainly vegetables and fruits (or drink fruit juices) and emphasize protein-rich foods, eggs or fish for instance. You will soon be eating better and enjoying your food more.

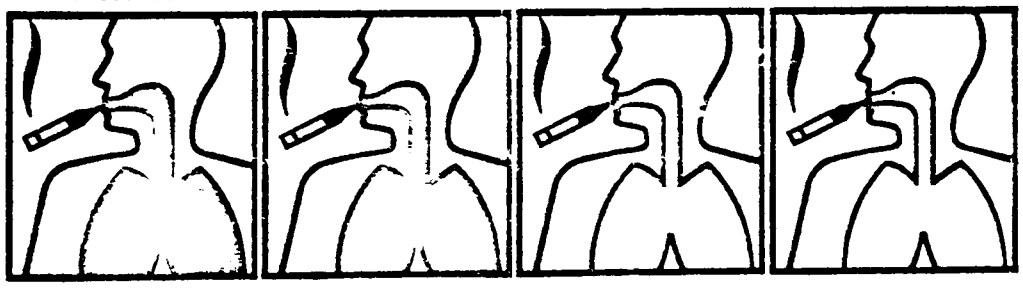
Then, after a few weeks, slowly adjust back to your normal diet, or rather your new diet as you will now be treating your body more kindly. And clean your teeth regularly with a strong-tasting toothpaste or mouthwash; you won't want any smoke in there afterwards.

A general concern for your health will also come to you; develop it. Learn to breathe again properly; you could start with this simple exercise. Sit quite upright with your thighs slightly apart. Breathe slowly, deeply and regularly through your mouth. Then blow out a little more, pulling in your stomach to empty your lungs completely. Breathe in slowly through your nose, filling your lungs from the stomach upwards, while slowly standing up and throwing back your shoulders.

Physical exercise of whatever type happens to suit you is vital, even if it's only a fifteen-minute walk each day.

But finally, and probably most important, change your habits. Travel in 'No Smoking' compartments, avoid the company of heavy smokers for a time; and do something different in dangerous periods–the time of your favourite cigarettes. Take a walk after dinner for instance, try to avoid the pub, but don't think negatively. For better, and certainly not for worse, you are a different person now, healthier, richer and much, much nicer to know.

Tar and nicotine reductions have been validated by independent laboratory tests in three countries using internationally accepted methods of analysis:– in U.K., by Hazleton Laboratories Europe Ltd., Harrogate; in the USA by Pitelson Laboratories Inc., New York; in Switzerland by Laboratoire Chimique du Doctor L. Herzfeld, Basle.



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MILES

FIGURE 1 : Cutaway diagram of the MD4 ventilated cigarette holder and associated manufacturer's literature.

Estimation of nicotine/tar delivery

Assuming that the concentration of nicotine/tar available in inhaled smoke is a continuously increasing function of the quantity of tobacco burnt (not necessarily a linear function[1]) the following technique gives an estimation of the nicotine/tar presented to the smoker.

The effect of variation in nicotine concentration along the tobacco rod, as a source of error in estimating the amount of nicotine presented to a smoker, is unlikely to be of great significance in the present experiment. This is because the smoking style results from this and the previous experiments indicate that the time based profiles of puffing frequency remain relatively constant irrespective of arousal condition (cf. smoking style results, Experiments 1, 2, 3, 4) or of the nicotine delivery of the cigarette smoked (cf. smoking style results for the present experiment). The effect of variations in the exact pressure profile of each puff represent an unknown source of error, this effect is most likely to be on the tar/nicotine ratio as discussed earlier.[1] Absolute puff pressure as opposed to pressure profile is likely to be important as a nicotine regulator, as clearly shown in Experiment 3.

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[1] This is not necessarily a linear function either in terms solely of nicotine or of tar or of their ratio. The concentration of nicotine and tar along the tobacco rod will vary in the course of smoking a cigarette, the tobacco rod acting analogously to a fractionation column during smoking. Tar and nicotine will accumulate towards the butt, hence the health advice to leave longer butts. In addition, the tar to nicotine ratio may vary as a function of pressure and duration of each puff. Since nicotine volatolizes at a lower temperature than the higher molecular weight tars, more nicotine will be present as opposed to tar in that smoke derived from the initial heating up of the burning cone of tobacco, i.e. from the beginning of the puff. Other factors such as the differential filtration efficiency of the tobacco rod and filter, for nicotine versus tar, may be important as well.

An estimate of variation in the tar/nicotine delivery of the same type of cigarette produced when smoked through the two types of holders (high nicotine $\underline{\Omega}$ 100% delivery versus low nicotine $\underline{\Omega}$ 20% delivery) can be derived by comparing the relative weights of tobacco burnt over fixed time intervals (in this case 5 minutes) when cigarettes are allowed to burn freely in the holder as opposed to being smoked in a standard fashion (i.e. fixed number of puffs, duration of puffs, negative pressure of puffs, inter-puff interval and total burning time including puffing time). Thus, comparison of tobacco weight burnt when a cigarette is allowed to burn freely in the holder with the tobacco weight burnt when the same type cigarette is puffed through the holder over the same time interval, allows the calculation of a value for the extra weight of tobacco burnt which is ascribable solely to puffing. Further, comparison of variations for this latter value between cigarettes smoked in different ventilated holders enables the calculation of the relative reduction in nicotine delivery caused by dilution of the smoke with air from the filter vent.

A small experiment was carried out to demonstrate that this method for estimating tar/nicotine delivery is sensitive and accurate. The weight losses of a sample of cigarettes were compared when burning freely in ventilated holders and when subjected to standardised smoking. A simple smoking 'robot' was constructed consisting of a single cylinder, electrically driven (rotary cycle) suction pump which could provide a fixed negative pressure for a certain duration of time - the withdrawal of the piston from the cylinder mimicing the expansion of the lungs during smoking. Each cigarette was 'puffed' ten times, the first five puffs being at 20 second intervals, the last five at 30 second intervals in order to approximate the increase in inter-puff interval during

smoking observed in this and other experiments (see Figure 8). The rate and maximum depth of withdrawal of the piston from the cylinder was adjusted by trial and error in order to obtain an increased weight of tobacco burnt equivalent to that produced by human smoking of the same type of cigarette, through a 100% cigarette holder, over five minutes. A comparison of the tobacco weight losses obtained by robot smoking and actual smoking in the experiment (Table 1 below and Table 10 in the Results section for the 100% filter) shows that tobacco weight losses and number of puffs produced by machine smoking are similar to those observed during smoking by subjects in the present experiment. It is therefore reasonable to assume that the smoking machine produced a fair approximation to the average smoking style for 100% filter. By means of repeating this procedure with the same pump settings but using a 20% filter an estimate is made of the loss of smoking efficiency caused by dilution of the smoke from the filter vent. This in turn can be compared to the manufacturer's estimates which are based on direct chemical analyses of tar/nicotine concentrations in the smoke.

This derivation of a value for the filter efficiency of the 20% Medac filter closely agrees with the manufacturers estimate[2]. The "extra" 7.2% filtering capacity inherent in the manufacturer's estimate compared with that derived from tobacco weights is probably due to the fact that a certain degree of tar/nicotine is deposited in the condenser and never leaves the filter. This is treated as a small and relatively constant 'error' for the purposes of this experiment.

Recording procedures

Heart rate, respiration rate, depth of inhalation and EEG 'α' were recorded as detailed in Experiments 3 and 4. SC was recorded as in

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[2] Tar and nicotine reductions estimated in Hazleton Laboratories (UK), Fitelson Laboratories (USA), Laboratoire Chimique du Doctor L. Herzfeld (CH).

TABLE 1

Sensitivity of tobacco weight burnt as a means for assessing filter efficiency

Filter	Mean weight of tobacco burnt in 5 mins, zero puffs. Wf[1] (g)		Mean weight of tobacco burnt in 5 mins, 10 puffs. Wp (g)		Δg = Wp - Wf (Wf = .350)
	m	SD	m	SD	
100%	.355	.035	.475	.050	.125
20%	.345	.064	.384	.055	.034

[1](mean Wf = .350g)

($\bar{m}$ weight cigarettes = 1.066, SD = .046, n = 14)

$$\text{Efficiency of 20\% filter in terms of 100\% filter} = \frac{\Delta g\ 20\%}{\Delta g\ 100\%} \times 100\% = 27.2\%$$

Experiment 3 using slightly larger effective electrode area, and light abrasion of the skin surface prior to thorough cleaning with 10% alcohol in water. This technique was judged advisable since the results in Experiment 4 indicated that the use of small electrodes and not abrading the skin reduces intersession reliability for SCL. Tobacco weight was measured as in Experiment 3.

Scoring procedures

Heart rate, respiration rate, SCL, SFs, and EEG 'α' were scored as detailed in Experiment 3. Puffing rate, tobacco burnt weight, and depth of inhalation was scored as in Experiments 1 and 2. The results of Experiment 2 indicated that depth of inhalation as assessed from a Hg strain gauge around the chest was a fairly accurate measure of inhalation volume as measured directly by spirometer. Although non-linearities of Hg strain gauge as a measure of inhalation were observed in some subjects, since subjects in this experiment were acting as their own controls this potential distortion of inhalation results was ignored for the purposes of simply comparing depth of inhalation of smoke from high as opposed to low nicotine delivery holders.

Subject procedures

Ten habitual smokers were recruited by word of mouth and advertisement. Subjects received standard payment after the experiments. Each subject was familiarised with the test room and electrodes procedure during recruitment a few days prior to the experiment. Subjects were habituated to the effects of the cigarette holder and to a middle range nicotine cigarette by smoking 1.3 mg cigarettes in a 100% holder in the days prior to the first and second experimental sessions. Subjects were re-tested at the same time of day, same day of the week and for women subjects not during the week of actual menstruation. All subjects were

requested not to smoke or drink tea/coffee for one hour and not to drink alcohol for twenty-four hours immediately prior to each experimental session. Subjects were informed that the purpose of the experiment was to examine the effects of cigarette smoking on brain activity and that the reason for cigarette holders was to standardise smoking between subjects. Subjects were not informed that the nicotine delivery would be varied by means of the holder. In practice, it appeared from questioning after the experiment that subjects noticed that cigarettes seemed 'weaker' or 'cooler' during the low nicotine condition although most subjects stated that cigarettes 'tasted' the same (presumably because it was the same brand of cigarette in each case).

Subjects were instructed to smoke so as to gain maximum enjoyment, they were not made to feel that they had to smoke a lot or a little but simply smoke as much of the cigarette as they liked. Subjects were requested to inhale all the smoke that they puffed, this was verified during the experiment by direct observation through one-way window, together with simultaneous observation of Hg strain gauge output to check for inhalation.

Subjects lay prone on a bed with their heads supported by a pillow. The room was warm, sound dampened and light level was at a constant low level.

Each subject completed two experimental session during each of which he/she smoked two 1.8 mg cigarettes, one session using a 100% holder (high nicotine condition), the other using a 20% holder (low nicotine condition). The order of these sessions was randomised between subjects. Each session followed the same pattern, apart from changes of holder. After 20 minutes relaxation, the last five minutes of which

were recorded as pre-smoking baseline, subjects were instructed over an intercom to start smoking. Five minutes after lighting up they were instructed to stub out their cigarettes. A further seven minutes of recording were taken. Subjects were then free to move around and chat with the experimenter for ten minutes, during which they could drink a small cup of orange squash if they so desired. Any smoke in the test room was cleared with an extractor fan. Following this the same cycle, relaxation, smoking,relaxation,was repeated.

RESULTS

1 Personality and cigarette consumption.

2 Reliabilities of pre-smoking baseline

3 Main effects of smoking on physiological measures irrespective of nicotine strength.

4 Comparison between high and low nicotine delivery physiological effects.

5 Smoking style difference between high and low nicotine:

(i) Overall differences

(ii) Calculated titration efficiency.

Personality and Cigarette Consumption

Perusal of Table 2 reveals that personality scores (Eysenck, 1975) and cigarette consumption of the subject sample (n = 10) of the present experiment are similar to those recorded for the subject samples in Experiments 1, 2, 3 and 4.

Reliabilitity of Baseline (Pre-Smoking) Measures.

(RESP, HR, SFs, SCL, EEG 'α')

Since the main object of this experiment is to compare the direction and magnitude of the effects of varying nicotine delivery of cigarettes and since high versus low nicotine cigarettes are smoked on different sessions it is necessary that the pre-smoking baselines of the various measures (RESP, HR, SFs, SCL, EEG 'α') be as near identical as possible between the High and Low nicotine sessions. This is especially necessary for the study of the effects of cigarette smoking since there

TABLE 2

Personality and Cigarette Consumption

Variable	m	SD
Cigarettes per day	18.2	(6.5)
P	7.4	(3.1)
E	10.4	(2.7)
N	12.9	(3.6)
L	3.9	(2.2)
Age range years	19–28	

(Marginal Significances in Brackets and Standard Deviations)

Variable	FIRST CIGARETTE					SECOND CIGARETTE				
	High Nicotine Mean (S.D.)	Low Nicotine Mean (S.D.)	T-Test 2-Tailed Pairs DF = 9	Pearson Corr. Coeff.	P	High Nicotine Mean (S.D.)	Low Nicotine Mean (S.D.)	T-Test 2-Tailed Pairs DF = 9	Pearson Corr. Coeff.	P
Respiration Rate (b.p.m.)	16.5 (2.8)	16.1 (3.1)	N.S. F = 1.23 N.S.	.77	.009	15.1 (5.9)	15.9 (5.0)	N.S. F = 1.39 N.S.	.93	.0001
Heart rate (b.p.m.)	69.6 (7.5)	67.9 (9.9)	N.S. F = 1.74 N.S.	.93	.001	77.0 (10.0)	71.6 (10.6)	.024 F = 1.12 N.S.	.82	.004
Spontaneous Fluctuations	21.2 (19.4)	22.4 (20.8)	N.S. F = 1.06 N.S.	.92	.0001	13.4 (14.3)	13.3 (12.8)	N.S. F = 1.25 N.S.	.89	.001
Skin Conductance (µmhos)	19.8 (8.3)	18.2 (6.6)	N.S. F = 1.58 N.S.	.84	.003	24.2 (12.7)	20.4 (8.6)	N.S. F = 2.18 N.S.	.68	.031
EEG Alpha (% Time>Criterion)	16.2 (13.3)	17.0 (14.2)	N.S. F = 1.02 N.S.	.75	.012	12.3 (10.9)	19.2 (24.5)	N.S. F = 5.05 P = 5% 2-Tailed	.55	(.102)

TABLE 3

TABLE 3 (Continued)

F ratios PRE-smoking baseline comparisons - High versus low nicotine sessions

The following changes in variance POST versus PRE smoking are significant:

EEG 'α' (% time criterion); second cigarette, $F = 5.05$; $df = 9,9$; $p < .05$, 2-tailed.

All other F ratios are non-significant.

is evidence (Ashton and Watson, 1970; Ashton et al. 1974) that subject starting state (as determined by personality and situation) may direct patterns of smoking to produce different effects and that the same rate of dose of nicotine may produce different effects depending upon the starting state. The most crude "variable starting state x fixed dose of nicotine" interaction to produce variable effects is that of tachyphylaxis. Other variations possible include the effect of diurnal rythmn (eliminated by re-testing at the same time of day), prior drug usage (tea, coffee, alcohol, etc. hopefully controlled sufficiently by word of honour), habituation to the laboratory environment (by prior familiarisation of the subject with the laboratory environment, and controlled for any systematic effects on results by randomisation of order between high and low nicotine sessions), menstrual cycle amongst women subjects (controlled for by not testing during menstruation) etc. N.B. the test-retest reliability (over one month) of the EPQ is only .80 (Eysenck and Eysenck, 1975).

The reliability of baseline (pre-smoking) measures was examined in two ways - comparison (T-Tests), variance analysis (simple F Ratio), and correlation (Pearson correlation coefficient) between sessions of the mean baseline scores (minutes 1-5, pre-smoking). Examination of Table 3 reveals that all measures; Respiration Rate, Heart Rate, Spontaneous Fluctuations, Skin Conductance and EEG 'α', show good reliability on the pre-smoking first cigarette baseline as indicated by non-significant mean differences (T-Test), non-significant variation differences (F Ratio) and minimum Pearson correlations amongst all measures, $r = .75$, $p = .012$ for EEG 'α'. However, half an hour later (post light-up of first cigarette) the between session baseline reliabilities of these measures deteriorated to the extent that a significant baseline heart rate difference ($p < .024$),

a significant change in variance EEG 'α' ($p = .05$) and a non-significant EEG 'α' correlation (p = .102) occurred prior to the second cigarette. This is no doubt (see Figures 2, 3, 4) due to the lingering differential effects of the first high and low nicotine cigarettes as reflected by the significantly elevated heart rate pre-second cigarette baseline for the high nicotine condition. This view is supported by the fact that unlike other measures respiration rate and SFs reliabilities showed little change over the session - cigarette smoking has the least effect on respiration rate of all measures and thus variations in nicotine delivery of the first cigarette predictably do not differentially perturb the second cigarette baseline for respiration rate (the same being true to a lesser extent for SFs).

Main Effects of Cigarette Smoking on Psychophysiological Measures Irrespective of Nicotine Strength

In general terms the results for the effects of cigarette smoking appear to be stimulant, resembling those effects observed for smoking during sensory isolation in Experiments 1, 2, and 3. Thus, for both high and low nicotine conditions, cigarette smoking significantly increases heart rate (both mean and peak), significantly increases SCL (for peak but not mean), and significantly decreases EEG 'α', while having no significant overall effect on respiration rate or SFs (cf. Table 4). There is some evidence that the effects of smoking the second cigarette (whether high or low nicotine) are not so pronounced as the first cigarette. The second cigarette produces only half the heart rate elevation that the first cigarette produces, irrespective of nicotine strength. The diminution of smoking effect on EEG 'α' is even more marked, the second cigarette producing no significant stimulant effects. This is doubtless due to tachyphylaxis (rapid receptor tolerance), a well known phenomenon for

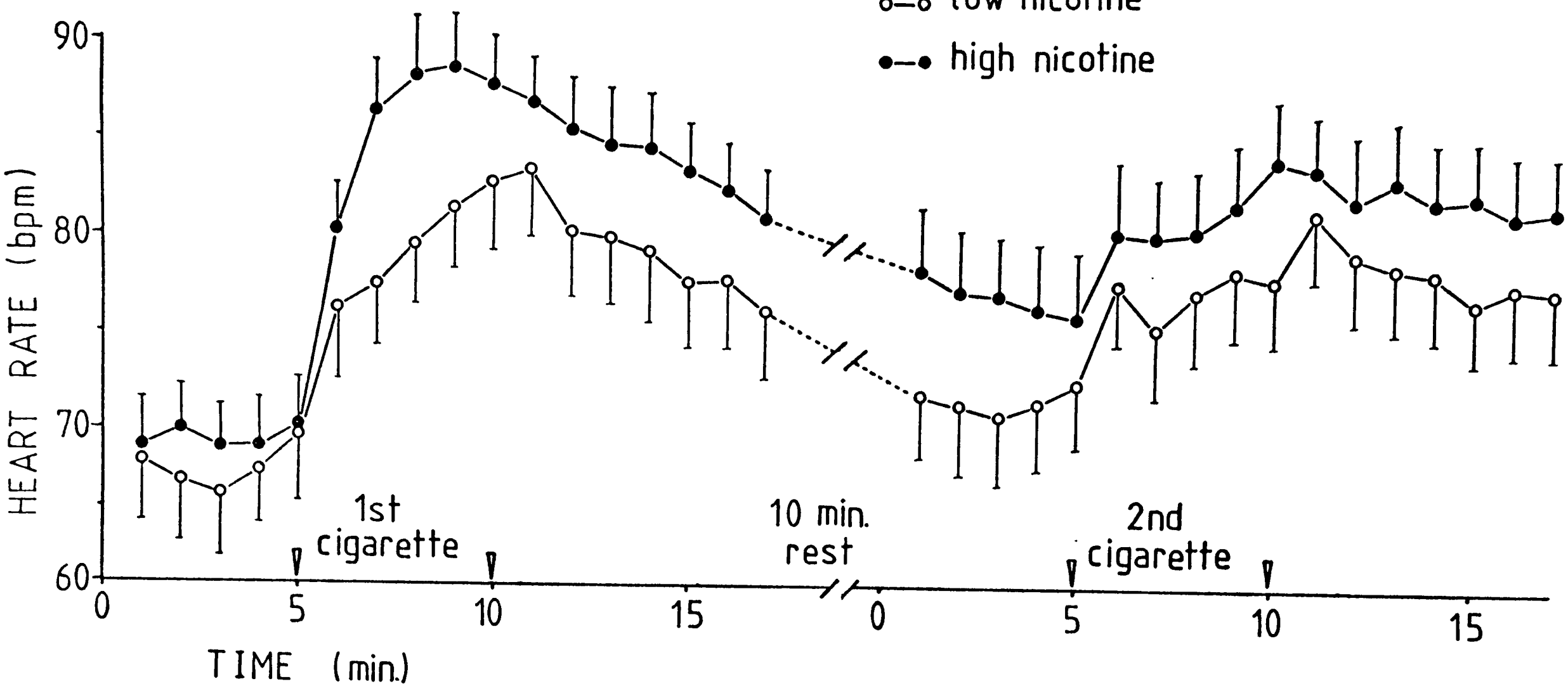


FIGURE 2 : Mean Heart Rate (S.E. bars) versus Time for (n = 10) subjects smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

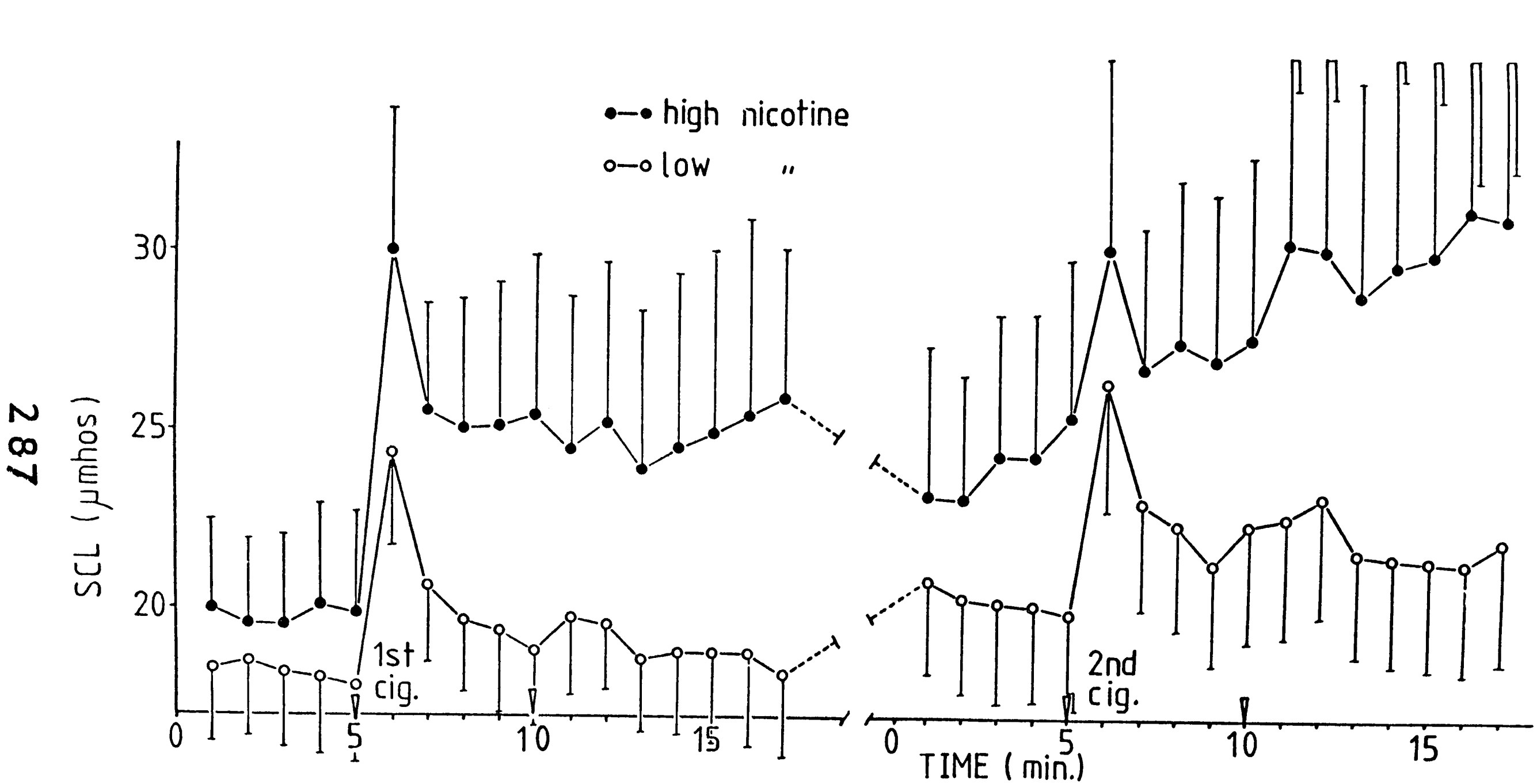


FIGURE 3 : Mean SCL (S.E. bars) versus Time for (n = 10) subjects smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

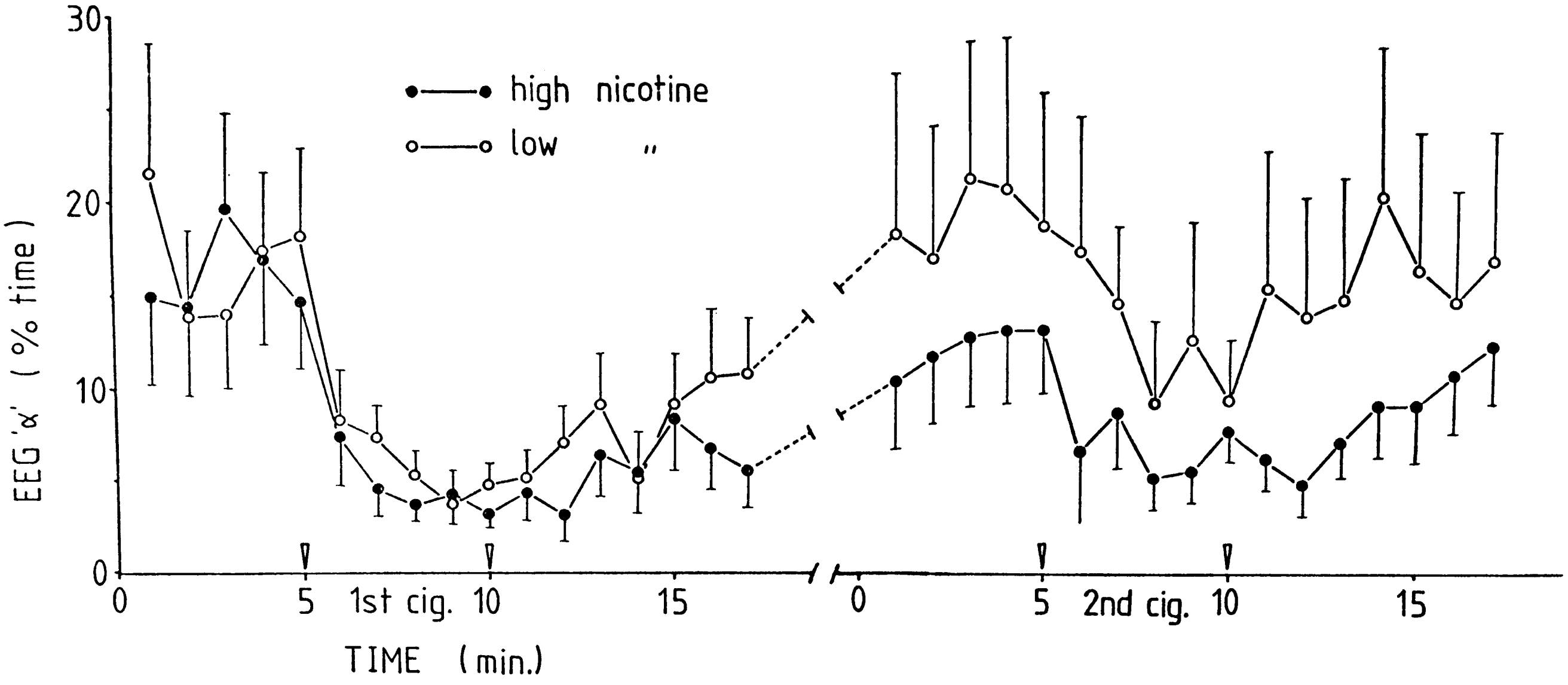


FIGURE 4 : Mean EEG 'α', % time > criterion, (S.E. bars) versus Time for (n = 10) subjects smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

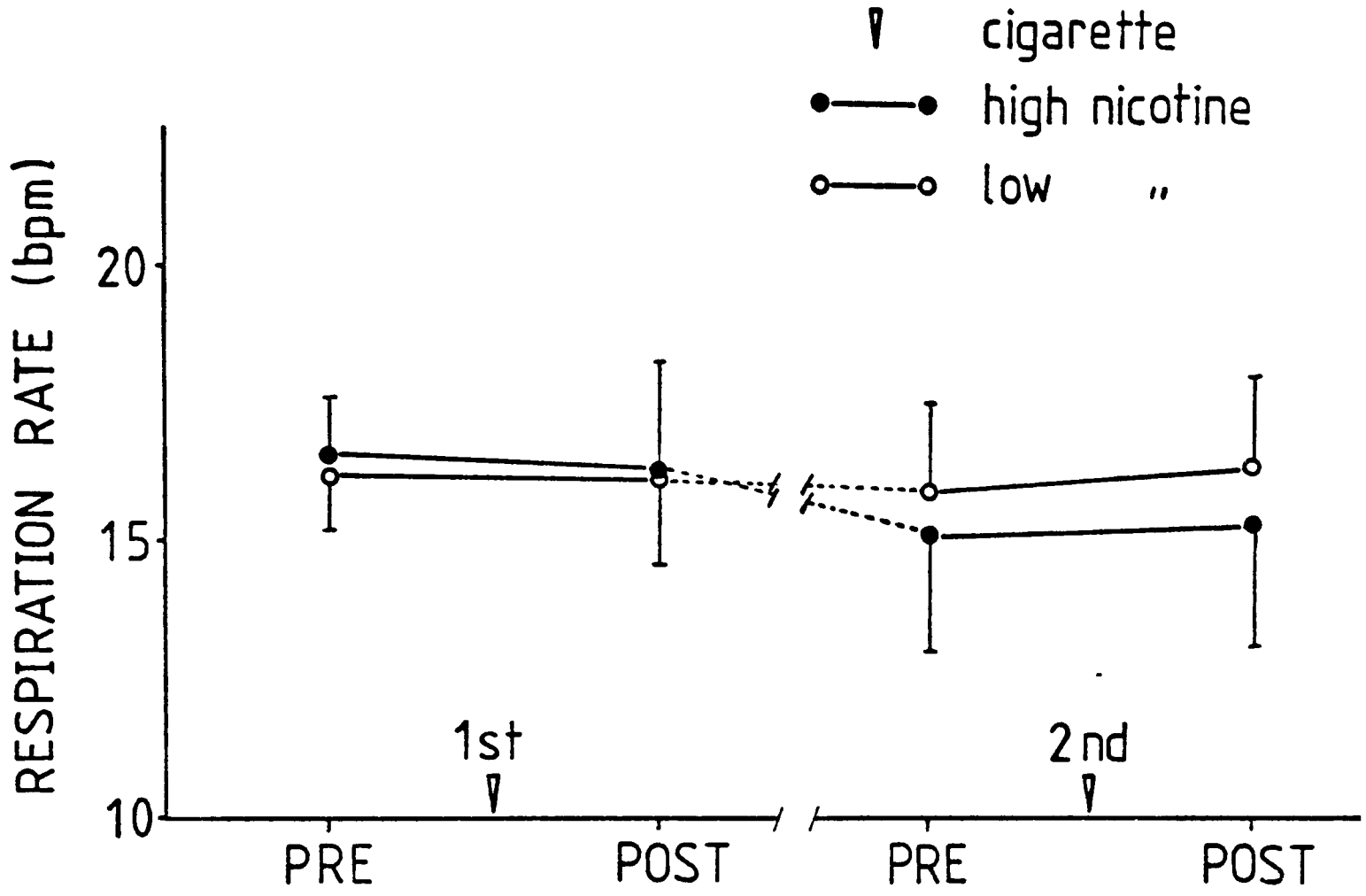


FIGURE 5 : Mean Respiration Rate (S.E. bars) for (n = 10) subjects, PRE and POST smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

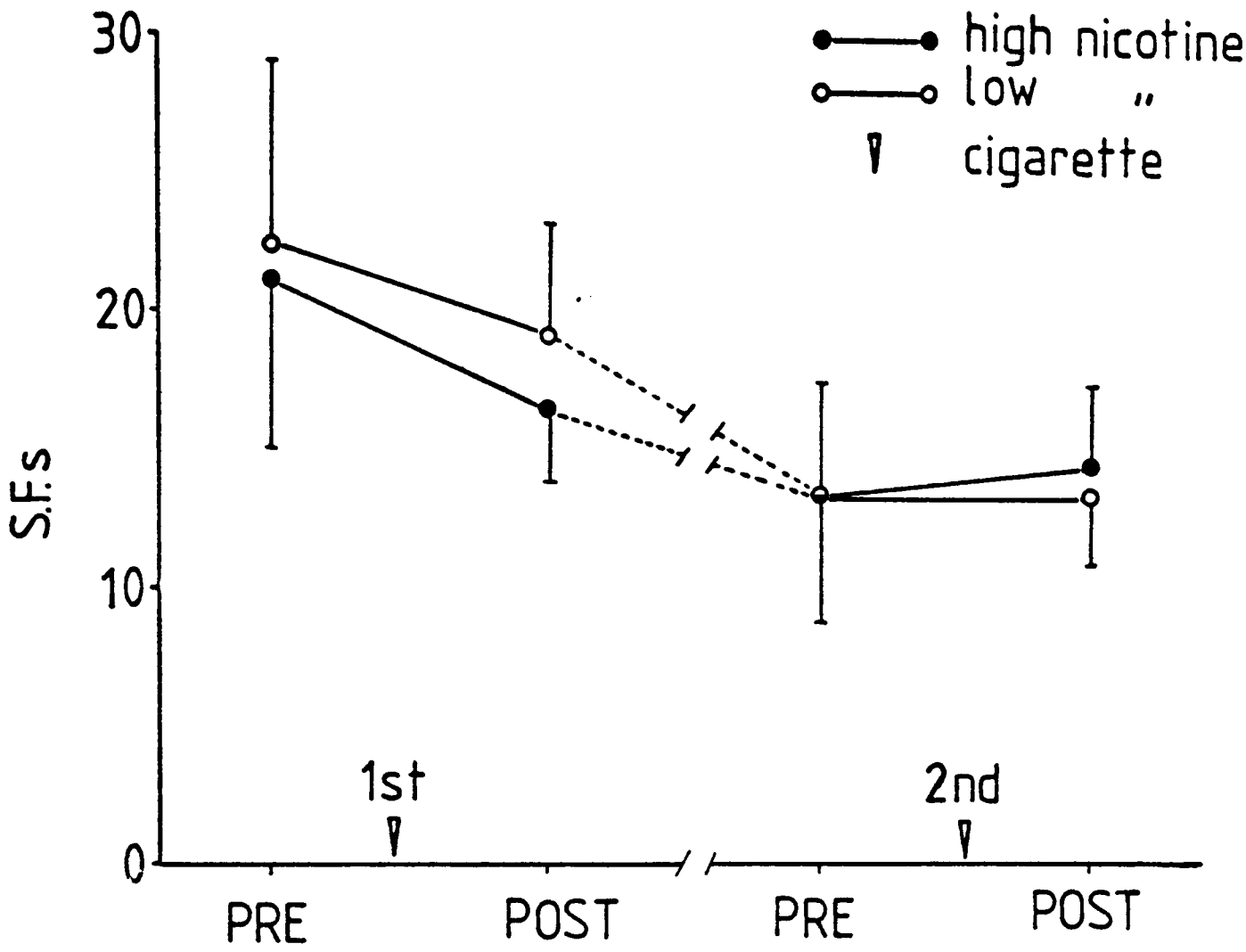


FIGURE 6 : Mean Spontaneous Fluctuations S.F.s (S.E. bars) for (n = 10) subjects, PRE and POST smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

VARIABLE	HIGH NICOTINE CIGARETTE								LOW NICOTINE CIGARETTE							
	First Cig. PRE	First Cig. POST	Δ POST-PRE	T-test P	Second Cig. PRE	Second Cig. POST	Δ POST-PRE	T-test P	First Cig. PRE	First Cig. POST	Δ POST-PRE	T-test P	Second Cig. PRE	Second Cig. POST	Δ POST-PRE	T-test P
Respiration Rate (b.p.m.)	16.5 (2.8)	16.1 (5.6)	-.4 (4.1)	NS	15.2 (5.9)	15.3 (6.1)	.1 (.8)	NS	16.2 (3.1)	16.2 (4.7)	0.0 (3.0)	NS	16.0 (5.0)	16.4 (4.7)	.4 (3.6)	NS
Heart Rate (b.p.m.) Mean Post-Smoking	69.5 (7.5)	87.4 (7.9)	17.9 (4.7)	.0001	77.0 (10.0)	83.7 (9.1)	6.7 (2.4)	.0001	67.9 (9.9)	83.2 (10.5)	15.3 (6.7)	.0001	71.6 (10.6)	79.5 (10.2)	7.9 (4.1)	.0001
Heart Rate (b.p.m.) Peak	69.5 (7.5)	92.0 (7.4)	22.5 (3.8)	.0001	77.0 (10.0)	86.2 (9.2)	9.2 (3.4)	.0001	67.9 (9.9)	85.2 (10.4)	17.3 (6.6)	.0001	71.6 (10.6)	81.5 (10.3)	9.9 (4.9)	.0001
Spontaneous Fluctuations	21.2 (19.4)	16.6 (8.4)	-4.6 (21.3)	NS	13.4 (14.2)	14.6 (9.3)	1.2 (12.4)	NS	22.4 (20.8)	20.1 (13.0)	-2.3 (10.6)	NS	13.3 (12.8)	13.4 (7.2)	.1 (10.4)	NS
Skin Conductance (μmhos) Peak Smoking	19.8 (8.3)	30.5 (12.7)	10.7 (6.6)	.001	24.2 (12.7)	30.2 (17.4)	6.0 (6.2)	.012	18.2 (6.6)	24.4 (8.0)	6.2 (3.7)	.001	20.4 (8.6)	26.5 (11.5)	6.1 (4.8)	.003
Skin Conductance (μmhos) Mean Post-Smoking	19.8 (8.3)	24.7 (14.8)	4.9 (10.5)	NS	24.2 (12.7)	29.9 (20.6)	5.7 (14.8)	NS	18.2 (6.6)	19.2 (6.8)	1.0 (1.9)	NS	20.4 (8.6)	22.2 (9.9)	1.8 (3.0)	(.093)
EEG 'alpha' (% Time>Criterion)	16.2 (13.3)	5.7 (5.6)	-10.5 (8.4)	.0001	12.3 (10.9)	8.4 (7.1)	-3.9 (8.6)	NS	17.0 (14.3)	8.2 (6.4)	-8.8 (9.4)	.016	19.2 (24.5)	15.9 (22.0)	-3.3 (7.6)	NS
EEG 'alpha' (Range Corrected % Time>Criterion)	1.00 (0.0)	0.27 (0.19)	-.73 (0.19)	.0001	2.57 (4.9)	1.63 (2.6)	-94 (3.3)	NS	1.00 (0.0)	0.73 (0.63)	- .27 (0.63)	NS	1.12 (0.65)	1.00 (0.87)	- .12 (0.47)	NS

(S.D.s and Marginal Significances in Brackets)

TABLE 4

Paired 'T'-Tests on Main Effects POST versus PRE smoking DF = 9, 2-Tailed

TABLE 4 (Continued)

F ratios POST versus PRE Smoking

The following changes in variance POST versus PRE smoking are significant:

Respiration Rate; First High Nicotine Cigarette: a significant increase in variance $F = 4.0$; $df = 9,9$; $p < .05$; 2-tailed

Spontaneous Fluctuations; First High Nicotine Cigarette: a significant decrease in variance $F = 5.33$; $df = 9,9$; $p < .05$; 2-tailed

EEG 'α' (%time>criterion); First High Nicotine Cigarette: a significant decrease in variance $F = 5.64$; $df = 9,9$; $p < .05$; 2-tailed

EEG 'α' (%time>criterion); First Low Nicotine Cigarette: a significant decrease in variance $F = 4.99$; $df = 9,9$; $p < .05$; 2-tailed

EEG 'α' (range corrected); Variance Analysis not applicable since range correcting affects variance.

All other F ratios are Non-Significant.

nicotine (Frankenhaeuser et al. 1968). There is also some slight evidence from burnt tobacco weight that smokers took less from the second cigarette (cf. Smoking Style results), so that the attenuated smoking effect for the second cigarette may be due to a combination of both reduced nicotine intake and tachyphylaxis, the latter effect probably being the most important.

Table 5 gives the correlations between the two measures of smoking induced heart rate elevation, peak heart rate elevation and mean heart rate elevation. In general terms, mean heart rate elevation, although lower than peak heart rate elevation (cf. Table 4), predicts the latter measure very well, since all peak x mean correlations are significant (cf. Table 5).

Other points of interest are revealed in the F ratio results (cf. Table 4). It appears that while having no significant effect on the mean, the first high nicotine cigarette significantly increased the variance of respiration rate. This would indicate that a sufficiently heavy dose of nicotine will effect respiration rate, although the direction of effect (stimulant,depressant) varies between individuals. By contrast the first cigarette reduces variance for SF rate and EEG 'α', this being significant for both first high and first low nicotine cigarettes in the case of EEG 'α', but only for first high nicotine cigarette in the case of SFs (a large variance reduction of SFs does occur for first low nicotine but this just fails significance, cf. Table 4). This significant variance reduction of EEG 'α' and SFs might be likened to a 'ceiling' or 'Law of Initial Values' effect. Figure 4 illustrates this very nicely, the S.E. bars for EEG 'α' literally appear to be squeezed against the X (Time axis) by the first cigarettes. This type of effect has been noted by EEG workers, some authors suggesting that for alpha

TABLE 5

Correlation between two measures of smoking induced heart rate elevation: Peak heart rate elevation x Mean heart rate elevation

Source of heart rate elevation	N	Mean heart rate elevation x peak heart rate elevation r_p	P
High nicotine first cigarette	10	+ .66	.05
High nicotine second cigarette	10	+ .87	.01
Low nicotine first cigarette	10	+ .98	.001
Low nicotine second cigarette	10	+ .84	.01

it is advisable to use log transformations (Cooper, Osselton and Shaw, 1974). This simple scaling problem has some relevance.

A slightly different type of data analysis (range-correcting) reveals that the effect of cigarette smoking on the EEG is less evident after this treatment of the data (cf. EEG 'α' scores, Table 4 , Figure 4 and 7). In other words, those individuals with the largest EEG 'α' scores show the greatest degree of stimulant effect from cigarette smoking. Given that some individuals show depressant EEG 'α' (or SF) reactions to cigarette smoking, and that these tend to be individuals who are expressing very high basal arousal (low EEG 'α', high SFs), the interpretation of overall smoking effect i.e. stimulant or depressant may depend markedly on the particular type of data processing used.

Consideration of Pre x (Post-Pre) correlations for EEG 'α' and SFs which support similar findings in Experiment 4, demonstrates this point again. Negative Pre x (Post-Pre) correlation coefficients indicate that the higher the pre-smoking level of arousal, the more likely it is that an individual will show depressant responses to smoking and vice versa (cf. Table 6).

If the results for SFs and EEG 'α' are considered in terms of smoking induced change in means and variance together with Pre x (Post-Pre) correlations, then one can see that the SFs and EEG 'α' results conform very closely to two of the hypothetical cases postulated in Experiment 4. The first cigarette effects are similar to 'type (b)', those for the second cigarette being similar to 'type (c)' (cf. Figure 1, Experiment 4).

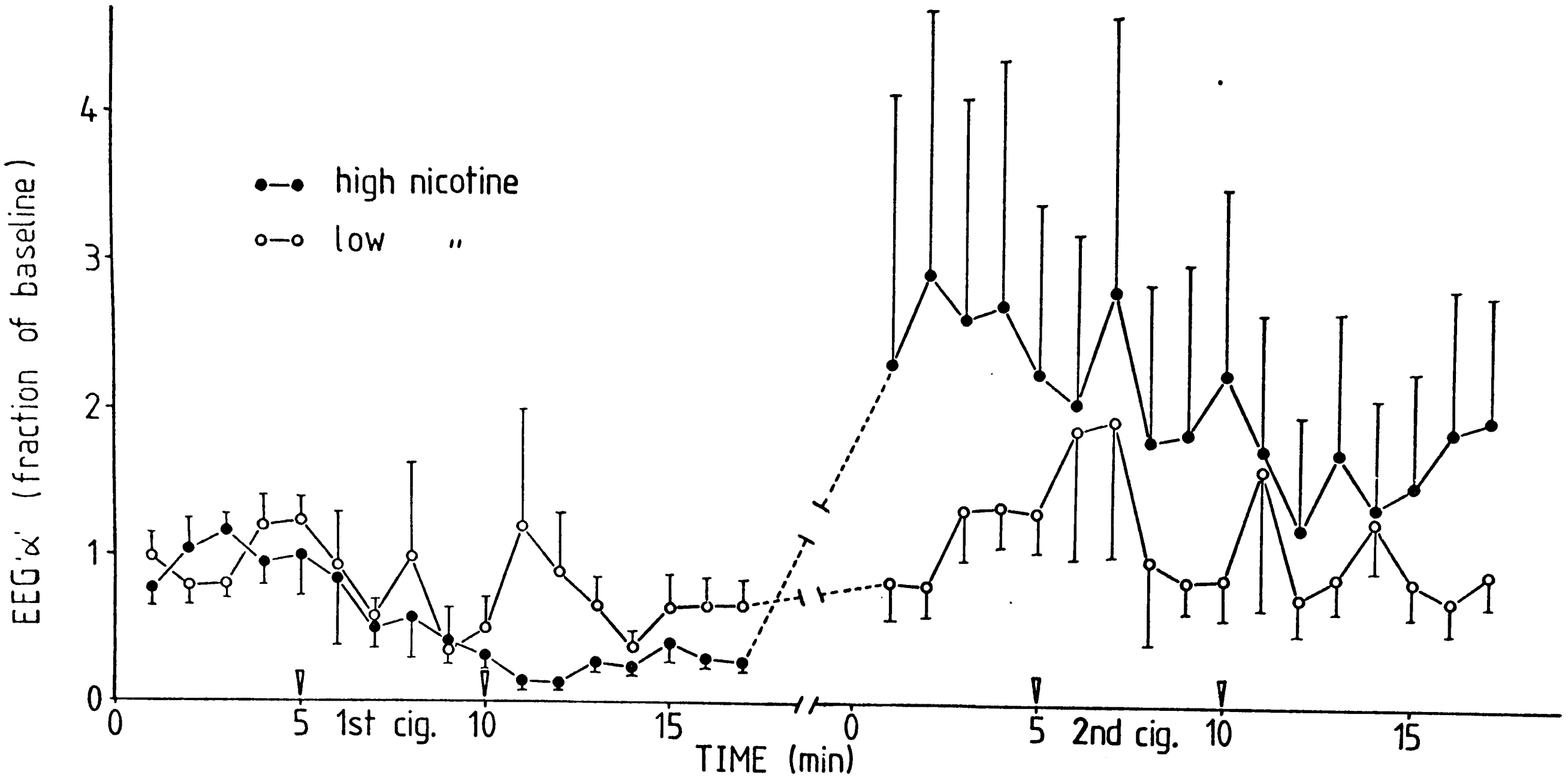


FIGURE 7 : EEG 'α' (fraction of baseline, S.E. bars) versus Time for (n = 10) subjects smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

TABLE 6

PRE x (POST-PRE) correlations for EEG 'α' and SFs

Activity		N	SFs		EEG 'α'	
			r_p	P	r_p	P
High Nicotine	1st cigarette	10	-.92	***	-.96	***
	2nd cigarette	10	-.77	**	-.81	**
Low Nicotine	1st cigarette	10	-.85	***	-.95	***
	2nd cigarette	10	-.83	**	-.42	N.S.

* p < .05
** p < .01
*** p < .001

DF = 9

Comparison between high and low nicotine delivery for effects of cigarette smoking on physiological measures

High and low nicotine delivery cigarette effects on the various psychophysiological measures are compared on the basis of magnitude (means) and scatter (F ratio), (cf. Table 7).

It is apparent that the higher nicotine delivery cigarette is producing greater effects on heart rate, SCL, and EEG 'α', for the first cigarette but not for the second cigarette. However, none of the comparisons of means between high and low nicotine delivery cigarettes achieve significance at the 5% level apart from peak heart rate elevation for the first cigarette ($p = .014$, cf. Table 7). The most striking feature of the high versus low nicotine comparisons is in fact the lack of almost any significant difference in magnitude of smoking effect. This in spite of the fact that the predicted variation in nicotine delivery was 5 : 1, i.e. 1.8 mg : 0.36 mg nicotine. 'Extra' variables (heart rate peak, latency to peak heart rate, peaking of SC, post smoking drop in heart rate) were calculated from the data in the attempt to produce some significant high versus low nicotine comparison, of these only peak heart rate significantly discriminated high versus low nicotine, and then only for the first cigarette.

The attempt to find significant differences between high and low nicotine effects on the basis of scatter (F ratio) was more successful. Four significant F ratios occurred (cf. Table 7). While no significant differences in mean change (Post-Pre) of respiration rate occurred, the smoking effect for the second low nicotine delivery cigarette had significantly greater variance than the variance for the second high nicotine effect. The meaning of this is unclear, however, it might be noted that where significant differences in respiration rate have previously

VARIABLE	FIRST CIGARETTE			SECOND CIGARETTE		
	High Nicotine Mean (S.D.)	Low Nicotine Mean (S.D.)	Paired T-test 2-Tailed DF = 9	High Nicotine Mean (S.D.)	Low Nicotine Mean (S.D.)	Paired T-test 2-Tailed DF = 9
Heart Rate Elevation (POST-PRE) - Mean (b.p.m.) (Mins. [9 + 10]/2)	+ 17.9 (4.7)	+ 15.2 (6.7)	(.072)	+ 6.7 (2.4)	+ 7.9 (4.1)	N.S.
Heart Rate Elevation (PEAK-PRE) - Peak (b.p.m.)	+ 22.5 (3.8)	+ 17.3 (6.6)	.014	+ 9.2 (3.5)	+ 9.9 (4.9)	N.S.
Latency to Peak H.R. (Mins Post Light-Up)	4.4 (2.0)	4.5 (2.1)	N.S.	5.6 (1.6)	4.5 (2.4)	N.S.
Post Smoking Drop in Heart Rate (Mins [9 + 10] to [16 + 17]/2 b.p.m.)	- 5.7 (5.3)	- 6.2 (3.9)	N.S.	- 2.5 (3.4)	- 2.1 (3.2)	N.S.
Respiration Rate Change (Post-Pre)(b.p.m.)	- 0.4 (4.8)	0.0 (3.0)	N.S.	+ 0.2 (.8)	+ 0.5 (3.6)	N.S.
Spontaneous Fluctuations Change (Post-Pre)	- 4.6 (21.3)	- 2.3 (10.6)	N.S.	+ 1.2 (12.4)	+ 0.1 (10.4)	N.S.
Rise in Skin Conductance: Peaking to Light-Up (mins 6 - PRE) (µmhos)	+ 10.7 (2.1)	+ 6.2 (1.2)	N.S. (.102)	+ 6.1 (6.2)	+ 6.1 (4.8)	N.S.
Rise in Skin Conductance (Post-Pre) (µmhos)	+ 4.9 (10.5)	+ 1.0 (1.9)	N.S.	+ 5.7 (14.8)	+ 1.8 (3.0)	N.S.
Change in EEG 'α' Post-Pre (%Time of Criterion α)	- 10.5 (8.4)	- 8.8 (9.4)	N.S.	- 3.9 (8.6)	- 3.3 (7.6)	N.S.
Change in EEG 'α' Post-Pre (Range corrected % Time of Criterion α)	- .73 (.06)	- .27 (.20)	(.067)	- .94 (3.30)	- .12 (0.47)	N.S.

(Marginal Significances in brackets)
(Standard Deviations [S.D.] in brackets below each mean)

TABLE 7

Paired 'T' Tests between High and Low nicotine on First and Second Cigarettes (Comparison of High versus Low Nicotine Cigarettes)

TABLE 7 continued

F ratios on smoking-induced changes for High versus Low Nicotine Cigarettes: (POST-PRE) High Nicotine versus (POST-PRE) Low Nicotine

The following changes in variance for (POST-PRE) High versus Low Nicotine cigarette smoking are significant:

Respiration Rate; Second Cigarette, High versus Low Nicotine (POST-PRE); significantly greater variance for Low:

$F = 20.25$; $DF = 9,9$; $p < .05$; 2-tailed

Spontaneous Fluctuations; First Cigarette, High versus Low Nicotine (POST-PRE); significantly greater variance for High:

$F = 4.04$; $DF = 9,9$; $p < .05$; 2-tailed

SCL; First Cigarette, High versus Low Nicotine (POST-PRE); significantly greater variance for High:

$F = 30.54$; $DF = 9,9$; $p < .05$; 2-tailed

SCL; Second Cigarette, High versus Low Nicotine (POST-PRE); significantly greater variance for High:

$F = 24.34$; $DF = 9,9$; $p < .05$- 2-tailed

All other F ratios are non-significant

occurred these are in terms of variance. The other three significant F ratio results are clearer in interpretation. These indicate that the high nicotine delivery cigarette is producing a greater perturbation of SFs (first cigarette) and SCL (first and second cigarettes) as reflected in the variances for (Post-Pre) smoking effect but not in terms of the means.

In the previous Experiment 4, some evidence was presented that subjects showed consistencies upon re-testing in their physiological reactions to smoking, this being especially marked for cigarette induced tachycardia, a so-called 'Autonomic Fingerpoint'. This is examined in Table 8 and 9; intercorrelations for mean heart rate elevation. The intercorrelations are by and large very low, only mean heart rate elevation for first high x first low nicotine delivery cigarettes producing a significant correlation (r_p = .79, $p < .01$, DF = 8, cf. Table 8). The most likely explanation for the poor intercorrelations is that both the effects of order (first versus second cigarette) and nicotine delivery (high versus low) represent confounding sources of variance. In Experiment 4, intercorrelations for smoking induced heart rate elevation were presumably higher than in the present experiment because the aforementioned sources of 'noise' (i.e. tachyphylaxis produced by the first cigarette perturbing heart rate elevations to the second cigarette, and also high versus low nicotine delivery) were eliminated by design: the same nicotine strength cigarette was smoked under identical conditions (no tachyphylaxis).

Smoking Style Differences Between High and Low Nicotine Delivery Cigarettes

It would appear that subjects adapted their smoking style in the expected direction i.e. they attempted to obtain more tar/nicotine from

TABLE 8

Smoking-induced heart rate elevation (mean) intercorrelations (r_p)

High nicotine first cigarette	(1)	.			
High nicotine second cigarette	(2)	.29	.		
Low nicotine first cigarette	(3)	.79**	.14	.	
Low nicotine second cigarette	(4)	.41	.36	.46	.
		(1)	(2)	(3)	(4)

** $p < .01$ DF = 8

TABLE 9

Latency to peak heart elevation intercorrelations (r_p)

High nicotine first cigarette	(1)	.			
High nicotine second cigarette	(2)	.49	.		
Low nicotine first cigarette	(3)	-.45	-.13	.	
Low nicotine second cigarette	(4)	-.26	.14	.28	.
		(1)	(2)	(3)	(4)

the low nicotine delivery cigarettes[3]. This is reflected by the greater number of puffs and greater depth of inhalation for the low as opposed to high nicotine cigarettes although these comparisons are of marginal significance (see Figure 8,9, Table 10). By contrast there is a small but significant difference for first cigarette and marginal significance for second cigarette in the weight of tobacco burnt for high versus low nicotine delivery. This suggests that smokers are receiving less nicotine from the low delivery holder. In other words, some attempt at compensation for low nicotine delivery occurs in terms of puffing, this is not entirely successful (viz. weight of tobacco burnt) and further compensatory activity is shown in the greater depth of inhalation for reduced nicotine delivery smoke. The critical variable in self regulation of nicotine intake is probably puff pressure rather than number of puffs or inhalation depth. It is difficult to believe that the relatively small and non-significant changes in puffing rate and inhalation depth would be sufficient to compensate for a nominal 5:1 ratio for nicotine delivery between the high versus low nicotine conditions. Efficient compensation by the smoker for the experimental variation of nicotine delivery is obvious from the close similarity of the physiological effects caused by smoking through high and low nicotine delivery holders (cf. previous section of results).

As can be seen (cf. Table 11) there is a tendency for increasing number of puffs to predict increasing weights of tobacco burnt when smoking. However, it should also be noted that even on the highest corre-

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[3] N.B. For ease and clarity of discussion the term 'low nicotine delivery cigarettes' or 'low nicotine condition' refer to 1.8 mg nicotine cigarettes smoked through the 20% delivery holder, and similarly 'high nicotine cigarette' or 'high nicotine condition' refers to 1.8 mg nicotine cigarettes smoked through the 100% delivery holder.

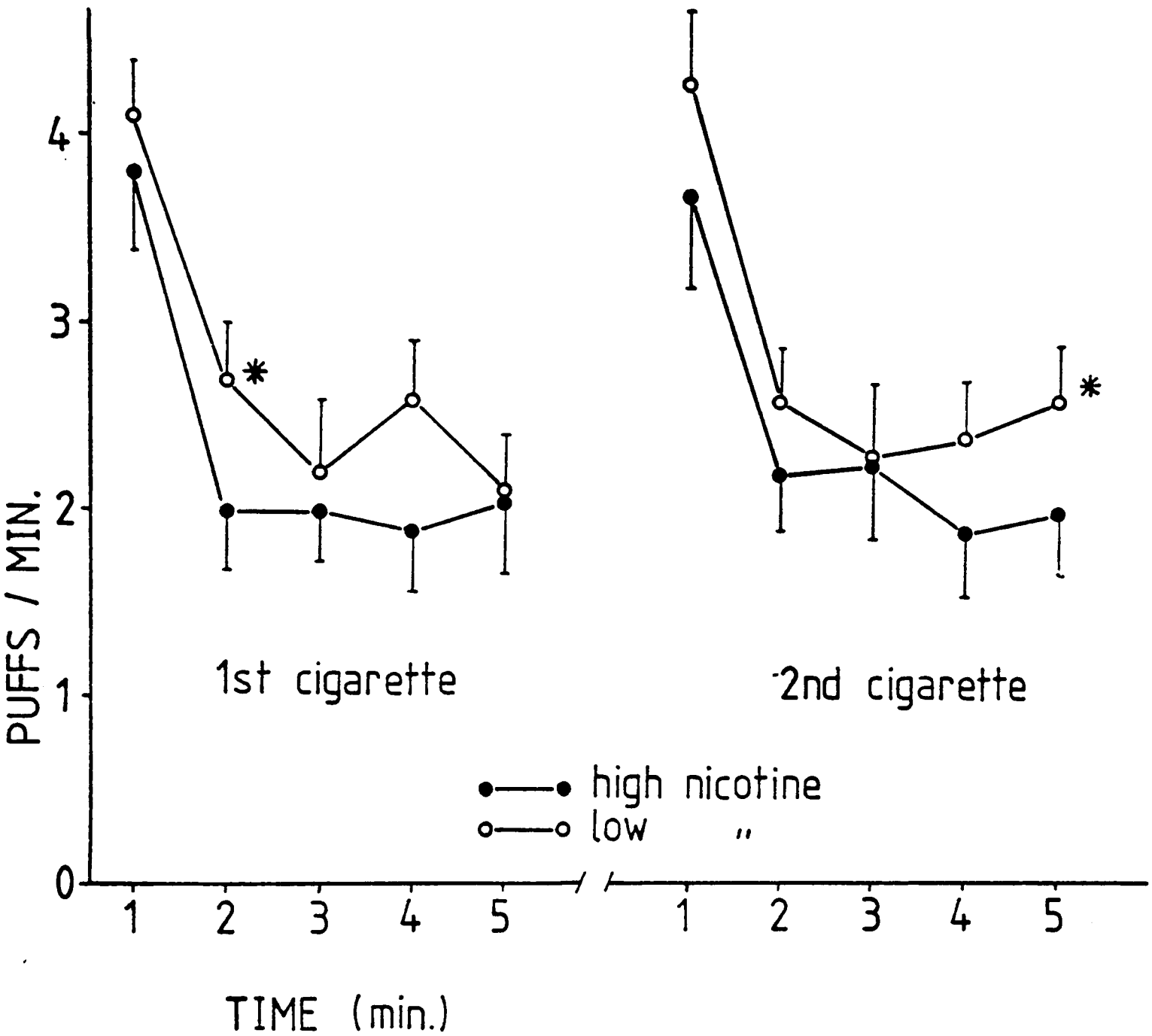


FIGURE 8 : Mean Puffs per minute (S.E. bars) by 1 minute epochs, for (n = 10) subjects smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

(* p = .035, Sign Test, 1-tailed)

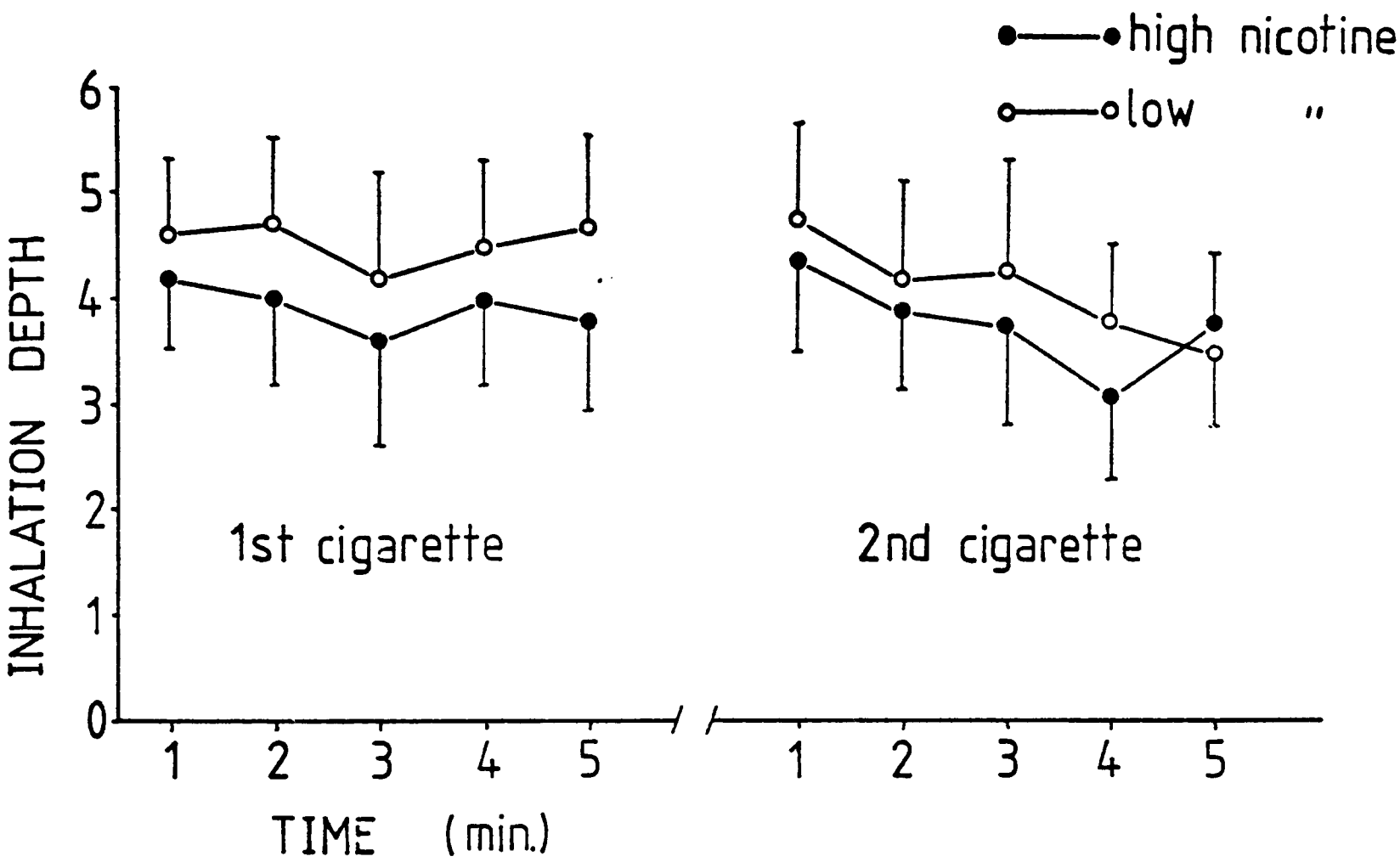


FIGURE 9 : Mean Depth of Inhalation (arbitrary Hg Strain Gauge Units, S.E. bars) by 1 minute epochs, for (n = 10) subjects smoking 2 High and 2 Low Nicotine delivery cigarettes on two experimental sessions.

VARIABLE	FIRST CIGARETTE			SECOND CIGARETTE		
	High Nicotine Mean (S.D.)	Low Nicotine Mean (S.D.)	P High versus Low	High Nicotine Mean (S.D.)	Low Nicotine Mean (S.D.)	P High versus Low
Tobacco Burnt (g)	.538 (.08)	.468 (.066)	.006	.500 (.071)	.461 (.072)	(.098)
Puffs (number)	11.8 (4.9)	13.9 (4.1)	(.081)	12.1 (5.0)	14.2 (5.0)	.017
Inhalation (Arbitrary Hg. Strain Gauge Units)	40.1 (22.5)	45.5 (27.1)	(.087)	39.9 (22.1)	41.2 (26.6)	N.S.

Paired T-Tests, DF = 9, 2-Tailed.

Standard Deviations (S.D.) in brackets below each mean.

Marginal probabilities in brackets.

TABLE 10

Smoking Styles: comparison between high and low nicotine cigarette T-TESTS.

TABLE 11

Correlations between number of puffs and weight of tobacco burnt, taken by subjects smoking the first and second high and low nicotine delivery cigarettes r_p

CIGARETTE	CORRELATION BETWEEN NUMBER OF PUFFS AND WEIGHTS OF TOBACCO BURNT r_p
First high nicotine	.58
Second high nicotine	.62
First low nicotine	.76 *
Second low nicotine	.58

* $p < .05$ DF = 8

lation for puffs x weight of tobacco burnt ($r_p = .76$, $p < .05$, DF = 8; First low nicotine cigarette; cf. Table 11) only 58% of the variance is accounted for. The source of the residual variance is most likely to be the intensity with which each puff is taken. An estimate of a smoker's 'titration efficiency', i.e., the degree to which a smoker can obtain the same amount of nicotine from smoking a cigarette through a high versus a low delivery holder, is given (cf. Table 12), based on the method described earlier (cf. Methodology : 'Estimation of nicotine/tar delivery'). The degree to which smokers are compensating for the filtering effect of the 20% holder is very evident.

Subjects are extracting on average 70%[4] of the nicotine/tar from

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[4] The similarity between the values generated for titration efficiency both on the basis of mean tobacco weights burnt or by taking the mean of individual titration efficiencies, reflects the fact that although the variances for weights of tobacco burnt are quite large (see Table 12) the correlations between tobacco weight burnt are quite high (see Table 14). Thus to take a very simple example one could imagine two sets of data with the same means and variances generating two very different values for any ratio measure depending on the correlation between them. Thus:

Subject	100%	20%	Ratio $20/_{100} \times 100\%$	Subject	100%	20%	Ratio $20/_{100} \times 100\%$
A	1	2	100	A	1	1	100
B	2	3	150	B	2	3	100
C	3	1	33.3	C	3	3	100
$\bar{m}$.	2	2	127.8		2	2	100
S.D.	1	1	85.5		1	1	0

CIGARETTE	TOTAL WEIGHT OF TOBACCO BURNT SMOKING (g) m	SD	WEIGHT OF TOBACCO BURNT ASCRIBABLE TO PUFFING (g)(-.35g)*	TITRATION EFFICIENCY (%) BASED ON GROUP MEANS	BASED ON INDIVIDUAL EFFICIENCES m	SD	PREDICTED FROM SMOKING MACHINE
First 100% Filter	.538	(.080)	.188	62.8	65.7	(40.5)	27.2
First 20% Filter	.468	(.066)	.118				
Second 100% Filter	.500	(.071)	.150	74.0	75.5	(44.4)	27.2
Second 20% Filter	.461	(0.072	.111				

* Weight of Tobacco Burnt Ascribable to Puffing = Total Weight of Tobacco Burnt Smoking − Weight of Tobacco Burnt over 5 mins without any puffing (0.35g)

TABLE 12

'Titration efficiency': calculation of increased extraction of nicotine/tar from cigarettes smoked through 20% versus 100% holders

cigarettes smoked through the low delivery filter than they extracted with the high delivery filter. If they had not engaged in any compensatory activity they would have obtained 27.2% (as predicted on the basis of machine smoking). A further, but less significant boosting of this effect is occurring by the subsequent increased inhalation depth of the tobacco smoke. Some small (non-significant) degree of 'learning' is apparent, the mean titration efficiency increasing from 65.7% for the first cigarette to 75.5% for the second cigarette smoked (cf. Table 12). It is possible that with further practise, subjects could have approached 100% efficiency, i.e. totally overcome the filtering effect of the low delivery holder. However, the most striking feature of the results is the speed with which subjects compensated for the variation of nicotine delivery, a large part of the possible compensatory activity occurring within the time period of first cigarette. This possibly reflects on the speed with which nicotine reaches CNS receptors; for inhalation style smoking this occurs within 10 seconds of smoke inhalation (Russell, 1976). This perhaps enables the smoker to obtain rapid feedback as to the concentration of nicotine in the smoke and so adjust various aspects of smoking style accordingly; primarily intensity of puffing and secondarily the frequency of puffs and depth of inhalation. An additional factor which may be of importance is the concentration of tar particles in the tobacco smoke since these will bear a fairly close relationship to nicotine concentration. Subjects may be using indirect taste and olfactory cues to assess nicotine content of the smoke. This is plausible since some subjects stated that they found the smoke from the low nicotine holder seemed less 'strong' or 'cooler'.

In spite of the compensatory activity indulged in by subjects, smoking high versus low nicotine delivery cigarettes, the idiosyncracies

TABLE 13

Intercorrelations for the number of puffs taken by subjects smoking the first and second, high and low nicotine delivery cigarettes (r_p)

Puffs first high nicotine cigarette	(1)	.			
Puffs second high nicotine cigarette	(2)	.88***	.		
Puffs first low nicotine cigarette	(3)	.74*	.80**	.	
Puffs second low nicotine cigarette	(4)	.81**	.90***	.89***	.
		(1)	(2)	(3)	(4)

* p < .05
** p < .01
*** p < .001

DF = 8

TABLE 14

Intercorrelations for the weight of tobacco burnt by subjects smoking the first and second, high and low nicotine delivery cigarettes (r_p)

Weight of tobacco burnt first high nicotine cigarette	(1)	.			
Weight of tobacco burnt second high nicotine cigarette	(2)	.87***	.		
Weight of tobacco burnt first low nicotine cigarette	(3)	.65*	.74*	.	
Weight of tobacco burnt second low nicotine cigarette	(4)	.47	.56	.93***	.
		(1)	(2)	(3)	(4)

* p < .05
** p < .01
*** p < .001

DF = 8

TABLE 15

Intercorrelations for the depth of inhalation taken by subjects smoking the first and second, high and low nicotine delivery cigarettes (r_p)

Depth of inhalation first high nicotine cigarette	(1)	-			
Depth of inhalation second high nicotine cigarette	(2)	.89***	-		
Depth of inhalation first low nicotine cigarette	(3)	.95***	.82**	-	
Depth of inhalation second low nicotine cigarette	(4)	.86**	.76*	.95***	-
		(1)	(2)	(3)	(4)

DF = 8

* p < .05
** p < .01
*** p < .001

of smoking style appeared to be remarkably consistent across cigarettes. This is revealed by the large numbers of significant intercorrelations between the four cigarettes for number of puffs (cf. Table 13), weight of tobacco burnt (cf. Table 14), and depth of inhalation (cf. Table 15). This indicates that although subjects do change their smoking style in response to the nicotine delivery of the cigarette, they do so in a consistent manner. The marked and relatively stable smoking style idiosyncracies amongst different subjects have been noted previously in the face of the effects of white noise versus sensory isolation (Experiments 1, 2 and 3), in the face of experimental repetition (Experiment 4), and even in the face of the cigarette being unlit - sham smoking x real smoking (Experiment 4).

General Discussion

Overall the most striking feature of the results was the similarity between the physiological effects produced by smoking the low and high nicotine delivery cigarettes. Analysis of smoking style clearly demonstrated why this should be so. Subjects were making significant attempts to extract more nicotine from the low delivery cigarette and the implication of the relatively small increases in puffing rate and depth of inhalation for the low as opposed to high nicotine cigarettes was that increased puff pressure for low nicotine cigarettes was a critical factor. Compensation for smoke dilution in the low nicotine cigarette was large (Titration efficiency' $\underline{\Omega}$ 70% as indicated by weights of tobacco burnt) and rapid (occurring within the time space of the first cigarette).

These results thus strongly support the hypothesis that a smoker aims to obtain some 'optimum' dose of nicotine. This 'optimum' dose of nicotine may represent the correct dose for a particular individual to obtain stimulant rather than depressant effects during a low arousal

situation, this being an 'Arousal Modulation' interpretation. Alternatively, it is possible to argue that the smoker seeks to titrate him or herself with sufficient nicotine to achieve nicotine homeostasis at CNS receptors which signal punishment when nicotine depleted i.e. 'Nicotine Addiction'. The variation in nicotine intake observed in Experiments 1, 2 and 3 to obtain high (depressant) or low (stimulant) doses of nicotine during stress and sensory isolation supports the former interpretation. However, there may be some truth in both types of hypotheses. Figure 10 plots titration efficiency for individual subjects against average cigarette consumption of each subject. Although the overall correlation is small (r_p = +.13, DF = 8, non-significant), the trend in the data (apart from one outlier) is clear. The heavier the smoker, the more efficiently he or she compensates for the smoke dilution by the low delivery holder. This result is best explicable in terms of 'Nicotine Addiction'. The heavier smoker is simply addicted to a higher level of nicotine and thus puts more 'effort' into obtaining his or her 'optimum' nicotine supply in the face of smoke dilution. Judging by the fact that the two heaviest smokers actually appear to extract more from the second low versus second high nicotine cigarette (Titration efficiency > 100%), their extra efforts are well rewarded.

In general terms these results conform to those reported elsewhere using plasma nicotine levels (Sutton, Russell, Feyerabend and Saloojee; 1978) for the effects of ventilated holders. However, subjects in the present experiment are more 'successful' in their self titration for nicotine as judged from the tobacco weight burnt ascribable to puffing and the actual observed physiological responses to smoking. Two possible reasons suggest themselves. Firstly, smokers are no doubt titrating 'downwards' from the nominal 1.8 mg nicotine of the high nicotine cigarette

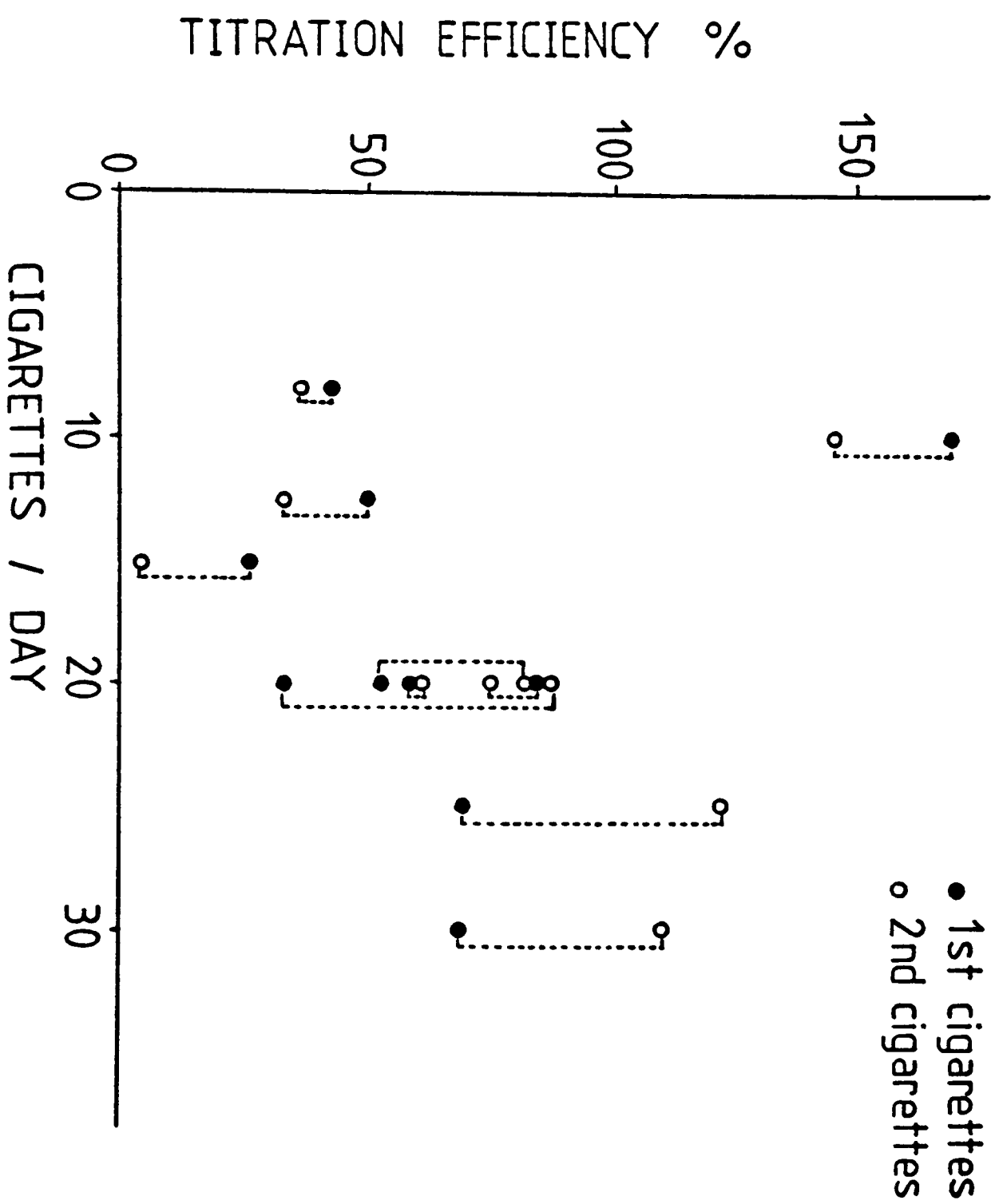


FIGURE 10 : Scattergram of Titration Efficiency versus Cigarettes/Day for n = 10 individuals. Dotted lines connect 1st and 2nd cigarette observations for each individual.

$$\text{Titration Efficiency} = \frac{\text{Weight of tobacco burnt by puffing: Low Delivery}}{\text{Weight of tobacco burnt by puffing:High Delivery}} \times 100\%$$

as well as titrating 'upwards' from the nominal 0.36 mg nicotine of the low nicotine cigarette, towards the nominal 1.3 mg nicotine delivery cigarette that the subjects habitually smoked. Secondly, subject differences may well be important - if, as was argued earlier, heavier smokers are more efficient self-titrators for nicotine. Subjects in the present experiment were slightly heavier smokers (18.2 cigarettes/day) than the subjects participating in the Sutton et al. (1978) experiment (15.8 cigarettes/day), and might thus be expected to be more 'efficient'.

Given that subjects appear to obtain almost the same amount of nicotine from the low as opposed to high nicotine delivery cigarette, and in practice obtained very similar physiological effects as assessed by a comprehensive battery of measures (EEG, SCL, SFs, Heart rate, Respiration rate), why should low tar/nicotine cigarettes be relatively unsuccessful in terms of their usage by the smoking population? The probable answer is that smokers are simply unwilling to put the extra effort into obtaining their 'optimum' dose of nicotine (if they did, they would not have gained much of a health advantage either).

E X P E R I M E N T 6

SOME EFFECTS OF CIGARETTE SMOKING ON SCALP DC POTENTIALS : CONTINGENT NEGATIVE VARIATION (CNV)[1].

Rationale

If electrodes are placed on the scalp vertex and mastoid or ear lobe it is possible to record a small negative DC potential between these two sites. Although the source of this negative DC potential is unclear, such DC potentials (as opposed to AC) are not uncommon in the body: there is DC potential of approximately 6mV that exists between the front and rear poles of the eye (Cavonius, 1973), and skin potential levels (SPL) ranging up to 60-70mV exist between indifferent forearm and palmar sites (Venables and Martin, 1967).

Small negative event-related perturbations of this DC level occur - sometimes referred to as event related slow potentials (ERSP) or contingent negative variation (CNV), as first described by Walter, Cooper, Aldridge, McCallum and Winter (1964). The CNV consists of a small negative potential which slowly builds up between a warning signal and an imperative signal requiring the subject to carry out some response, usually a motor response such as pressing a button. The CNV thus occurs in an expectancy situation and is sometimes referred to as an expectancy wave.

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[1] Work carried out at the Clinical Psychopharmacology Unit, University of Newcastle-upon-Tyne.

The immediate source of the CNV (and presumably the steady negative DC potential upon which it 'rides') probably resides in the cortex, although there is evidence that the origin of the CNV is in the arousal systems of the brain, including the ascending reticular activating system (Rebert, 1972) and probably the limbic system (Routtenberg, 1968). Direct recording from these sites in animals and perhaps in the future the use of non-invasive magnetic field techniques on humans (Reite, Zimmerman, Edrich and Zimmerman; 1976)[2] will no doubt resolve this uncertainty. The magnitude of the CNV is thought to reflect the degree of activity in these systems and so is related to the degree of alertness of the subject. There is evidence that CNV is increased or decreased by stimulant and depressant drugs respectively (Ashton et al. 1978) and that while there is a monotonic positive relationship between CNV and performance efficiency (e.g. reaction time), the relationship between CNV and other measures of 'arousal' is of the familiar 'inverted U' form (Tecce, Savignano-Bowman and Meinbresse, 1976).

The CNV is of particular interest as regards research concerning the effects of cigarette smoking, since it is one of the few techniques which have demonstrated definite stimulant and depressant effects of cigarette smoking on electrocortical activity in man (as opposed to animals), and also biphasic stimulant and depressant dose response effects of nicotine (given in the form of injected 'shots') in man (Ashton et al. 1978).

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2 The brain produces magnetic fields due to current flow of the order of 10^{-8} gauss. These have been correlated with EEG and have the potential advantage of enabling the investigator to 'see' beneath the cortex, without actually placing electrodes in or on the subject's head.

The aim of the present work reported was twofold:

A Firstly, an attempt to use the CNV as a 'probe' to assess the effects of nicotine arrival at CNS sites after cigarette smoke inhalation. This has been predicted to arrive in the form of a nicotine rich blood 'bolus' 8 seconds (approximately) after cigarette smoke inhalation (Russell, 1976). On this basis it was predicted that, since CNV has been demonstrated to be a sensitive measure of the effects of both cigarette smoking and also nicotine injection as measured before and after smoking or nicotine injection, a large effect would be observed (whether stimulant or depressant) during as opposed to after smoking. This is because if each CNV trial is timed to occur 8-10 seconds post-inhalation of cigarette smoke, then the CNV will be recorded from the brain at the time of arrival and uptake of the nicotine 'bolus'. Ten or so averaged CNV trials are necessary to obtain good signal to noise ratio, so only ten puffs and inhalations need be used (well within the average number of puffs per cigarette). Control is sham-smoking by the same subject.

B Secondly, it was hypothesised that the sequence of actions in smoking, of lip contact → puff → inhalation represents a sequence of stimuli and motor responses analogous to that used in the CNV paradigm i.e. warning signal (S_1) → imperative signal (S_2) → motor response. It was proposed to examine whether this produced a 'CNV-like' effect and, if so, whether any observable differences could be found between sham smoking, low delivery nicotine cigarettes and high delivery nicotine cigarettes.

A further possibility examined was whether the arrival of the nicotine bolus at the brain shortly after smoke inhalation produces some 'involuntary' change in DC level i.e. a 'bump' or 'dip' in the DC trace eight seconds or so post-inhalation.

METHODOLOGY

Equipment and recording procedures : General

The method of recording CNV followed that as described by Ashton et al.(1974). The CNV was recorded from surface Ag/AgCl electrodes on the vertex and linked mastoids, with an earth electrode on the forehead. An additional electrode was placed at the nasion to pick up voltages generated by eye movements and blinks. A proportion of the nasion signal was then subtracted from the vertex signal in order to compensate for any artefacts due to eye movements.

The voltages were amplified by a high gain AC amplifier with a long time constant (9 seconds). The amplified signals were fed into a PDP8/E computer, programmed to average ten time-locked individual CNVs. The averaged CNVs were displayed on an oscilloscope and traced out by an X-Y recorder fed from the computer. The whole assembly was driven by a timing circuit which was itself triggered manually by a push button operated by the experimenter.

EXPERIMENT A

Procedures (A)

Generators for the warning and imperative signals were triggered by the timing circuit. The warning signal (S_1) was a tone (4,000 Hz, 20ms) and the imperative (S_2) signal was another tone (1500Hz, 400ms). The interval between the two signals was 1.25 seconds. For the purposes of this experiment the timing circuit was triggered manually by the experimenter each time the subject puffed his or her cigarette, as assessed by observation through a one-way window into the subject room. After a fixed time delay of 12 seconds the timing circuit triggered S_1. This value of 12 seconds was chose so as to place the $S_1 \rightarrow S_2$ CNV sequence

at the postulated time of arrival of the nicotine bolus at the brain (4 seconds for puffing and inhalation, plus 8 seconds for nicotine bolus 'travel time' to the brain).

The first ten puff-driven CNV trials were averaged, with the limitations that the initial 'lighting-up' puffs and any puff which occurred within 16 seconds of the immediately preceding puff were discarded. In practice, since the first few puffs of cigarette smoking are usually massed together, the puff-driven CNV was averaged from puff number 2 to puff number 12.

Subject procedures (A)

Five subjects were recruited by word of mouth. Subjects were asked to refrain from alcohol for 24 hours and tea, coffee and cigarettes for half an hour prior to the experiment. Each subject smoked a 1.3 mg cigarette and also sham smoked a similar cigarette during the same session. Order was randomised between subjects for sham and real smoking. An interval of approximately 30 minutes separated sham and real smoking.

Results (A)

The averaged CNVs recorded 12 seconds post cigarette lip-contact for sham and real smoking for two of the five subjects are presented in Figure 1. The evoked potentials associated with S_1 and S_2 are clearly visible, together with the intervening negative wave envelope (CNV). Individual differences are marked in the size of CNV. The horizontal line is drawn from the computer averaged baseline derived from the 3 seconds immediately preceding S_1. The size of the CNV envelope in μV seconds (representing the area enclosed between the evoked potential waves and the baseline) is given in Table 1 for real and sham smoking.

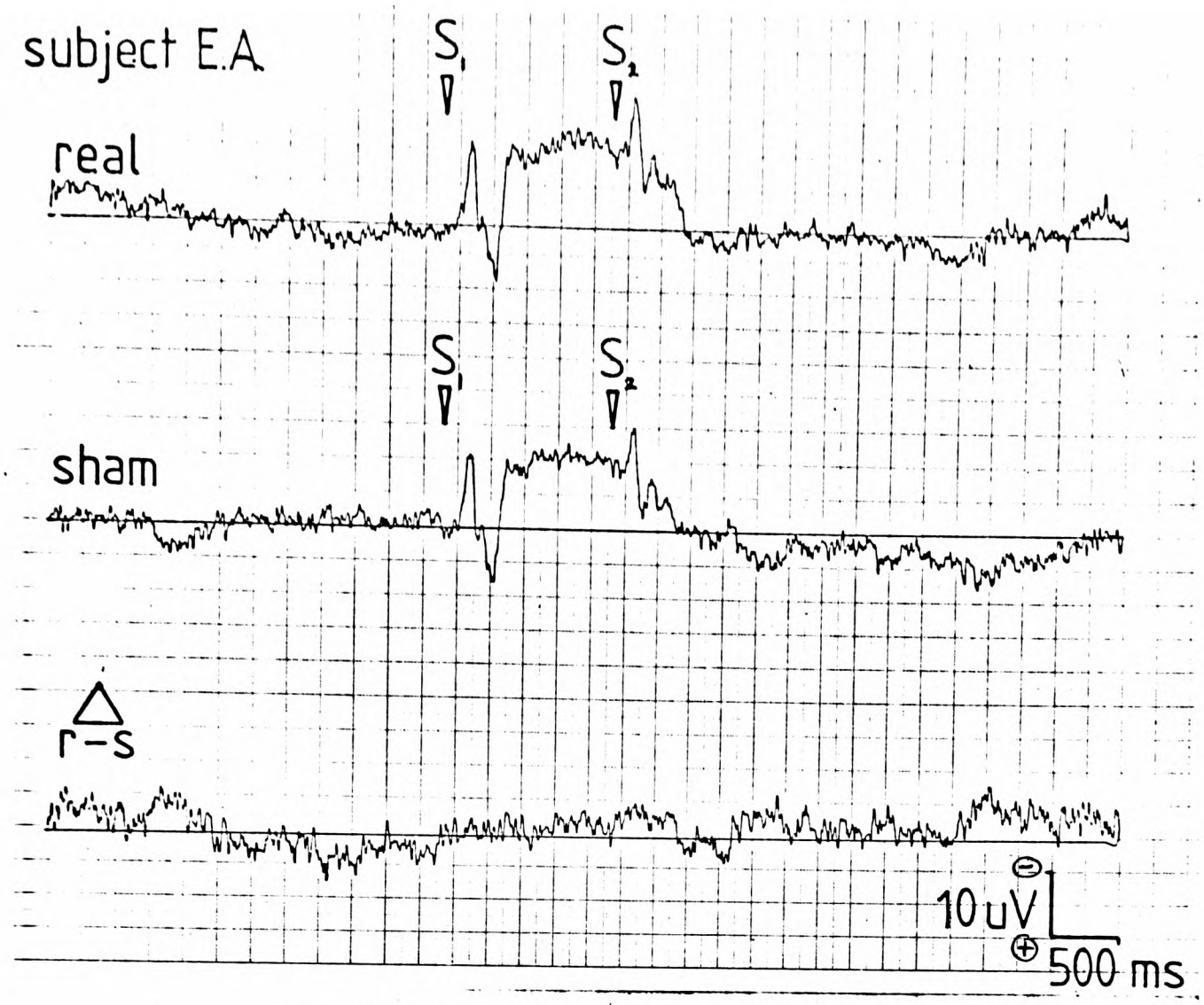


FIGURE 1 : 'Puff-driven' CNVs obtained from two subjects showing the range of effect. Subject E.A. shows virtually no change real (1.3 mg nicotine) versus sham smoking whereas subject B.C. shows a clear increase in CNV magnitude.

While the differences between real and sham puff-driven CNVs are not large, there is a definite trend for the real smoking CNVs to be larger than sham smoking CNVs. For five subjects this trend just fails significance (cf. Table 1: n = 5, x = 0, p = .062, 2-tailed Sign Test).

Discussion (A)

The trend of the CNV data indicated a minimal increase of CNV size at the time locations during cigarette smoking at which the nicotine bolii are said to arrive (Russell, 1976). This result was not predicted on two counts. Firstly, the magnitude of changes, irrespective of direction, in CNV size, real versus sham smoking were small in comparison to those reported for cigarette smoking or nicotine 'shots' (Ashton et al. 1978). Secondly, it might be predicted that depressant as well as stimulant effects should have been observed, even in a sample of five subjects (N.B. the sign test in Table 1 is significant if set for 1-tail i.e. predicting stimulant effects of real versus sham smoking: p = .031).

The most probable explanation for both the smallness of CNV change and its direction is that the nicotine bolus arrives at the brain just after 8 seconds post-light up. In other words, nicotine from the blood bolus is only just beginning to arrive at receptors at the post-inhalation time location studied in the present experiment. This accounts for both the smallness of effect (only the first part of the nicotine bolus has reached the CNS receptors) and also the direction of effect (stimulant since for depressant effects the whole of a large nicotine bolus would have to arrive at CNS receptors to reach the 'correct' part of the biphasic dose-response curve). Other confounding variables are possible individual differences in blood flow and nicotine absorption

TABLE 1

CNVs for Real and Sham Smoking

N	CNV μV seconds			P 2-Tailed Sign Test
	REAL m (SD)	SHAM m (SD)	Δ REAL-SHAM m (SD)	
5	10.320 (3.978)	9.036 (3.531)	+1.284 (1.489)	.062

kinetics, together with the possibility that nicotine induced tachycardia for real smoking may progressively shorten the latency of nicotine bolus arrival at the brain from puff numbers one to ten. The obvious way to test some of these possiblities is to use a β-blocker (e.g. propranolol) to prevent the nicotine-induced tachycardia, and also to use post-puff CNV time lags of both shorter and longer duration compared to the value suggested by Russell (1976).

EXPERIMENT B

Procedures (B)

This was a passive recording experiment. No stimuli were given to subjects. DC potential from the vertex and nasion sites on the subject were continuously recorded on two channels of magnetic tape (FM, Racal recorder). Each time the subject puffed on his or her cigarette, the experimenter pressed a button signalling a pulse to a signal channel on the magnetic tape that was also recording DC potentials from the subject. This marker signal occurred at the time of lip contact by the subject's cigarette as observed through a one-way window.

After the experiment, the magnetic tape was replayed and the signal marker used to operate the PDP8/E averager. This enabled a series of 16 second epochs of smoking record to be averaged for each subject, with time zero being lip contact for each puff. Eight puff epochs were averaged, discarding the lighting-up puffs and any puff followed by another puff within 17 seconds. Eye movement compensation was carried out on the resulting trace as detailed earlier for CNV.

Computer averaging across subjects was utilised to demonstrate effects.

Subject procedures (B)

Subjects comprising the sample (n = 12) were drawn from two sources. The first (and larger, n = 8) group of subjects were participating in another experiment being carried out by other workers concerning the effect of smoking high and low delivery cigarettes on the CNV, recorded before and after smoking. Consequently, it was possible to utilise the actual smoking period of this experiment to carry out the passive recording technique detailed earlier.

This group of 8 subjects smoked high (1.8mg) nicotine delivery cigarettes (n = 5) and/or low (0.8mg) nicotine delivery cigarettes (n = 5) on different experimental sessions. Three of these subjects were observed smoking both types of cigarettes.

The second (smaller, n = 4) group of subjects were recruited directly. These subjects smoked middle (1.3mg) nicotine delivery cigarettes and also sham smoked on the same experimental session. The interval between real and sham smoking was approximately 30 minutes. The order of real and sham smoking was randomised between subjects.

Results (B)

The averaged DC potential traces associated with cigarette puffs are presented in Figures 2, 3 and 4. Specimen individual traces are presented for real versus sham smoking and high versus low nicotine delivery cigarettes in Figure 2 and 3. Note the negative shift which occurs post cigarette lip contact and lasts for 2 seconds approximately. Note also the highly individual patterns of responding which are consistent for a particular subject irrespective of whether sham or real smoking.

This idiosyncracy of responding was apparent in all the four

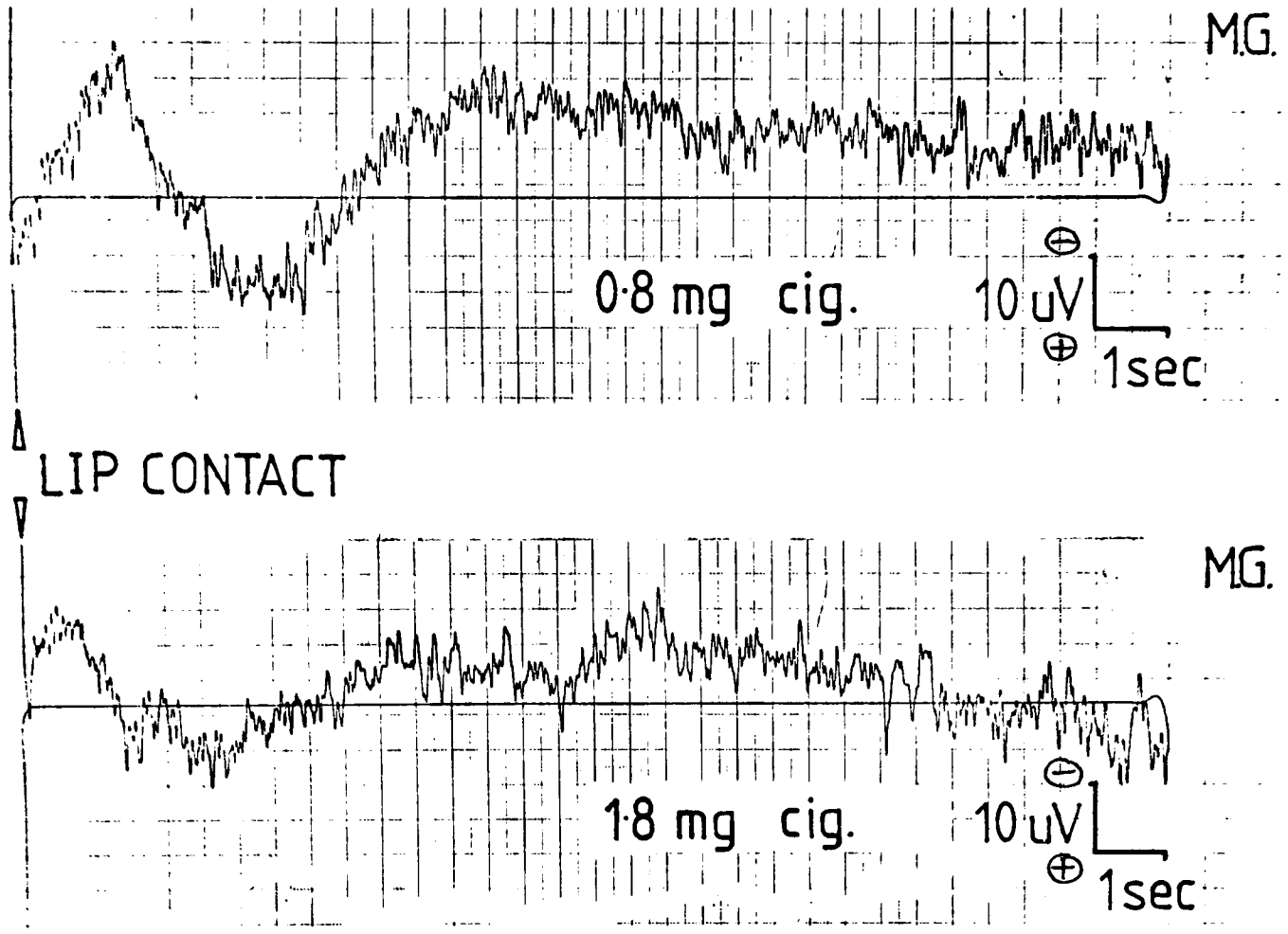


FIGURE 2 : D.C. waveform averaged over 8 puffs, for 16 seconds post lip contact. Subject M.G. smoking 0.8 mg and 1.8 mg nicotine delivery cigarettes.

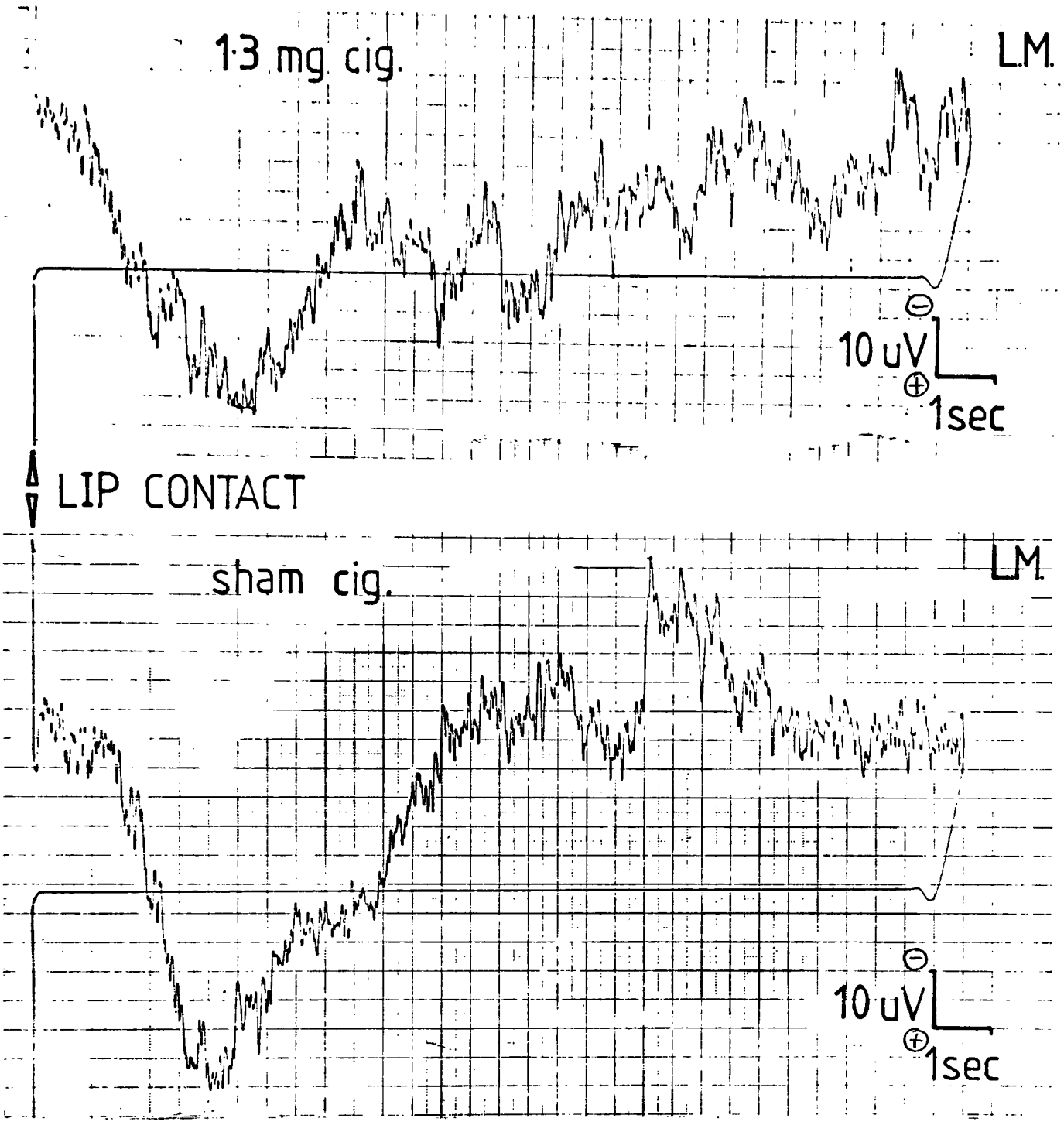
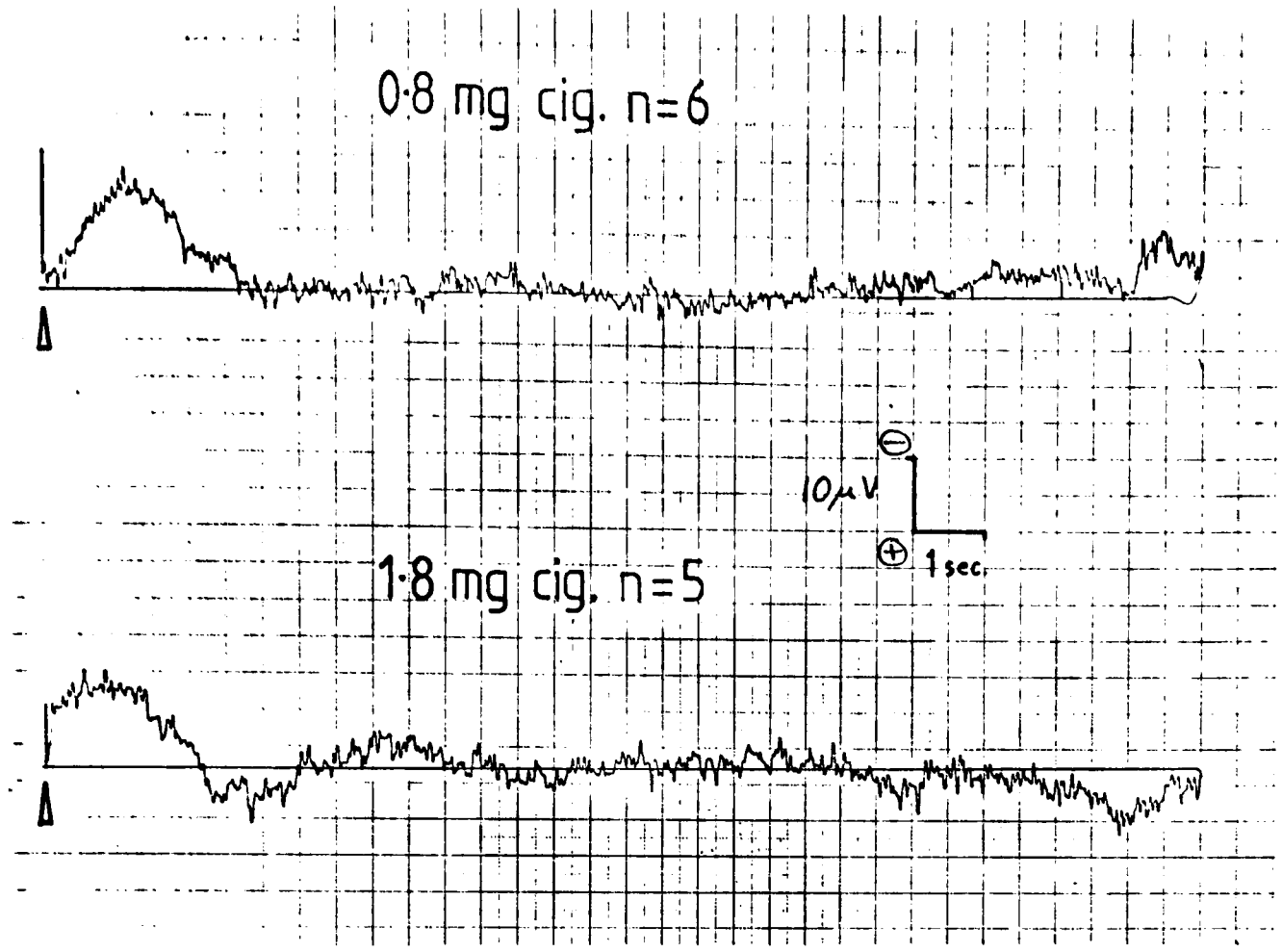


FIGURE 3 : D.C. waveform averaged over 8 puffs, for 16 seconds post lip contact. Subject L.M. real smoking (1.3 mg nicotine delivery cigarette) and sham smoking an unlit cigarette.



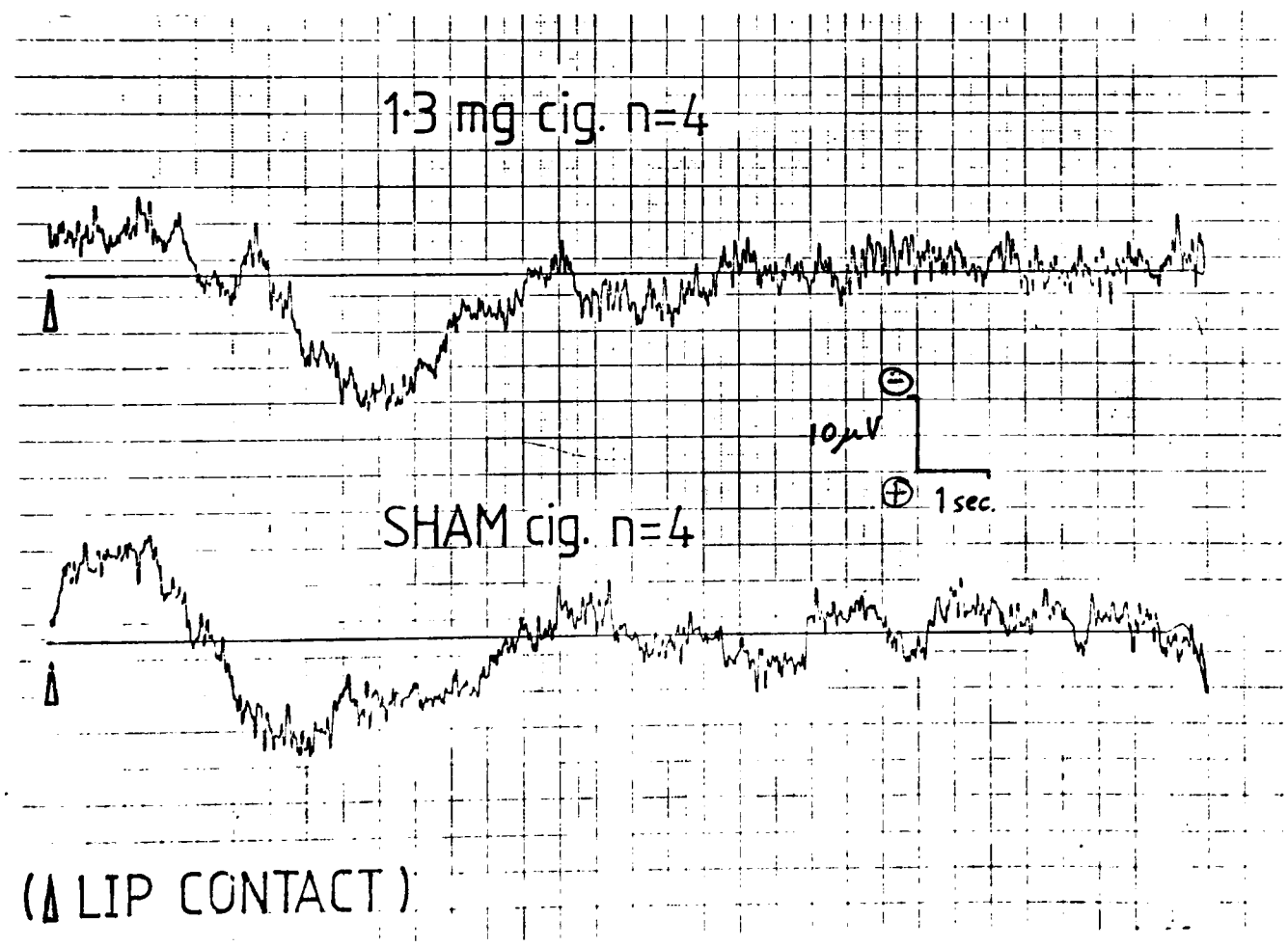


FIGURE 4 : D.C. waveform averaged over 8 puffs for 16 seconds post lip contact. Grand Means for; TOP, (n = 6,5) subjects smoking 0.8 mg & 1.8 mg nicotine delivery cigarettes; BOTTOM, (n = 4,4) subjects both sham smoking and real smoking (1.3 mg nicotine delivery cigarette).

subjects who both real and sham-smoked, and also in the three subjects who smoked both high and low nicotine delivery cigarettes. Consistent individual differences in smoking style have been observed in subjects for Experiments 1 - 5 in the face of variations of situation (stress versus sensory isolation; Experiments 1 - 3), of nicotine delivery (high versus low delivery; Experiment 5) and also for real versus sham smoking (Experiment 4). The idiosyncracies in DC potential traces, associated with puffing, noted in the present experiment may have their origin in the aforementioned individual differences of smoking style, the particular smoking style variable of major importance perhaps being puff intensity i.e. pressure and duration, since this occurs at the same time as the negative shifts observed in the present experiment (cf. Figure 4, first 2 seconds after lip contact).

The grand means averaged across subjects smoking 0mg (sham), 0.8mg, 1.3mg, and 1.8mg nicotine delivery cigarettes (cf. Figure 4) suggest that this negative shift,which occurs post lip contact,does not differ substantially according to the type of cigarette smoked, (the N of subjects are too small for valid statistical comparison across types of cigarette).

There was no evidence for a perturbation in the DC potential 8 seconds post inhalation (12 seconds post lip contact) as can be seen in the averaged traces (cf. Figure 4).

Discussion (B)

The results clearly show that there is a mean DC negative shift Ω 10μV in the two second period following lip contact of the cigarette and just prior to inhalation. Although the n of observations for each type of cigarette are small, the data suggest that this negative shift

is very similar across all types of cigarette smoked (0mg, 0.8mg, 1.3mg, 1.8mg nicotine delivery). This suggestion was additionally supported by the observation that, for the subjects who acted as their own control, the large individual differences in the shape and magnitude of this negative shift were stable in the face of variations in cigarette nicotine delivery (cf. specimen traces Figure 2 and 3). Two possible explanations, for this negative shift, are puffing associated motor artefact or an 'expectancy' wave analogous to the CNV. If this negative shift is general motor artefact it is difficult to explain why the puffing associated negative shift disappears during subsequent inhalation (cf. Figure 4, 2 to 4 seconds post lip contact) also during which time the smoker's arm moves the cigarette away from the mouth. Both of these actions, inhalation and arm movement, are associated with larger changes of muscle activity by comparison to muscle activity during the actual puff when inhalation is minimal and the arm steady. On the other hand, the negative shift might be produced by the specific motor activity of facial muscles during puffing, which may not be eliminated by the eye movement compensation routine based upon subtraction of nasion electrode signals.

The alternative explanation, of the negative shift, is that it represents a CNV-like 'expectancy' wave where S_1 is lip contact and S_2 is the change in buccal cavity volume as gases arrive from the cigarette. S_2 is then the 'imperative' signal for inhalation. If this is true, it raises the possibility that the negative shift observed immediately post cigarette lip contact is an objective measure of the so-called 'secondary reinforcing' or 'conditioned' properties of cigarette smoking. The use of sham-smoking controls in Experiments 1 - 5 demonstrated that for the time period of actual smoking in particular, sham smoking could account

for up to half of any real smoking effect, with the exception of smoking-induced tachycardia, which appeared to be entirely accounted for by the actions of nicotine. The effects of motor activity, and possibly the secondary reinforcing properties of smoking behaviour, would thus appear to be important.

The logical test of whether the negative shift associated with puffing, observed in the present experiment, is the muscle artefact or an 'expectancy' wave is to repeat the experiment with groups of subjects who are requested not to inhale but to merely suck every so often on a pencil. As a further control for the possibility that sucking activity is excessively conditioned to nicotine reinforcement for smokers, it would be advisable to include a group of non-smokers (pipe smoker sometimes can be observed to suck on an empty pipe, apparently with some degree of enjoyment).

Conclusions: A and B experiments

The data presented in A and B experiments suggest that:

1) Cigarette smoking as opposed to sham smoking produces a slight increase of CNV magnitude 8 seconds post inhalation. The nicotine 'bolus' may arrive or produce its major effects at some time after this time.

2) There is a negative shift associated with the act of puffing. This may simply be motor artefact from facial muscles or may represent a 'CNV-like' expectancy wave.

3) There is no evidence for a change in DC potential for a 14-second period after the puffing associated DC negative shift.

CHAPTER 4

SMOKING, PERSONALITY AND PHYSIOLOGY - INTERACTIONS

1) Cigarette consumption and smoking induced heart rate elevation.

2) Interaction of stress with smoking induced heart rate elevation and cigarette consumption.

3) Personality and cigarette consumption - general data and interactions:

(i) Preferences in tar/nicotine delivery of cigarette

(ii) Social Class

(iii) Age

(iv) Sex

(v) Cigarette consumption

(vi) Personality - General

(a) Personality comparison of the subject sample with normative data

(b) Personality correlations with cigarette consumption and smoking style

(c) Personality correlations with physiological effects

1) Cigarette consumption and smoking induced heart rate elevation

Alone, amongst the effects of cigarette smoking which were observed in Experiments 1 to 6, smoking induced tachycardia was the physiological measure of smoking effect that both efficiently discriminated the effects of cigarette smoking from sham smoking (the latter producing zero effect) and also reliably occurred with virtually no change in magnitude in the face of variations of experimental situation (i.e. 'sensory isolation' versus 'boredom' versus 'stress'; conditions). The effects of cigarette smoking on other physiological measures were either non-significant (respiration rate, irregularity) or, while being significant, were approximately 50%+ accounted for by sham smoking (EEG 'α', SCL, SCR, SFs, EMG, CNV) and also the magnitude and direction of effect were strongly determined by pre-smoking levels of arousal (EEG 'α', SCL, SFs).

As such, smoking induced tachycardia, while throwing little light on the problem of 'why people smoke', represents an ideal marker response for the effects of cigarette smoking (and by implication for the effects of nicotine). This marker can be used to combine data for real-smoking from all experiments (i.e. Experiments 1, 2, 4, 5; heart rate data was not collected for Experiments 3 and 6).

The correlation of interest is between self reported average cigarette consumption and smoking induced tachycardia. Consideration of scattergram (Figure 1) of mean heart rate elevation versus cigarette consumption reveals a significant relationship. The heavier smoker shows less smoking induced tachycardia ($r_p = -.380$, $N = 38$, $p < .05$). Two possible explanations for this effect are suggested. Firstly, the heavier smoker may take less nicotine from each cigarette; secondly, the heavier

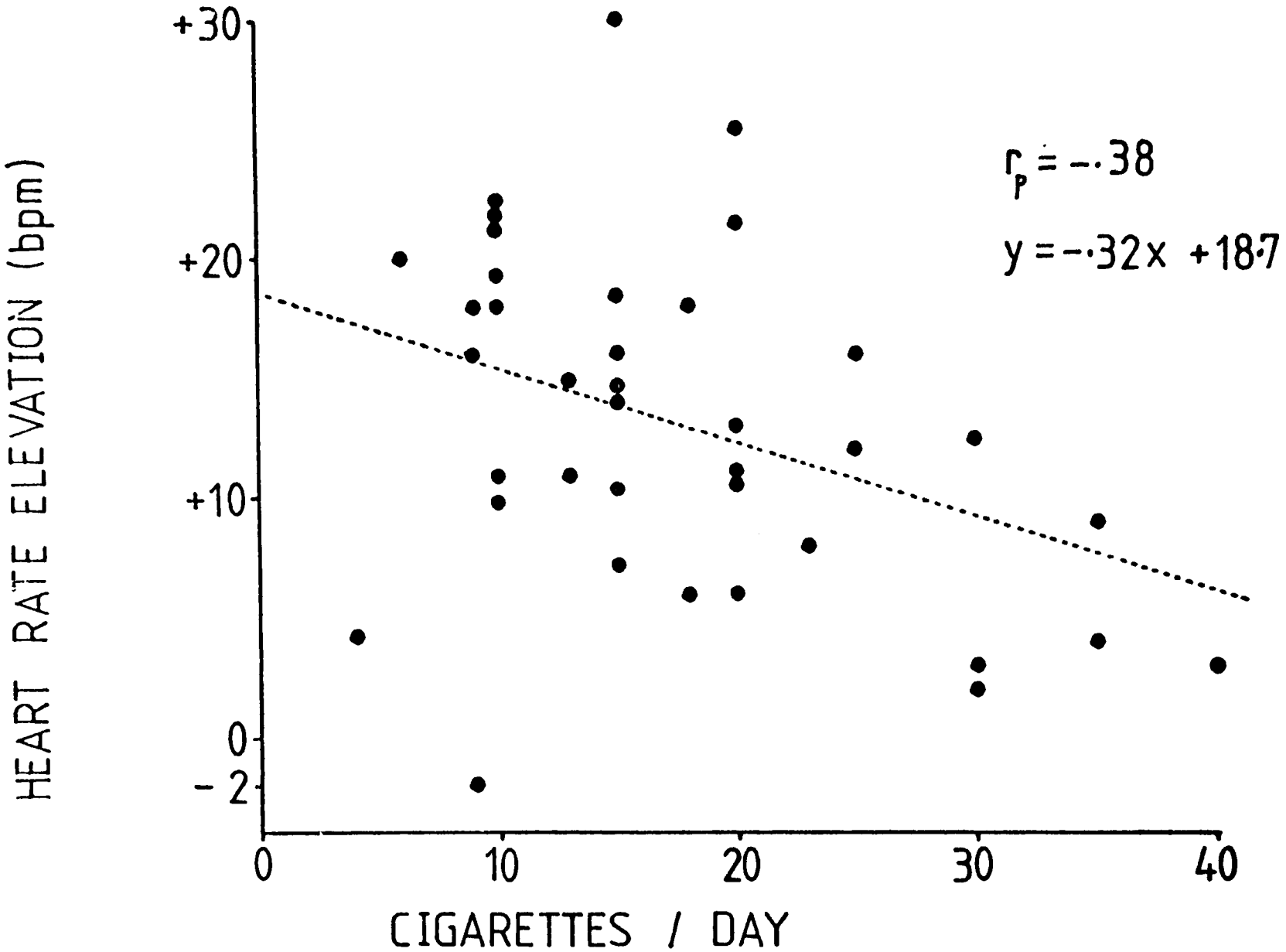


FIGURE 1 : Scattergram for n = 38 individuals of Heart Rate Elevations (POST-PRE) smoking a single cigarette during Low to Neutral Arousal Conditions versus Cigarettes/Day. ($r_p = -.38$, n = 38, $p < .05$)

Based on combined data for Experiments 1, 2, 4 and 5.

smoker may be less sensitive in the cardiovascular system (CVS) to nicotine.

The first possibility is unlikely (although plasma nicotine levels would be necessary to prove this) since while heavier smokers were observed to take no more or less puffs from each cigarette (cigarette consumption x puffs: r_p = +.054, n = 50, p = non-significant, combined real-smoking data for sensory isolation and boredom conditions), arguably they extracted slightly more (non-significant) nicotine per puff as revealed by greater weights of tobacco burnt over the 5 minute smoking period (cigarette consumption x weight of tobacco burnt: - sensory isolation - Experiment 2, r_p = +.06, n = 10, p = non-significant; Experiment 3, r_p = +.18, n = 12, p = non-significant; Experiment 5, r_p = +.29, -.04, +.26, +.38, high delivery first, second, low delivery first, second, respectively, n = 10, 10, 10, 10, p = non-significant. These cigarette consumption x weight of tobacco burnt correlations are presented separately because of differences in cigarette brand and differences in use of cigarette holders between experiments).

The second possibility - that the heavier smoker may be less sensitive to nicotine in the CVS - remains the most likely. Decreased nicotine sensitivity in the heavier smoker may be due to a variety of factors, long term tolerance to nicotine, including metabolic tolerance (Beckett et al., 1971), short term receptor tolerance - tachyphylaxis - (as noted in Experiment 5, or cf. Frankenhaeuser et al., 1968) and possibly even innate differences between light and heavy smokers and non-smokers in nicotinic receptor sensitivity (no strong evidence). In other words, the heavier smoker may smoke more cigarettes because he is less sensitive to nicotine, or because the heavier smoker consumes more cigarettes he becomes less sensitive to nicotine. In all probability

this becomes a vicious circle, the intervals between cigarettes being sufficiently close in the case of the heavy smoker to induce a semi-permanent state of tachyphylaxis, broken only by sleep. This tachyphylaxis in the CVS doubtless occurs to some lesser extent for other physiological responses (EEG 'α', SCL, etc., cf. Experiment 5). If tachyphylaxis is the crucial factor underlying the negative correlation between cigarette consumption and smoking-induced tachycardia, experiments in which smokers are <u>not</u> requested to refrain from smoking prior to testing (for Experiment 1 to 5 and 6A this requested abstinence period was 1 hour+) should produce better negative correlations. (The heavier smoker is more likely to have smoked immediately prior to testing and thus to be in a state of tachyphylaxis.)

Data are presented for cigarette consumption and smoking induced tachycardia, where subjects are not instructed to refrain from smoking prior to testing[1]. Consideration of Figure 2 reveals, that while the regression slope of the relationship between cigarette consumption versus tachycardia is virtually identical to that of Figure 1 based on data for Experiments 1 to 5, the correlation coefficient is much higher (r_p = -.86, n = 12, p < .001 cf. Figure 2). This evidence supports the above hypothesis - that the heavy cigarette smoker is in a semi-permanent state of tachyphylaxis, and so shows poor CVS response to cigarette smoking. However, further consideration of the raw data base for these Newcastle subjects (n = 12) reveals that this picture may be an oversimplification. Table 1 presents a correlation matrix for five variables; heart rate elevation (b.p.m.); age (years); cigarette consumption (number per day); cigarettes smoker prior to testing on the day of experiment (number); time elapsed since last cigarette smoked (minutes).

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[1]Cigarette consumption and heart rate data from subjects participating in TRC study January to June 1978, Clinical Psychopharmacology Unit, Newcastle upon Tyne. Courtesy of R. Stepney and by kind permission of Professor J.W. Thompson (1978).

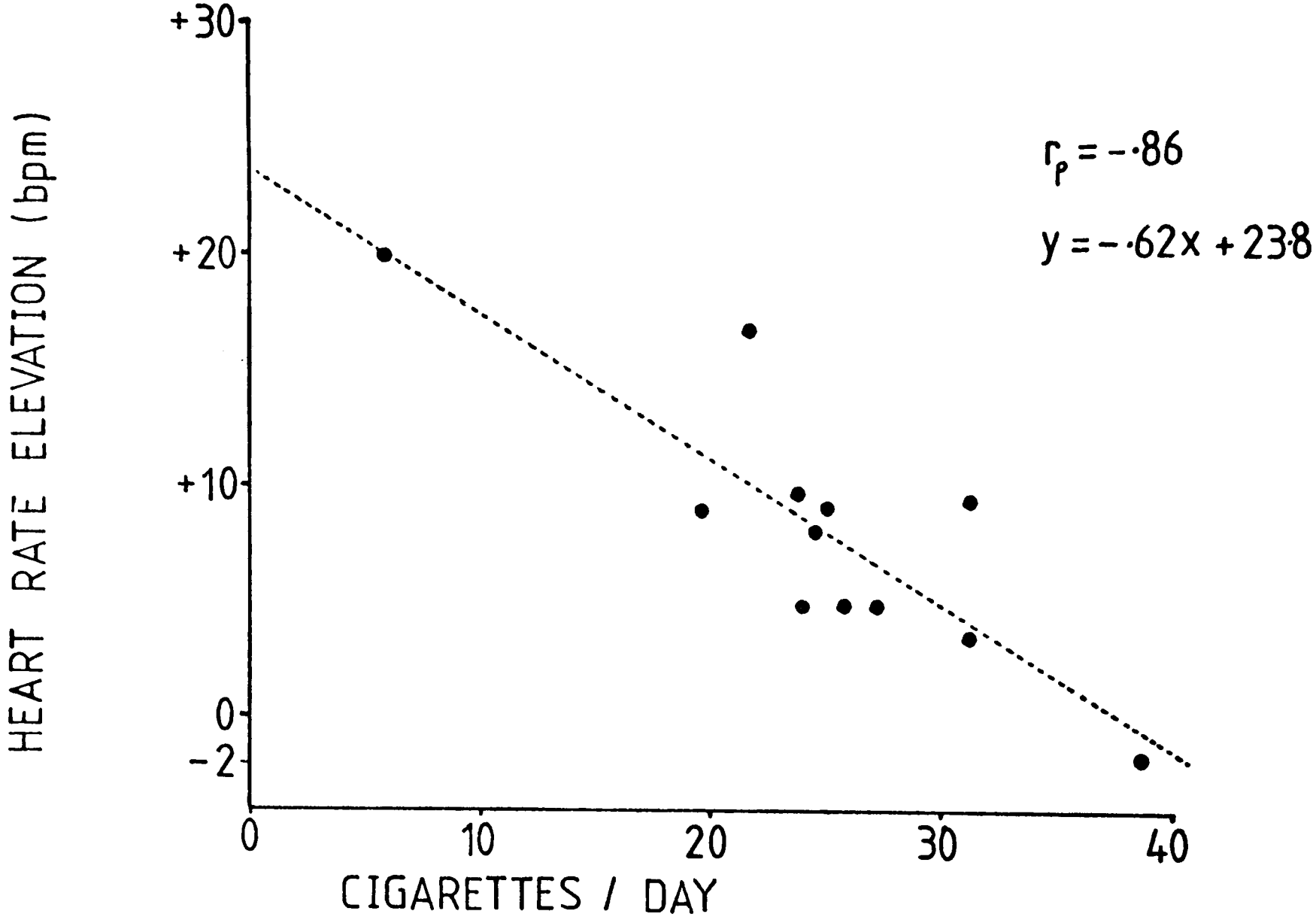


FIGURE 2 : Scattergram, for n = 12 individuals, of Heart Rate Elevation (POST-PRE) smoking a single cigarette, during Neutral Arousal Conditions, versus Cigarettes/Day. T.R.C. data based upon repeated observations.

(r_p = -.86, n = 12, p < .001)

TABLE 1

Reworked T.R.C. Heart Rate data:

Correlation matrix r_p (n = 12)

VARIABLE					
HR elevation (bpm) (1)	.				
Age (years) (2)	-.64*	.			
Cigarette consumption (number per day) (3)	-.86***	+.49	.		
Number of cigarettes smoked prior to testing (4)	-.64*	+.22	+.78**	.	
Time elapsed since last cigarette (minutes) (5)	+.01	-.02	+.28	+.18	.
	(1)	(2)	(3)	(4)	(5)

* p < .05
** p < .01
*** p < .001

TABLE 2

Comparison of TRC[1] data (n=12)

and data for Experiments[2] 1,2,4,5 (n=38)

	TRC m	TRC SD	EXPERIMENTS 1, 2, 4, 5 m	EXPERIMENTS 1, 2, 4, 5 SD
Heart rate elevation (bpm)	+8.28	± 5.77	+13.09	± 7.16
Age (years)	28.58	± 9.83	19 - 28	
Cigarette consumption (number per day)	24.80	± 7.89	17.68	± 8.58
Number of cigarettes smoked prior to testing (number)	4.47	± 2.76	-	
Time elapsed since last cigarette (minutes)	39.87	±30.64	> 60	
Arousal situation	'Neutral'		'Low → Neutral'	

[1]TRC data based on repeated observations
[2]Experiments 4, 5, data based on repeated observations

Perusal of the correlation matrix (Table 1) reveals higher cigarette consumption predicts lower smoking induced tachycardia, as mentioned before (r_p = -.86, $p < .001$). Additionally, increasing age and increasing number of cigarettes smoked prior to testing also predict lower smoking induced tachycardia (r_p = -.64, $p < .05$; r_p = -.64, $p < .05$, respectively). Both these variables also predict higher cigarette consumption (age x cigarette consumption r_p = +.49, p = non-significant; cigarettes smoked prior to testing x cigarette consumption, r_p = +.78, $p < .01$). Surprisingly, time elapsed since the last cigarette prior to testing, does not predict anything, least of all cigarette-induced tachycardia. This may be because plasma nicotine levels, after the last cigarette prior to testing, may have reached a fairly slow decline stage, $T_{\frac{1}{2}}$ versus nicotine $\underline{\Omega}$ 20-30 minutes post-smoking (Russell, 1976) cf. Table 2, mean time elapsed since last cigarette $\underline{\Omega}$ 40 minutes.

A picture emerges in which a cluster of positively interrelated variables - cigarette consumption, number of cigarettes smoked prior to testing and age - predict lower cigarette induced tachycardia. The two crucial source variables are probably number of cigarettes smoked prior to testing and age, which combine to 'produce' the high negative cigarette consumption x tachycardia correlation. The former variable no doubt determines a 'steady state' plasma nicotine level which produces tachyphylaxis, whereas the latter variable (age), while 'feeding' the cigarette consumption x tachycardia correlation (age x cigarette consumption, r_p = +.49), produces direct effects on its own account (age x smoking induced tachycardia, r_p = -.64). These may be both direct aging effects on the reactivity of the CVS, and also perhaps the debilitating effects of years of cigarette smoking on CVS reactivity.

Comparison of cigarette consumption, age and smoking induced

tachycardia supports this contention (cf. Table 2). Subjects in Experiments 1, 2, 4 and 5 were younger and lighter smokers than the TRC subjects and (consequently) showed greater overall smoking induced tachycardia.

The importance of this finding is that it emphasises the importance of such general background factors as cigarette consumption and age on CVS sensitivity to nicotine. By contrast, the importance of cigarette consumption on EEG and SCL reactivity to cigarette smoking appears to be less marked. This may reflect both the higher concentrations and faster clearance times for nicotine in the CNS as opposed to general circulation, (cf. Russell, 1976, for review) and also the importance of effects of smoking behaviour in the absence of nicotine on EEG and SCL (sham smoking effects).

(Correlations of cigarette consumption x EEG or SCL effects of smoking or sham smoking are inconsistent and small. *e.g.*: cigarette consumption x EEG (POST-PRE) for boredom: Experiment 4: first session $r_p = -.30$, second session $r_p = +.15$, cigarette consumption x SCL (POST-PRE): first session $r_p = -.25$, second session $r_p = +.13$. However, cigarette consumption x smoking induced tachycardia correlation is highly significant for subjects in Experiment 4: first session $r_p = -.89$, second session $r_p = -.63$ n = 10 in each case.)

2) <u>Interaction of stress with smoking induced heart rate elevation and cigarette consumption</u>

Cigarette smoking was observed to have significant depressant effects (EEG 'α', SCR) or no significant effect (SCL, EMG, Respiration rate, irregularity) on measures of physiological arousal during white noise stress, as detailed in Experiments 1, 2 and 3. As such, there is

objective evidence for the subjective reports of cigarette smoking having tranquillising properties during stressful situations. In sharp contrast to these 'beneficial' effects of cigarette smoking during stress is the marked tachycardia associated with cigarette smoking during stress. Stress itself produces a mean heart rate elevation of approximately +10 b.p.m., on top of which smoking induced tachycardia adds another +10 b.p.m. (approximately), although there are considerable individual differences in reactivity, the implications of which will be discussed shortly (cf. Table 3). The combination of stress and cigarette smoking produced mean heart rates after smoking of around 90 b.p.m. (normal resting heart rate $\underline{\Omega}$ 70-75 b.p.m.; for young healthy subjects during sensory isolation, resting heart rates $\underline{\Omega}$ 65 b.p.m., cf Experiments 1, 2, 4 and 5). Over the range of heart rates observed, there was no strong evidence for a Law of Initial Values or 'ceiling effect' for smoking induced tachycardia; the effects of smoking and stress on heart rate appeared to be additive. In a passive situation with no strenuous physical activity, this combined stress and nicotine induced heart rate elevation can only be regarded as an unwelcome strain on the CVS. For some subjects, who were observed to have mean post-smoking heart rates during stress > 100 b.p.m., it is possibly dangerous in the long term. Schachter (1973) uses a 'cognitive relabelling' theory to suggest that the stressed or anxious cigarette smoker actually 'enjoys' the autonomic feedback from this nicotine produced tachycardia. However, the observation that peripheral sympathetic blockers (β blockers) which reduce stress induced or nicotine induced tachycardia are also anxiolytic (cf. Thesis Introduction), suggests that the further augmentation of stress induced heart rate elevation by cigarette smoking is merely an unpleasant side-effect, which the smoker tolerates in order to obtain the central depressant effects of nicotine

TABLE 3

Mean effects of stress and

cigarette smoking on heart rate

Data	N	Source of Effect	ΔHR (bpm) m	SD
T.R.C. (1968)	12	Cigarette smoking during neutral arousal	+ 8.28	± 5.77
Experiments 1, 2, 4, 5	38	Cigarette smoking during low to neutral arousal	+13.09	± 7.16
Experiments 1 and 2	18	Cigarette smoking during stress	+10.80	± 3.97
Experiments 1 and 2	34	Noise stress versus sensory isolation	+ 9.52	± 7.52
Pilot study	5	Shock stress versus sensory isolation	+ 9.80	± 7.60

(depressant; i.e. large dosage).

During low to neutral arousal conditions, the heavier smoker showed significantly less smoking induced tachycardia than the lighter smoker (cf. earlier: 'cigarette consumption and smoking induced heart rate elevation). This relationship reverses for cigarette smoking during stress (cf. Figure 3). Comparison of the regression coefficients for the relationship between cigarette consumption and smoking induced tachycardia during low to Neutral Arousal (cf. Figure 1) versus Stress (cf. Figure 3) reveals that this reversal is significant (y = smoking induced tachycardia, x = cigarette consumption, b_{xy} = -.317, Low Arousal n = 38; b_{xy} = +.144, Stress, n = 18; stress versus low arousal regression coefficients, $p < .05$, corrected for differences in variance using formulae 51 and 53, Bailey [1959]).

The interpretation of this significant finding is complicated. Firstly, it must be noted that the heavier smoker tends (non-significant) to be less reactive in the CVS to the effects of stress per se (Δ_{stress} HR = +10.76 b.p.m., n = 28, heavy smokers ≥ 20 cigarettes/day, Δ_{stress} HR = +4.30 b.p.m., n = 6; comparisons are non-significant). Secondly, the evidence that the heavy smoker is obtaining more nicotine during stress than the light smoker is weak (non-significant) (Stress: puffs x cigarette consumption, r_p = +.143, n = 34; tobacco weight burnt x cigarette consumption, r_p = +.39, +.23; n = 10, 12; Experiments 2 and 3 respectively). This is because the heavier smoker tends to take slightly more puffs and burn more tobacco irrespective of whether smoking during stress or low arousal situations. The major effect is that all smokers make significant attempts to obtain more nicotine during stress (cf. Experiments 1, 2 and 3).

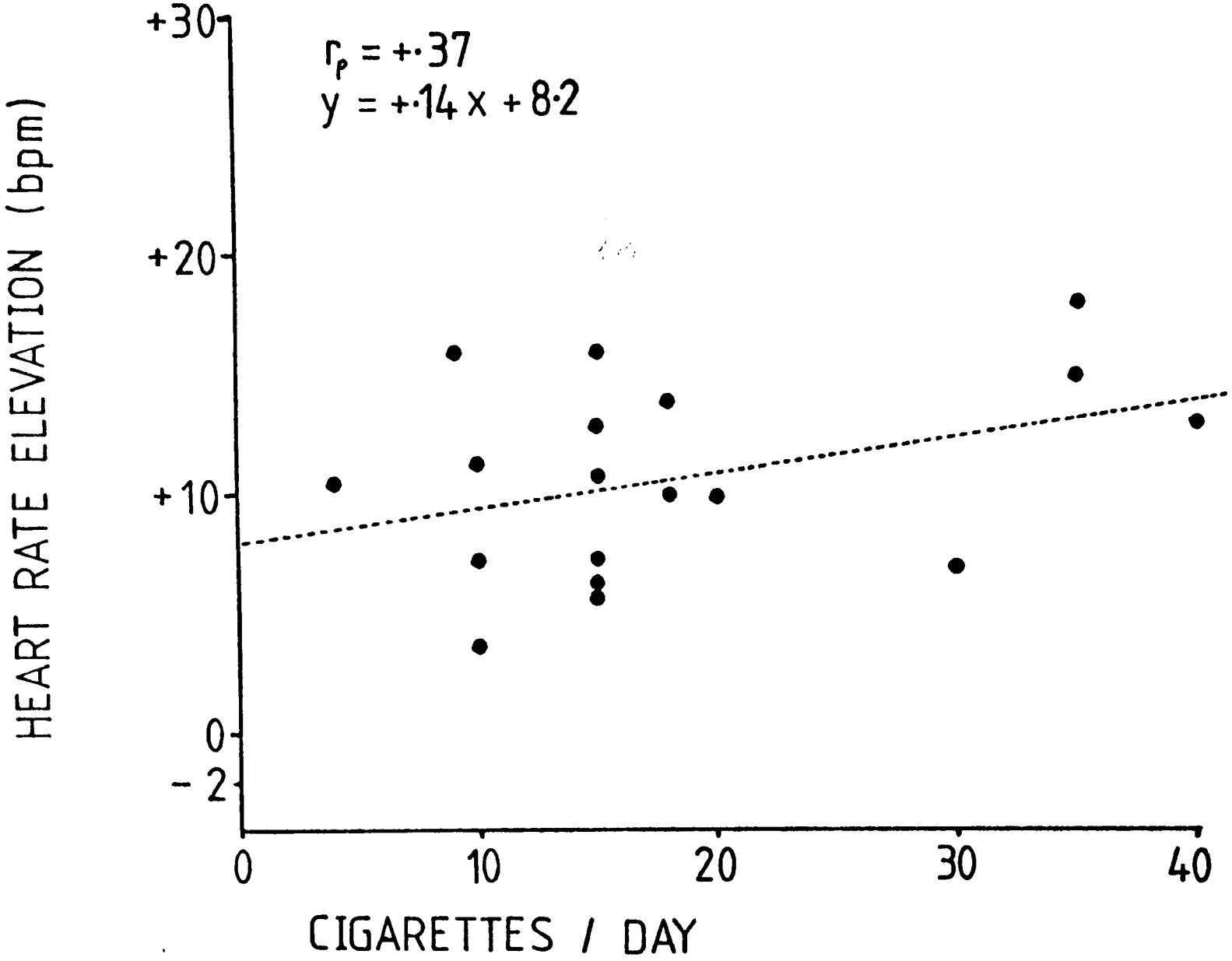


FIGURE 3 : Scattergram, for n = 18 individuals, of Heart Rate elevation (POST-PRE) smoking a single cigarette during High Arousal (Stress) Conditions versus Cigarettes/Day.

(r_p = +.37, n = 18, p = N.S.) Based upon combined data for Experiments 1 and 2.

One possible interpretation, for the potentiating effects of stress on smoking induced tachycardia in the heavy smoker, is that it causes a more rapid clearance of 'tonic' nicotine from the general circulation. This postulated increase in nicotine clearance could occur both by the stress-induced baseline heart rate elevation and also by increasing renal excretion rates via stress mediated urinary pH mechanisms (Schachter et al., 1977). The stress-induced increase in nicotine clearance rate would differentially reduce the effect of 'chronic' tachiphylaxis caused by higher plasma nicotine levels in the heavy smoker, in effect changing the 'tonic' plasma nicotine levels of the heavy smoker to that of a lighter smoker. Whether or not this postulated mechanism is sufficiently rapid, to account for the significant potentiating effects of stress on the cigarette induced tachycardia of the heavy smoker, is debatable. Irrespective of the exact mechanism by which it occurs, this observation may have some implications for the health of a heavy smoker who leads a stressful life, although doubtless that smoker would obtain subjectively calming effects from smoking, via central nicotine actions.

3) Personality and cigarette consumption - general data and interactions

Age, cigarette consumption and personality data for the subjects participating in Experiments 1 to 5, together with other relevant comparison data and a selection of Eysenck (1975) personality norms are given (cf. Tables 4 and 5).

(i) Preferences in tar/nicotine delivery of cigarettes

Although the great majority of the subjects habitually smoked low to middle and middle tar delivery cigarettes, a small number (n = 15) either occasionally or habitually smoked high, middle-to-high, low tar delivery cigarettes or 'roll-ups'. These smokers were maintained on 1.3 mg

GROUP	SEX	N	AGE (Years)	CIGARETTE CONSUMPTION (Number/Day)	Personality : Eysenck (1975) E.P.Q.		
					P	E	N
Experiments 1-5	♂	52	19-28	16.37 (8.31)	7.52 (3.29)	12.62 (4.60)	11.92 (4.48)
	♀	20	19-28	15.06 (6.36)	5.89 (2.70)	13.83 (4.36)	13.82 (4.62)
	Sex Combined	72	19-28	15.82 (7.77)	7.18 (3.22)	13.03 (4.59)	12.31 (4.62)
MRC Cannabis Project Phase III	Sex Combined[1]	12	23.8 (3.6)	13.0 (6.5)	5.6 (4.3)	13.8 (5.5)	13.6 (6.3)
Valium and Cigarette Smoking Project	Sex Combined[1]	15	20-30	15.10 (5.77)	4.87 (2.82)	14.33 (2.72)	10.80 (3.71)
Adult Norms	♂	768	20-29	Smokers & Non-Smokers[3]	4.19 (3.26)	13.72 (4.79)	9.81 (5.09)
	♀	1366	20-29	" " " "	2.79 (2.41)	12.89 (4.70)	12.87 (4.99)
Students (General)[2]	♂	231	20-29	Smokers & Non-Smokers	4.84 (3.33)	13.80 (2.24)	9.93 (5.08)
	♀	203	20-29	" " " "	3.02 (2.54)	13.49 (4.74	12.16 (5.85)
Students (Art)[2]	♂	27	20-29	Smokers & Non-Smokers	7.67 (4.06)	12.26 (5.34)	12.69 (3.88)
	♀	41	20-29	" " " "	4.52 (3.23)	13.00 (5.01)	13.46 (5.73)
Psychotics[2]	♂	104	35.1	Smokers & Non-Smokers	5.66 (4.02)	10.67 (5.22)	13.39 (6.06)
	♀	72	39.3	" " " "	4.08 (3.19)	10.58 (4.66)	14.56 (5.23)
Drug Addicts[2]	♂	8	27.2	Smokers & Non-Smokers	6.94 (5.75)	8.88 (6.98)	17.88 (3.94)
	♀	4	32.5	" " " "	6.25 (3.20)	9.25 (4.86)	20.00 (1.15)

[1] Sex ratio 1 : 3, ♀ : ♂

[2] Normative data from Eysenck (1975)

[3] No data, reflects smoker/non-smoker distribution occurring 'naturally'.

(N.B. S.D.s in Brackets)

TABLE 4

Personality, cigarette consumption and comparison data

GROUP	SEX	N	AGE (Years)	CIGARETTE CONSUMPTION	PERSONALITY		
					P	E	N
Subjects[1] participating in psychophysiology experiments	1:1 ♀ : ♂ Combined	31	18-36	Smokers & Non-Smokers[3] Combined	7.05 (3.81)	13.48 (6.31)	9.76 (5.29)
Questionnaire[1] sample (small)	1:1 ♀ : ♂ Combined	174	18-36	Smokers & Non-Smokers[3] Combined	5.03 (4.11)	12.47 (5.28)	11.91 (5.83)
Questionnaire[2] sample (large)	♂	84	31.6 (13.0)	Smokers & Non-Smokers[3] Combined	3.58	12.20	9.12
	♀	193	26.2 (10.5)		2.58	12.92	12.13

(N.B. S.D.s in brackets)

[1] Source: T. Paisey, D.Phil Thesis - 'Individual Differences in Psychophysiological Response', 1980, Dept. of Experimental Psychology, Oxford.

[2] Source: T. Paisey, unpublished data, (1979)

[3] No data, reflects smoker/non-smoker distribution occurring 'naturally'

TABLE 5

Comparative personality data: samples from Oxford area and subjects participating in psychophysiology experiments at the Department of Experimental Psychology (Oxford)

nicotine cigarettes for several days prior to testing, as detailed in the experimental procedures. No habitual pipe or cigar smoker were recruited. 'Health Trends' data (Capell, 1978) relevant to the dates of experimental work (1975-1978) confirms that this distribution of preferred tar category is close to 'normal', (data for 1977 indicates that 70% of all U.K. manufactured cigarette sales were in the middle tar category, although, more recently, technical advances aimed at reducing tar whilst maintaining nicotine delivery have enabled low-to-middle tar category cigarettes to capture a greater share of the market. Low tar cigarettes account for a relatively small percentage of sales ($\approx$ 12%, 1977) presumably because of the technical difficulty in reducing tar whilst maintaining nicotine delivery and still producing an acceptable 'taste').

(ii) Social Class

While preferences in type of cigarettes smoked by the subject sample were close to the normal smoking population, social class was not. Although not formally assessed, it was abundantly clear that the subject sample had a disproportionate loading towards social classes I and II. Consequently social classes III, IV and V were underrepresented. This was doubtless a consequence of the fact that the population pool from which subjects were recruited lived in a University town, and, in particular, Oxford. Approximately half the sample had direct connections with the University and associated academic or clinical institutions (i.e. undergraduates, postgraduates, research workers, technicians, nurses), while the remaining half of the sample were composed of unemployed or part-time workers (e.g. secretaries, waitresses, barmen, gardeners, musicians, housewives, etc.). The single common factor (apart from smoking and age range) amongst all subjects was availability for day-time experiments. This inevitably

excluded smokers who were engaged in full-time non-academic employment. It is unlikely that this social class sampling bias had any distorting effect on physiological responding, factors such as age and general physical fitness (cf. Experiment 1: the notable tendency for 'sporting' individuals to have low tonic heart rates) being more important. Notwithstanding, one point of technical interest as regards the effect of occupation and physiological responding occurred with regard to the tonic electrodermal measure: SCL. Individuals with calloused hands, in particular fingertips, (i.e. some technicians, musicians and part-time gardeners) evidenced artificially high skin resistances even after thorough cleaning of the skin and allowing time for electrolytic jelly 'soak-through'. This factor was eliminated by light skin abrasion, the importance of which can be judged by the greater SCL test-retest reliabilities for abrasion as opposed to non-abrasion techniques (cf. relevant SCL sections in Experiments 4 and 5).

(iii) Age

A fairly young and narrow age range (19-28 years cf. Table 4) was deliberately chosen on the assumption that young healthy adults would evidence greater responsiveness on physiological measures. This assumption appears to have been correct, at least as regards smoking-induced tachycardia (cf. 'Cigarette consumption and smoking induced heart rate elevation').

Prevalence of cigarette smoking does not vary significantly with age over the range 16-59 years being roughly constant at 45-50% of the population at a particular age for both men and women (source TRC data, 1976; GHS data indicates the same age trend but that prevalence for smoking amongst women is lower than for men $\underline{\Omega}$ 40%, Capell, [1978]). Before and after the age range 16-59 years the prevalence of cigarette

smoking rises and falls dramatically, respectively. The former effect is no doubt a consequence of recruitment to the habit, and the latter effect a consequence of historical trends, giving up (and/or death?).

This means that, while the age range of subjects chosen(19-28 years) may produce greater smoking effect insofar as physiological measures are concerned (both because they are younger and have smoked for less years), choosing this particular age band does not lead to any gross bias insofar as the section of whole adult population from which smokers are drawn. Below 18 years and above 60 years there is good reason to believe that much of a hypothetical sample of smokers would not be truly representative of the bulk of the smoking population. This is because, irrespective of historical trends in consumption and aging effects on physiology, for the age of <18 years the majority of teenagers have tried smoking to a greater or lesser degree, roughly 50-55% 'giving-up' after a short time (e.g. Mangan, 1975-1978, unpublished SSRC school-children's survey) whereas for ages >60 years the percentage of the older adult population who are smokers falls rapidly from 48% of the 35-59 years-old population to 26% of the >60 years-old population.

(iv) Sex

The sex ratio of the subject sample was 1:2.6, ♀ : ♂(cf. Table 4), distributed randomly amongst experiments, but balanced within experimental sub-groups. It is noteworthy that female as opposed to male subjects are somewhat under-represented compared to the relative proportions of female and male smokers in the general population (percentage of 25-34 years population who are smokers, approximately the age range 19-28 years in the present sample, ♂= 48%, ♀ = 47%, TRC data, GHS data suggesting that ♂smokers are relatively more common than ♀ smokers: ♂ = 49%, ♀ = 42%, Capell, 1978). The greater number of males in the present

sample reflects the fact that female smokers were less willing to volunteer for psychophysiological experiments.

Sex differences for selected variables are presented in Table 6. No analyses by sex were carried out for individual experiments since, with the experimental design followed (small samples of subjects repetitively tested with a wide battery of measures), numbers in each cell, by sex, were insufficient. Consideration of Table 6 indicates that sex differences for a general selection of variables, with the exception of personality, are small and non-significant. The lower P scores and higher N scores for females are predictable from normative data (Eysenck, 1975). Somewhat surprising is the observation that female subjects are non-significantly more extraverted than males (cf. Table 6). Normative data would suggest the opposite trend, males being more extraverted than females. The relatively higher extraversion scores for females may indicate that the more confident and sociable female smokers tended to volunteer for a psychophysiological experiment (cf. the underrepresentation of females discussed earlier).

(v) Cigarette consumption

Mean cigarette consumption was 15.8 cigarettes/day (cf. Table 4). This is close to the average cigarette consumption for the general population (average consumption approximately 18 cigarettes per day, TRC data, 1978). As noted earlier for smoking induced tachycardia, heavy cigarette consumption may attenuate the magnitude of cigarette smoking effect. The cigarette consumption of the subject sample indicates that the magnitude of smoking effects observed in the present work are likely to be fairly representative of the bulk of the smoking population, insofar as cigarette consumption represents a potential confounding variable.

VARIABLE		N		♂ m	♂ SD	♀ m	♀ SD	P 2-Tailed T-test ♂ versus ♀
Cigarette consumption (per day)		52	20	16.37	(8.31)	15.06	(6.36)	NS
Personality	P	52	20	7.52	(3.29)	5.89	(2.70)	.05
	E	52	20	12.62	(4.60)	13.83	(4.36)	NS
	N	52	20	11.92	(4.48)	13.82	(4.62)	(.10)
Tonic heart rate low to middle arousal situations (b.p.m.)		36	18	66.50	(10.20)	68.39	(10.14)	NS
Rise in heart rate to stress versus sensory isolation (b.p.m.)		23	11	+8.65	(7.15)	+11.55	(7.57)	NS
'Real-smoking' smoking-induced tachycardia during low to middle arousal situations (b.p.m.)		24	14	+12.71	(6.79)	+13.75	(7.96)	NS
'Real-smoking' smoking-induced tachycardia during stress situation (b.p.m.)		11	7	+10.64	(4.30)	+11.11	(3.70)	NS
'Real-smoking' Puffs per cigarette:low to middle arousal		35	15	13.66	(4.85)	10.80	(3.99)	(.10)
'Real-smoking' Puffs per cigarette:stress situation		22	8	15.55	(5.66)	11.75	(3.24)	(.10)

TABLE 6

Sex differences: selected variables Experiments 1-5

(vi) Personality

General:

Personality scores for the subject sample, by sex and combined, are detailed in Table 4, together with normative data in Tables 4 and 5. Psychoticism (P), extraversion (E) and neuroticism (N) scores are stated by Eysenck (1975) to indicate the individuals disposition towards behaviours which reflect: P - tendency towards psychosis in particular tough-minded attitudes, E - tendency towards sociability and impulsivity, N - tendency towards emotionality and instability of moods in particular anxiety. Some degree of genetic determination for P, E and N is evidenced from twin studies and their biological bases are suggested to be: P - no definite evidence, E - low cortical arousal producing, in particular, slow punishment conditioning, N - lability of the limbic system and, in consequence, of the autonomic nervous system (Eysenck, 1977). Although individual personality scores are stated to be traits, i.e. relatively fixed and immutable, one month test re-test reliabilities for P, E, N, do not exceed 0.8 and considerable variation occurs with age, reflecting the common observation that older people do not 'go out' so much and are generally more cautious and emotionally less labile. As regards the implicit 'immutability' of personality traits, some theorists suggest that behaviour is far more determined by the immediate environment than by personality traits (Mischel, 1968). This proposition is supported to some extent by a cursory examination of EPQ scale items, e.g., it is entirely reasonable to suggest that prisoners and drug addicts (Eysenck, 1975, criterion sub-groups) score highly on "P" simply by endorsing (EPQ) items such as (item 55) 'Do most things taste the same to you?" and (item 23) 'Would you take drugs which may have strange or dangerous effects?' Endorsements of the former item may be determined by prison

food whilst the latter items is tautologous for the respective criterion sub-group.

Notwithstanding these criticisms, there is much evidence that personality traits have some validity and become relevant to the study of psychoactive drug use in general, and cigarette smoking in particular, by involving the concept of 'optimum arousal'. Briefly, it has been suggested that extraverts, being relatively underaroused, smoke in order to obtain stimulant effects; while introverts, being relatively over aroused, smoke in order to obtain depressant effects. "N", the dimension of emotional lability, acts as a multiplier for these effects, while "P" perhaps reflects both poor arousal control (cf. N) and low cortical arousal (cf. E), (Eysenck, 1973, 1975, 1977; Eysenck and O'Connor, 1979).

In general terms, personality interactions with smoking represent a particular facet of the determination of smoking effect outcome by starting state as examined in the present experiments, whether caused by differences in environment (stress versus sensory isolation) or individual variations in arousal (cf. Experiment 4 and relevant sections in other experiments).

Evidence in support of this contention, for personality in particular, has derived from studies of smoking and performance (Warburton and Wesnes, 1978), smoking and physiological measures of arousal (Ashton et al., 1974; Eysenck and O'Connor, 1979), and from patterns of cigarette consumption and smoking style itself (Eysenck, 1973; Ashton et al., 1974).

The relevance of personality to the causes of smoking behaviour, as suggested by the present work, are for convenience divided into three section: (a) Personality comparisons of the subject sample with normative data, (b) Personality correlations with cigarette consumption and smoking style, (c) Personality correlations with physiological effects.

(a) Personality comparison of the subject sample with normative data:

The most striking feature of the personality scores of the subjects are the significantly elevated P scores in relation to Eysenck's age-related norms, whether split by sex or combined (cf. Table 4; 'P' score of subject sample is >> Eysenck norm: $p < .001, ♂$; $p < .001, ♀$; 2-tailed T test). The E and N scores of the subject sample were not significantly different from age-related norms (cf. Table 4). However, N scores were slightly higher than might be predicted from age-related norms (cf. Table 4) and this small effect is consistent with the somewhat contradictory reports of a slight relation between elevated N and cigarette smoking (cf. Warburton and Wesnes, 1978, for review). Although there are some contradictory data (Weeks, 1979), the bulk of evidence suggests that smokers are more extraverted than non-smokers (cf. Warburton and Wesnes, 1978, for review). Failure of prediction (E should be elevated for the subject sample) in the present case may be due to a simple chance effect. However, a more plausible explanation, in view of sample size (n = 72), could involve the recent changed item content of the E scale. The original scale, which was used in most of the relevant smoking studies reported, was a combination of sociability and impulsivity sub-scales. In the more recent (1975) version, however, the impulsivity items, together with 'stimulation-seeking', 'risk-taking', 'tough-mindedness' and 'thought-disorder' items, have been assimilated into an orthogonal 'P' or psychoticism dimension. The E scale has thus been reduced mainly to a scale of sociability, although there are indications of a stimulation seeking component. This perhaps puts into perspective the lack of relationship between E and cigarette smoking, reported here. A lack of relationship between E (EPQ, Eysenck, 1975) and cigarette consumption has also been found in two other studies of cigarette smokers (cf. Table 4, MRC Cannabis Project, Phase III; Valium and cigarette smoking project).

The significantly elevated 'P' scores of the present subject sample, noted earlier, may derive from two sources. Firstly, it may reflect the fact that the subjects were cigarette smokers, by virtue of the item contents of P and E discussed earlier (i.e. 'stimulation seeking' type items). Secondly, and probably of more importance, elevated 'P' scores may be indicative of a 'volunteer effect'. This 'volunteer effect' for psychophysiology experiments appears to be important, since comparison of the P scores of the present sample of smokers with P scores of non-smokers and smokers combined participating in similar psychophysiology experiments carried out in Oxford, reveals no significant difference (cf. Table 4, 'Experiments 1 to 5', mean P = 7.18; Table 5 'Subjects participating in psychophysiology experiment', P = 7.05; and by contrast 'P' scores for the Oxford area in general P $\underline{\Omega}$ 3.0).

The elevated P scores of the subject sample cannot be taken as indicating that the subjects were pre-psychotic! In fact, many criticisms of the P scale focus on its failure to differentiate criterion groups such as psychotics (Bishop, 1977; Block, 1977), although these objections are countered by the claim that P measures a predisposition in the normal (premorbid) personality (Eysenck, 1977; Selected comparison data is given in Table 4 and 5). Elevated 'P' scores indicate rather that the subjects were slightly more inclined to be 'stimulation-seekers' and less 'defensive'. The analogous comparison group judging from published data would appear to be 'Art Students' (cf. Table 4, Eysenck [1975] comparison data).

(b) Personality correlations with cigarette consumption and smoking style:

Correlations of PEN with selected variables of consumption and smoking style are given in Table 7. No significant relationship exists between P, E or N and cigarette consumption, a finding which is consistent

Variable correlated with personality variables P, E and N	n	CORRELATION COEFFICIENT r_p AND SIGNIFICANCE					
		P x variable	Significance P	E x variable	Significance P	N x variable	Significance P
Cigarette consumption	70	+ .002	NS	+ .055	NS	- .130	NS
Puffs during low to neutral arousal	50	+ .090	NS	+ .163	NS	- .298	.05
Puffs during stress	30	+ .082	NS	- .055	NS	- .234	NS
Weight of tobacco burnt — Stress Exp. 2	10	+ .376	NS	- .127	NS	- .236	NS
- - - - Sensory Isolation Exp. 2	10	- .014	NS	+ .430	NS	+ .595	NS
- - - - Stress Exp. 3	12	+ .099	NS	+ .424	NS	- .516	NS
- - - - Sensory Isolation Exp. 3	12	- .042	NS	+ .232	NS	- .614	.05
Sensory Isolation Exp. 5							
- - - - FIRST HIGH NICOTINE	10	- .074	NS	- .515	NS	- .353	NS
- - - - SECOND HIGH NICOTINE	10	- .107	NS	- .60	NS	- .567	NS
- - - - FIRST LOW NICOTINE	10	+ .413	NS	- .213	NS	- .289	NS
- - - - SECOND LOW NICOTINE	10	+ .515	NS	+ .026	NS	- .139	NS
Valium and smoking experiment							
Mean butt length — control day	15	+ .426	NS	- .382	NS	- .180	NS
- - - control day	15	+ .350	NS	- .311	NS	- .217	NS
- - - valium day	15	+ .361	NS	- .415	NS	- .229	NS
- - - valium day	15	+ .363	NS	- .420	NS	- .211	NS

TABLE 7

Personality correlations with selected variables
- cigarette consumption and smoking style

with the non-significant findings (cf. earlier) as regarding mean P, E, and N scores.

As regards the correlations between personality scores and smoking style, correlations are largely non-significant (cf. Table 7). However, two trends are apparent.

Firstly, there is a trend for N to be negatively related to vigour of smoking as indicated by puffing rates and tobacco weight burnt. This trend reaches significance at .05 level for both N x Puffs during low to neutral arousal and N x Tobacco Weight Burnt, Experiment 3, Sensory Isolation (cf. Table 7). This relationship may have its origin in the suggested (Eysenck, 1967) basis of N - i.e. lability of the autonomic nervous system. It is possible that high N scorers are very sensitive to nicotine's effects on the autonomic nervous system and in particular wish to avoid excessive smoking-induced tachycardia. There is, however, little evidence that high N predicts high smoking induced tachycardia (cf. Table 8, next section).

Secondly, the relationship between 'E' and smoking style is less apparent than might be predicted on theoretical grounds. Since extraverts are postulated to be under-aroused, it is suggested that extraverts should preferentially take less nicotine in order to obtain small (stimulant) doses. Two factors may be decrementing this predicted relationship: (i) the previously discussed attenuation of the 'stimulation seeking' component of the more recent (1975) 'E' scale, (ii) the effect of personality may be so small (correlations between 'E' and physiological measures of cortical arousal or conditioning rarely rise above r = -.5) that it is necessary to present the extraverted smoker with the necessity to avoid 'over-dose' i.e., avoid obtaining depressant effects from nicotine, in order to observe strong relationships between 'E' and smoking style.

(This is analogous to the necessity of setting up the 'right conditions' during experiments in order to observe significant personality x physiology interactions, as stated by Eysenck (e.g., Eysenck, 1977, 1973.) The two negative correlations between 'E' and tobacco weight burnt for high nicotine delivery cigarettes, Experiment 5 (cf. Table 7), which just fail significance at the .05 level, suggest that the extravert titrates 'downwards' in order to obtain small stimulant doses of nicotine and so raise his or her state of underarousal towards an 'optimum'.

(c) Personality correlations with physiological effects:

Relationships between personality and physiological effect, whether caused by real smoking, sham smoking or stress, were generally small and non-significant. For brevity, a selection of correlations are given in Table 8 in order to illustrate trends.

Arguing from the postulated biological bases of PEN (cf. earlier) it is predicted that (i) extraverts should be less reactive to stress whereas (ii) individuals with high 'N' scores should be more reactive to stress, particularly in the autonomic system. The effects of cigarette smoking should tend to be (iii) more stimulant in the cortical system of extraverts, while (iv) high 'N' scorers should be particularly reactive to smoking in the autonomic system. Theory gives little guidance as to the direction of effects in high 'P' scorers.

There is some non-significant evidence for one of these predictions - (i) — cf. Table 8. Thus, (i) extraverts showed a tendency to less stress induced heart rate elevation.

Subjective mood ratings in Experiment 4 revealed that extraverts rated themselves as being more 'bored/underaroused' (r = -.46, -.44, mood

Variable correlated with personality variables P, E and N			n	P x variable	Significance P	E x variable	Significance P	N x variable	Significance P
Heart rate rise to stress versus sensory isolation			34	- .076	NS	- .127	NS	- .147*	NS
Heart rate rise to cigarette smoking - sensory isolation	Exp. 1, 2		18	- .303	NS	+ .219	NS	+ .017	NS
Heart rate rise to cigarette smoking - stress	Exp. 1, 2		18	+ .254	NS	+ .392	NS	- .041	NS
Heart rate rise to cigarette smoking - boredom Exp. 4		1' session	10	- .184	NS	- .312	NS	+ .025	NS
		2' session	10	+ .113	NS	- .388	NS	+ .465	NS
Heart rate rise to cigarette smoking - sensory isolation Exp. 5		1' High Nicotine	10	- .192	NS	- .165	NS	+ .337	NS
		2' High Nicotine	10	+ .128	NS	+ .449	NS	+ .179	NS
		1' Low Nicotine	10	- .371	NS	- .226	NS	+ .409	NS
		2' Low Nicotine	10	- .389	NS	+ .093	NS	+ .131	NS
Example for another variable (EEG):									
EEG 'α' (POST-PRE)	Real	1' session	10	- .140	NS	+ .130	NS	- .303	NS
		2' session	10	- .372	NS	- .027	NS	- .271	NS
Experiment 4	Sham	1' session	10	+ .101	NS	+ .006	NS	- .749	.05
		2' session	10	- .389	NS	- .408	NS	- .089	NS

TABLE 8

Personality correlations with selected variables

- general physiological measures and physiological effects of smoking

x 'E' pre-smoking, sessions 1 and 2) and extraverts reported that smoking had stimulant effects (r = +.24, +.38 ; (Post-Pre) mood x 'E'; sessions 1 and 2).

However, as discussed earlier (cf. Experiment 4; mood ratings), the relationship between subjective and objective measures of arousal was poor.

In summary, it appears that personality does not strongly determine smoking effect. This is in sharp contrast to the observation that differences of physiological starting state strongly determine smoking effect, whether caused by experimental conditions (stress versus sensory isolation), or occurring naturally through individual variation in basal measures, or, for heart rate, occurring by variations in cigarette consumption and age.

It is entirely possible that personality effects for relatively small samples can only be reliably demonstrated by rigorously selecting subjects to obtain large variations on one scale, e.g. 'E', whilst holding other scale scores constant (i.e. 'P' and 'N').

CHAPTER 5

SUMMARY DISCUSSION - EXPERIMENTS 1-6

The results of Experiments 1 to 6 (summarised in Tables I and II) reduce to four major findings.

(i) Both stimulant, depressant and mixed effects of cigarette smoking were demonstrated on a number of physiological variables (EEG, electrodermal and EMG). No consistent effect was found on respiration rate or irregularity. Heart rate was invariably increased by cigarette smoking.

(ii) The 'starting state' of the subject had important consequences as regards the magnitude and/or direction of smoking effect, stimulant versus depressant. Thus, for subjects in high arousal i.e. stress conditions, cigarette smoking produced either definitely depressant or mixed effects on EEG 'α' and SCL, while during low arousal i.e. sensory isolation conditions, cigarette smoking produced strong stimulant effects on these measures. Similarly, analysis of individual differences in levels of activity in various arousal systems, particularly EEG 'α' and SFs, demonstrated that individuals with low baseline levels of arousal tended to show stimulant effects from cigarette smoking, whereas individuals with high baseline levels of arousal tended to show depressant effects from cigarette smoking. Personality, as a starting state mediator of smoking effect, appeared to be of relatively minor importance. High cigarette consumption was a strong predictor of reduced cigarette induced tachycardia, perhaps as a consequence of tachyphylaxis or elevated 'tonic' plasma nicotine levels.

(iii) Sham smoking accounted for around 50% of all effects, in both directions (stimulant or depressant), with the exception of cigarette

TABLE I

PHYSIOLOGICAL VARIABLE MEASURED	EFFECT OF STRESS ON BASELINE	EFFECT OF CIGARETTE SMOKING UNDER VARIOUS CONDITIONS			APPROXIMATE PROPORTION OF EFFECT ACCOUNTED FOR BY SHAM SMOKING	IS MAGNITUDE AND/OR DIRECTION OF EFFECT DETERMINED BY PRE-SMOKING BASELINE RESPONSE LEVELS ?	COMMENT
		STRESS	NEUTRAL	SENSORY ISOLATION			
Heart Rate	Stimulant	Stimulant	Stimulant	Stimulant	0%	No (except for cigarette consumption of smoker)	Consistent with virtually every published finding. smoking effects appear exclusively due to nicotine.
Respiration Rate	Mixed	Mixed	Mixed	Mixed	100%	No	Marked stable individual differences and physical effects of smoking behaviour can be observed. A poor measure of 'Arousal' however.
Respiration Irregularity	Mixed	Mixed	-	Mixed	100%	Not studied	
SCL	Stimulant	Mixed	Stimulant	Stimulant	50%	Yes (to some extent - Law of Initial Values)	Replicates Agué (1974) report. 'Mixed' effects of smoking under stress are an original finding.
SFs	Stimulant (not reported)	-	Depressant not reported (Mangan & Golding 1978)	Mixed	50% - 100%	Yes	No other reports published.
SCR	-	Depressant	Depressant not reported (Mangan & Golding 1978)	-	50% - 100%	Not studied	Increased habituation rate consistent with Friedman et al. (1974) finding on EEG α blocking to stimuli.
Tonic EMG	Stimulant	Stimulant (Marginal)	-	Stimulant (Marginal)	0% - 50%	Not studied	Consistent with Fagerström & Götestam (1977) but contradicts animal work data on nicotine as EMG depressant.
Phasic EMG response (to noise bursts)	-	Depressant	-	-	50% - 100%	Not studied	Consistent with Domino (1973) Hutchinson & Emley (1973)
EEG 'α'	Stimulant	Depressant	Mainly Stimulant	Stimulant	50%	Yes	No equivalent experiments for stress or sensory isolation Consistent with many reports of stimulant effects under neutral conditions (Remond et al. 1979)
CNV 8-seconds post-inhalation	-	-	Stimulant (Marginal)	-	Only real versus sham smoking studied. Non-real or sham smoking baseline required	Not studied	No equivalent experiment available although stimulant and depressant post-pre smoking effects on CNV reported (Ashton et al. 1974).
Puffing Associated DC negative shift	-	-	? Stimulant	-	100%	Not studied	May represent facial muscle artefact or a true 'CNV-like' wave. Marked and stable individual differences.

TABLE II

SMOKING STYLE VARIABLE MEASURED	EFFECT OF STRESS	EFFECT OF VARIATION IN NICOTINE DELIVERY (LOW-HIGH) 1.8,0.36mg	MARKED AND RELATIVELY STABLE INDIVIDUAL DIFFERENCES? ('r' refers to test-retest correlations averaged over all experiments)	COMMENT ON PARTICULAR VARIABLE
Puffing Rate	Small increase (N.S.)	Small Increase (Marginal Significance)	Yes (r = +.8)	
Puff Pressure	Increase (Significant)	-	Yes (r = +.8)	Probably the single most important factor as regards obtaining stimulant or depressant effects (low versus high nicotine doses).
Puff Duration	Small Increase (N.S.)	-	Yes (r = +.5)	
Tobacco Weight Burnt	Increase (Significant)	Small Decrease (Significant)	Yes (r = +.8) (r = +.2 in Experiment 2)	Represents the combined effects of puff rate, duration and pressure
Depth of Inhalation	Small Increase (N.S.)	Small Increase (Marginal Significance)	Yes (r = +.8)	
Duration of Inhalation	Small Increase (N.S.)	-	Yes (r = +.8)	Replicates Rawbone (1978) study in direction of effect only. 'n' is larger than Rawbone study.
Smoke Exposure Index	Increase (N.S.)	-	Yes (r = +.6)	
Comment on Effect	Smokers attempt to obtain larger i.e. depressant doses of nicotine during stress.	Effects seen are in the direction of compensating for variations in nicotine delivery. This compensation is Ω 80% successful both in terms of tobacco weight burnt and physiological effects.	Individual differences in smoking style generally appeared marked and stable. They may either reflect 'habit' or their origins may lie in individual differences in nicotine sensitivity	

induced tachycardia, which appeared to be entirely accounted for by tobacco smoke inhalation, and thus by implication was entirely due to pharmacological actions of nicotine. In consequence, nicotine probably accounted for less than 50% of any smoking effect, with the exception of tachycardia, since sham smoking an unlit cigarette is only a poor approximation of a true nicotine-free smoking placebo.

(iv) Smoking style varied in the predicted directions. Increased vigour of cigarette smoking occurred during stress to obtain larger (depressant) dosages of nicotine. Increased vigour of cigarette smoking occurred in response to smoke dilution by ventilated holders. The latter 'self titration' for nicotine appeared to be extremely rapid, being 80% successful within the period of two successive cigarettes, from analyses of burnt tobacco weight, and approaching 100% successful as regards comparisons of smoking effect on physiological measures, including heart rate, between high and low delivery cigarettes. The crucial regulatory variable appeared to be puff pressure in both cases. Striking and stable idiosyncracies of the vigour of smoking style were evidenced which perhaps resulted from individual differences in nicotine sensitivity.

The implication of these results is that cigarette smoking represents an activity which could be used by a smoker to regulate his or her arousal level in the direction appropriate to the situation, i.e. to relax the anxious smoker and to stimulate the drowsy or bored smoker. The question of major interest is to what extent can the laboratory results be extended to the 'real world'? It is probable that the laboratory results give a fair indication of what range of effects may be achieved from smoking a cigarette by the solitary smoker when anxious, bored or drowsy. These effects would probably be reinforcing. However much cigarette smoking occurs in social situations and social situations are

often associated with other psychoactive drug taking, such as tea, coffee and alcohol consumption, and also food consumption. Extremely complex interactions are probable in these circumstances. Thus the cues for lighting a cigarette may simply become social cues in these situations - rather than any attempt at arousal regulation - a packet of cigarettes is offered around. Similarly, the multiple and simultaneous usage of psychoactive drugs may produce "balancing" of depressant versus stimulant effects, as demonstrated for alcohol consumption and cigarette smoking (Myrsten and Andersson, 1978) and also perhaps for the, as yet, poorly understood drug interactions in an extreme case - heroin self-administration and cigarette smoking (Mello, Mendelson, Sellers and Kuehnle, 1980) (also cf. in Appendix: 'The effects of short term diazepam administration on social drug use'). As regards smoking at meal times, the association between hunger and smoking is well known. Smoking alleviates hunger and smokers who give up often put on weight (both by reason of increased appetite and decreased metabolic rate, cf. Russell, 1976). Thus, smoking may alleviate hunger, but on this basis how can the observation that some smokers enjoy a cigarette immediately after a meal be explained? Perhaps the smoker can titrate himself for nicotine dosage so as to obtain the correct stimulant versus depressant effects of nicotine at lateral hypothalamic 'feeding' reward centres, before and after eating, respectively.

The real-world situation is obviously very complicated, and generalisation from the present laboratory studies reported must be limited to solitary cigarette smoking in the absence of any concurrent activities such as alcohol or food consumption.

SUMMARY DISCUSSION - GENERAL

Three main questions may be asked about the motivation for cigarette smoking (i) why do people start smoking?, (ii) why do cigarette smokers continue to smoke?, (iii) and why do smokers find it so difficult to give up smoking? The experiments in this thesis have been primarily directed towards answering the second question, i.e. what are the reinforcing factors underlying maintenance of cigarette smoking. However, these factors are doubtless important in determining why one individual becomes a smoker, another may briefly experiment with the habit as a teenager and then stop, and why one habitual long-term smoker may give up whereas another may not.

There are currently two main hypotheses as to the reasons for cigarette smoking - 'Arousal Modulation' and 'Nicotine Addiction'.

An Arousal Modulation model of cigarette smoking suggests that smokers use cigarettes as one means of regulating their mood i.e. to stimulate themselves when feeling bored or drowsy and to calm themselves when feeling anxious, irritable or angry. Viewed as such a mechanism of mood control, smoking is one of a similar class of common activities - including coffee and tea drinking (stimulant), alcohol consumption (primarily depressant). This class of mood control activities may also include such non-pharmacological activies as sucking sweets, chewing gum, 'excessive' television viewing, the reading of light material and physical/mental exercises such as Yoga. The primary agent of cigarette smoking's postulated mood controlling properties is suggested to be nicotine. Nicotine has a biphasic dose response curve, stimulant at low doses and depressant at higher dosages. This biphasic dose response has been clearly demonstrated on animals (cf. Introduction of thesis) by

studies on neurotransmitter release, electrocortical activity and behaviour measures. Proof for dose-related biphasic effects of nicotine (per se) in man virtually devolvesto one report (Ashton et al. 1978). This is because most studies utilising nicotine (injection) in man have had as their primary objective the demonstration of changes in cigarette consumption or smoking style, rather than observation of physiological and, in particular, electrocortical functioning. However, there are numerous reports of stimulant and depressant effects of cigarette smoking on various measures of physiological arousal; autonomic, muscle and electrocortical functioning (cf. Introduction of thesis). While the majority of reports suggest that cigarette smoking has stimulant effects, there are quite a number of reports of mixed and/or depressant effects of smoking; increased EEG and SCR habituation to tone stimuli, decreased SF rate, increased habituation of reflex or stress-induced EMG responding, decreased CNV amplitude for individuals postulated to be over-aroused, and increased alpha activity during stress (Friedman et al., 1974; Domino and von Baumgarten, 1969; Hutchinson and Emley, 1973; Ashton et al., 1974; Mangan and Golding, 1978). Studies of cigarette smoking and performance have tended to show 'enhanced' performance but some decrements of performance have been noted, on complex reasoning tasks, acquisition of low interference paired associate verbal material, (cf. Introduction of Thesis). However, the interpretation of cigarette smoking effects on performance as being stimulant or depressant are complicated by the well known 'inverted-u' curve relating performance to arousal, the so-called 'Yerkes-Dodson Law'

'Nicotine Addiction' models of cigarette smoking hypothesise that the cigarette smoker becomes addicted to a certain level of nicotine at CNS target receptors. When nicotine levels at these CNS receptors fall

below a certain level 'punishment' is signalled in an analogous manner to that operating for opiate addiction. The relief of unpleasant nicotine withdrawal symptoms is the primary stimulus for the smoker to light up another cigarette. Evidence in support of this view has come from a number of studies demonstrating appropriate increases or decreases in cigarette consumption and/or vigour of smoking behaviour in the face of experimental manipulations designed to vary nicotine levels at the postulated CNS target sites. The experimental manipulations have included; (Internal) use of central and peripheral nicotinic receptor blockade, additional nicotine presented by injection or orally, measures designed to increase and decrease the rate of nicotine excretion by manipulating urinary pH levels, and (External) variations (+ or -) in nicotine delivery of cigarettes by use of smoke dilution, increased filter efficiency, length of tobacco rod, choice of tobacco (cf. Introduction of Thesis).

Experiments utilising these methods have met varying degrees of success (on average demonstrating up to 30% of predicted variation). In particular the evidence seems to suggest that variations in smoking style (i.e. the vigour with which a cigarette is smoked) are more important than overall cigarette consumption, studies which have utilised only the latter measure demonstrating it to be relatively insensitive to internal or external manipulations of nicotine. Over and above this methodological comment, two general comments may be made. Firstly, that experiments designed to demonstrate compensatory (+ or -) variations in self-titration for nicotine by varying nicotine delivery of cigarettes (External) are more successful (e.g. Ashton et al. 1979) than those (Internal) experiments utilising injected nicotine, oral nicotine or nicotinic blockade (e.g. Kumar et al. 1978). Secondly, if a particular steady level of nicotine at CNS receptors is required, given the extremely short half-life

of nicotine in the CNS (probably of the order of a few minutes), why do not most smokers either chain smoke or opt for a method of smoking (e.g. cigar smoking) which would enable them to ahieve closer to 'steady-state' nicotine levels at the hypothesised 'nicotine addicted' CNS receptors? (cf. 'peak' versus 'trough' nicotine level seekers; Russell et al., 1978).

The most probable answer to both of these questions - the greater success of External versus Internal methods, and the implication of the short CNS half-lives of nicotine - is that the cigarette smoker is not attempting to maintain some steady level of nicotine at CNS receptor sites. The reasons for this are not difficult to find, and involve a synthesis of both Nicotine Addiction and Arousal Modulation models of cigarette smoking. Such a synthesis might be termed 'Arousal Addiction'.

Two crucial factors are at work. Firstly, it may be necessary only to achieve particular nicotine levels in the CNS for a short period of time in order to achieve secondary effects of relatively greater duration. The secondary effects are doubtless the well documented nicotine-induced release of neurotransmitters such as acetycholine, noradrenaline etc., (cf. Introduction of Thesis). Secondly, although nicotine is probably the ultimate reinforcer for cigarette smoking, the feedback from activity associated with smoking (puffing, inhalation, smell, etc.) produces marked effects both on its own account and by close association with the arrival of nicotine. One of the strongest demonstrations of effects not mediated by nicotine is that reported by Hall (1970). These results demonstrated that mecamylamine, a centrally acting nicotine receptor blocker, completely prevented EEG desynchronisation, caused by nicotine injection, of the cerebral cortex and olfactory bulb of both alert and also encéphale isolé cats, but failed to blockade these effects when nicotine was administered via smoke into the lungs (cf. Introduction of

Thesis for examples of sham-smoking effects on human EEG). Such non-nicotine mediated effects are generally subsumed under the heading of the 'secondary reinforcing' properties of cigarette smoking. It is perhaps not surprising then, that intravenous 'bolus' injections of nicotine at rates designed to mimic or exceed those obtained by cigarette smoking fail to alleviate either the subjective sense of missing cigarettes or the objective measure of cigarette puffing behaviour during or after nicotine shots (cf. Russell et al., 1978 for review). This 'secondary reinforcing' property of cigarette smoking behaviour is an important factor to be taken into account whether 'Nicotine Addiction' or 'Arousal Modulation' models of smoking are espoused.

As is often the case with opposing theories of some phenomenon, both of which can muster supporting evidence, the truth lies somewhere in between (cf. 'Wave' versus 'Particulate' nature of electromagnetic radiation). The view taken in the present thesis is that cigarette smokers are 'addicted'[1] to smoking and ultimately to nicotine which acts as a partial reinforcer for the habit. The nature of the addiction from the point of view of 'giving-up' is the same as in opiate or alcohol addiction. This is nicely demonstrated by Figure 1. However, 'withdrawal' symptoms from cigarette smoking in no way compare to those observed for going 'cold turkey' or 'drying-out'. It is postulated that the cigarette smoker is in fact addicted to certain levels of desired arousal, which probably varies both between individuals and within individuals as a function of situation. This is 'Arousal Addiction'.

There is some evidence that the smoker is in fact a person with poor arousal control, perhaps ultimately deriving from genetic factors. Thus twin studies demonstrate a strong genetic loading for smoking (Strickenberger, 1968), children who are more neurotic, anxious and

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[1] 'addicted' in the behavioural sense, the word 'addiction' in this sense, is equivalent to the general W.H.O. term 'drug dependence' (Laurence, 1973).

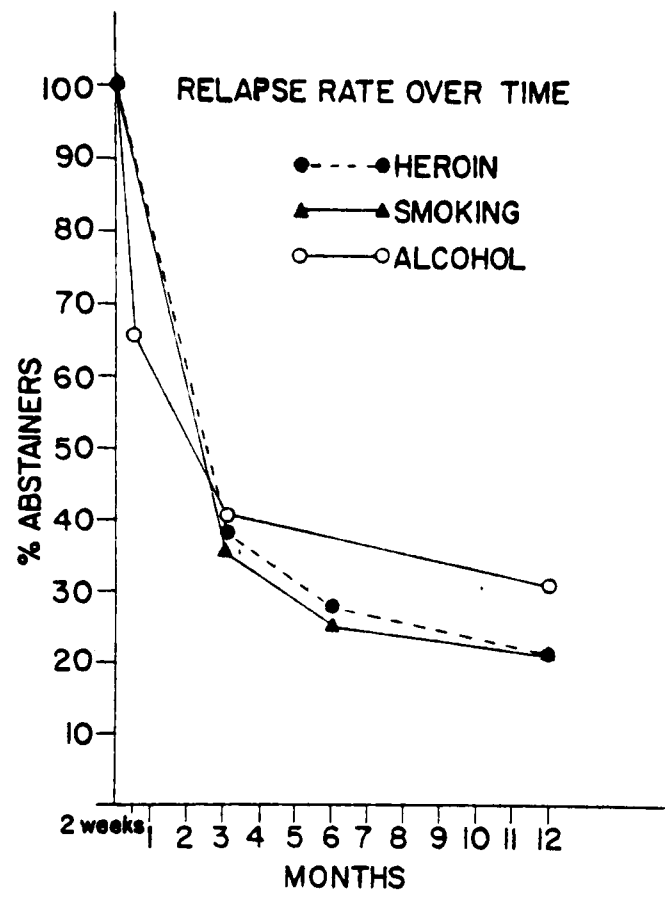


FIGURE 1 : Relapse rate over time for heroin, smoking and alcohol (from Hunt and Matarazzo, 1973)

extraverted are more likely to become smokers (Cherry and Kiernan, 1978; Mangan, 1975, unpublished SSRC Schoolchildren Survey) and cigarette smoking is linked to elevated usage of other commonly used arousal-control drugs such as caffeine and alcohol (Zucker and Van Horn, 1972; Prendergast, Thomas, Preble, and Tennant, 1973; Mangan, 1975). In addition, personality factors and general drug usage themselves have a degree of genetic loading (Eysenck, 1975; Strickenberger, 1968).

On this basis we might predict that the more emotionally stable smoker is more likely to successfully 'give'up'. There is indeed evidence that low neuroticism scores for men do, in fact, predict a greater likelihood of giving up the habit (Cherry and Kiernan, 1978). The evidence for women is less clear-cut, perhaps because they tend to be more emotionally labile and have higher 'N' scores than men in the first place (Eysenck, 1975). However, by far the strongest predictor for giving up, and the least mentioned in the literature, is social class.

Thus, perhaps, as a consequence of Smoking and Health Education campaigns, there has been an overall trend for smoking prevalence to have decreased over the last few years (Cappell, 1978). This reduction of smoking prevalence has been more a function of 'giving-up' rather than decreased recruitment to the habit. Taking figures for age, sex, historical trends and social class, based on TRC and GHS surveys (U.K.) into account, the major effect of health education campaigns has been to cause Social Class I to give up smoking. The reduction of smoking prevalence for Social Class I from 1961 to 1976 was 53% to 29% (men), 45% to 24% (women). For Social Classes II, III, IV and V, smoking prevalence reduction over the equivalent time period has been minimal: 59% to 45% (men), 48% to 42% (women, with very little gradation of effect from Social Class II to V, (source; Capell, 1978). This major reduction of smoking prevalence in Social Class I

perhaps reflects the fact that the Smoking and Health Education campaigns ultimately emanate from this class. There is no convincing evidence that Social Class I is emotionally more stable than Classes II to V or that their environments are less boring or stressful. Thus,it would be predicted from an Arousal Addiction model of smoking,that with declining prevalence of smoking the consumption of tea, coffee, alcohol, minor tranquillisers and perhaps other mood control activities such as Yoga should have differentially increased over the last few years in Social Class I as compared to Social Classes II to V. Data pertaining to this question do not appear to be easily accessible. In particular, data for the medical profession which has exhibited a dramatic decline in smoking prevalence and which also has ready access to minor tranquillisers (e.g. diazepams) and β blockers (e.g. propranolol) would be extremely interesting.

If this suggestion is true, it implies that the individual 'at risk' for cigarette smoking will compensate for the loss of cigarettes as a mood control device by increased alternative mood control activities, some of which e.g. alcohol consumption, may themselves be unhealthy in excess.

Perhaps in the long term the cigarette manufacturers will diversify some of their resources into providing 'safer' mood control activities. In the short term, continued efforts for producing a 'safer' cigarette, primarily by reduction of the more hazardous tar and carbon monoxide components of smoke,while maintaining nicotine delivery,would seem the appropriate course of action. (The unwanted and potentially hazardous cardiovascular side-effects of nicotine itself might possibly be ameliorated by inclusion of a β-blocker in the tobacco.)

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APPENDIX A : Specimen Chart Records

Figure 1 - 7 are photostats of chart record photographs. Response channels and time period are marked on each figure. For the EEG channel, dark coloured, small amplitude portions of the trace are β; lighter coloured, large amplitude portions of the trace are α (EEG channel is 8-13 Hz bandpass output). Cross-hatches on the SC channel indicate resets of "back-off". ("↑" : direction of inhalation)

Figures 1 and 2: note the strong α-blocking effect of sham smoking during sensory isolation (Figure 1) and increase of α for sham-smoking during stress (Figure 2). Real cigarette smoking effects usually last longer. Note also SCRs to noise stimuli (Figure 2).

Figures 3 and 4: cigarette smoking during boredom. Note that while subject G.G. (Figure 4) shows strong stimulant smoking effect on EEG α, subject L.M. (Figure 3) if anything shows the reverse.

Figures 5, 6 and 7: Although stimulant effects of cigarette smoking predominate during sensory isolation conditions, this to some extent depends on individual starting state. The pre-smoking baseline levels of EEG α are largest in subject J.D. (Figure 5) smaller in subject C.R. (Figure 6), and very small in subject K.C. (Figure 7). Consequently, the effects of cigarette smoking vary from strongly stimulant (Figure 5, subject J.D.), through stimulant (Figure 6, subject C.R.) to marginally depressant (Figure 7, subject K.C.)

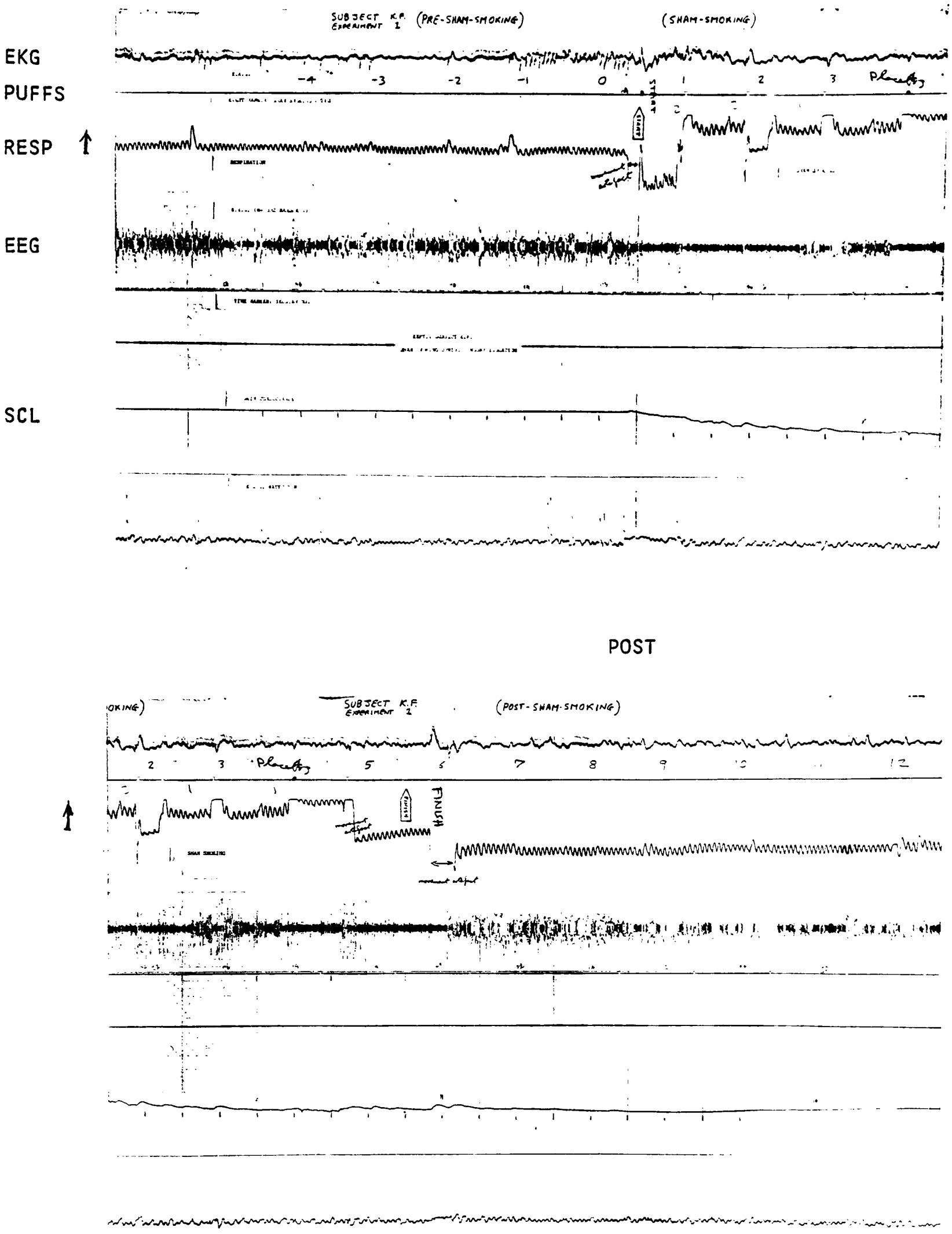


Figure 1: Subject K.F., Experiment 1, sham-smoking during sensory isolation.

PRE

SHAM SMOKING

EKG

PUFFS

RESP

EEG

SCL

WN

POST

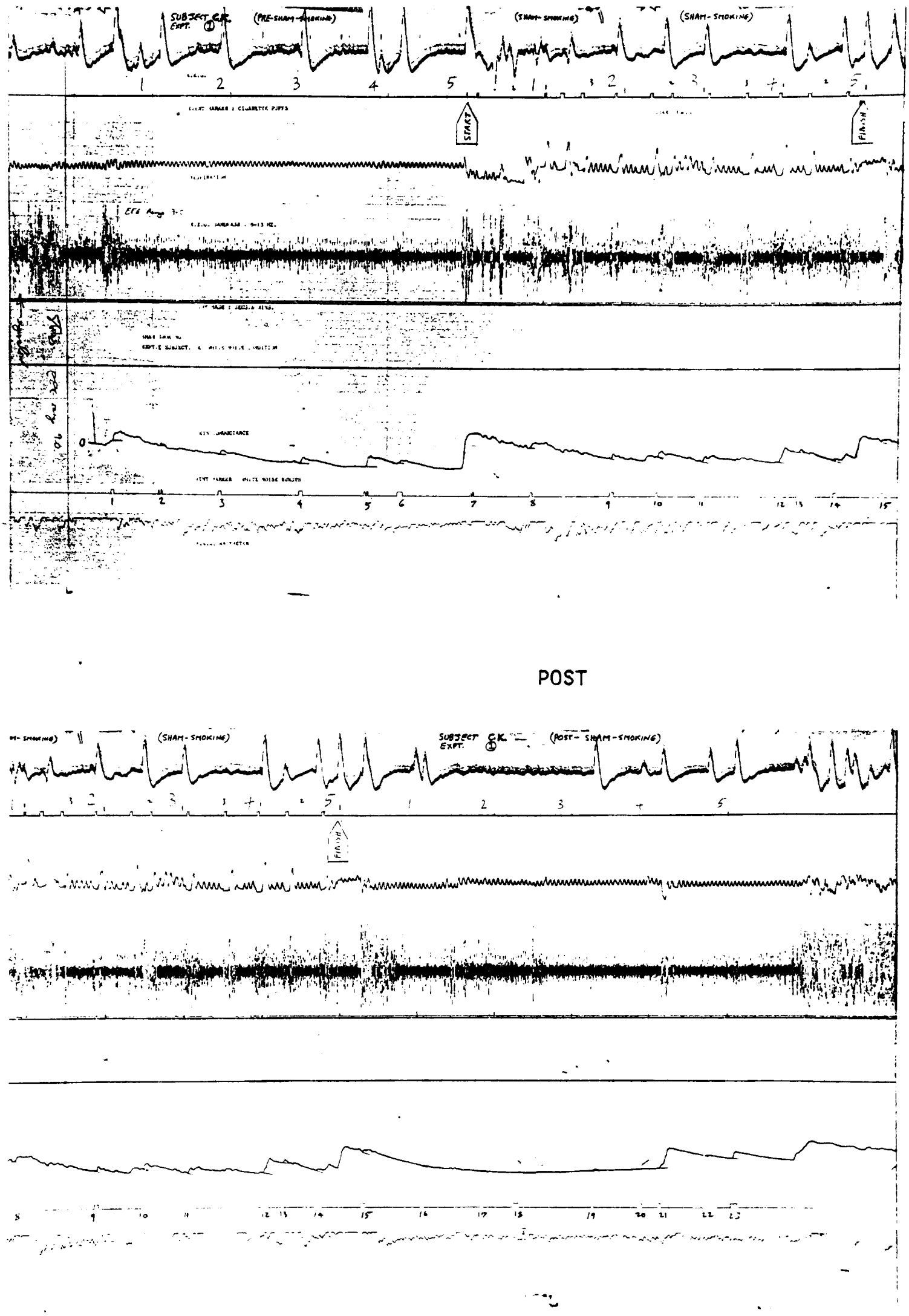


Figure 2: Subject C.K., Experiment 1, sham smoking during stress.

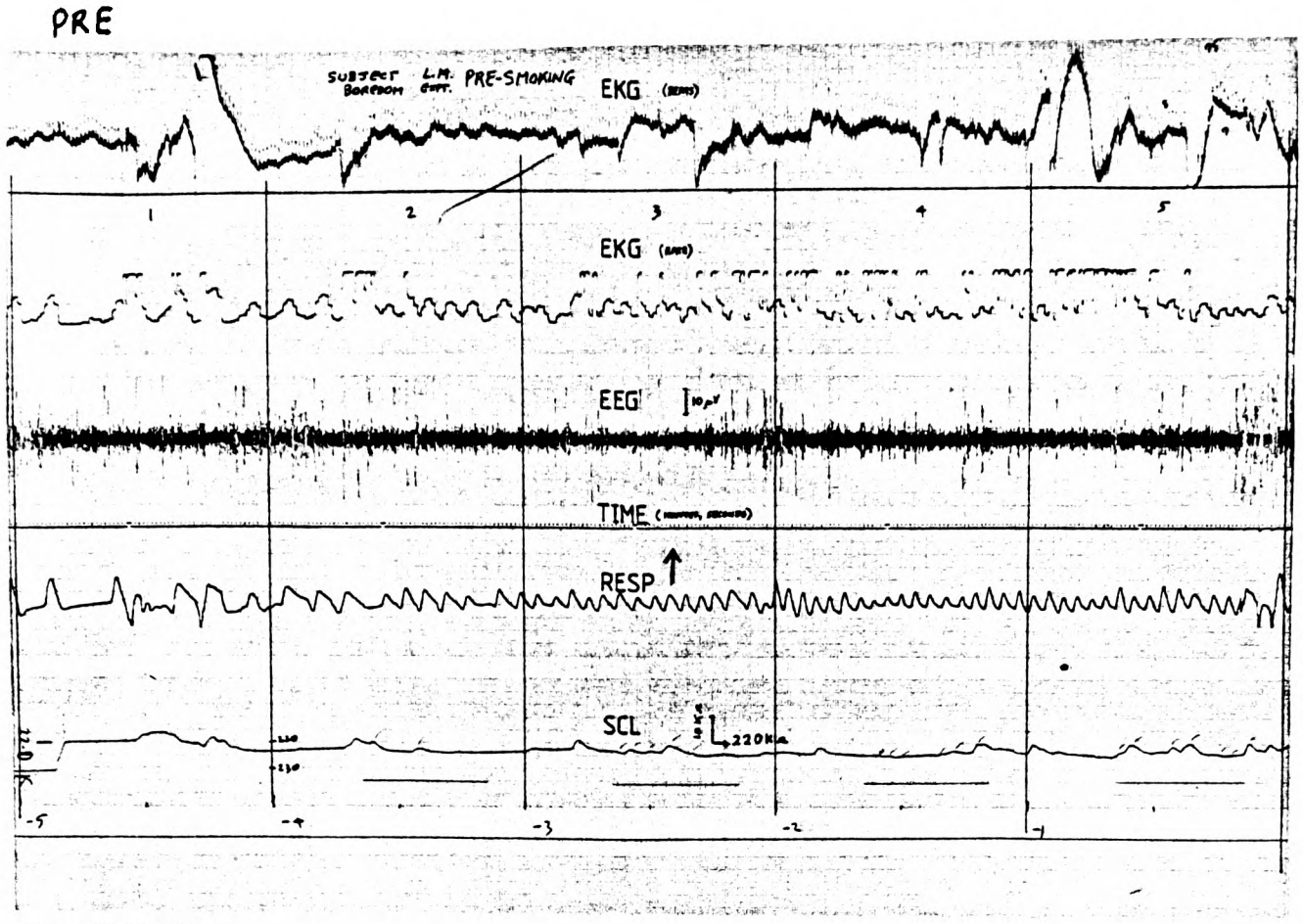


Figure 3: Subject L.M., Experiment 4, real-smoking during 'boredom'. Response modalities and time period are labelled on the figures.

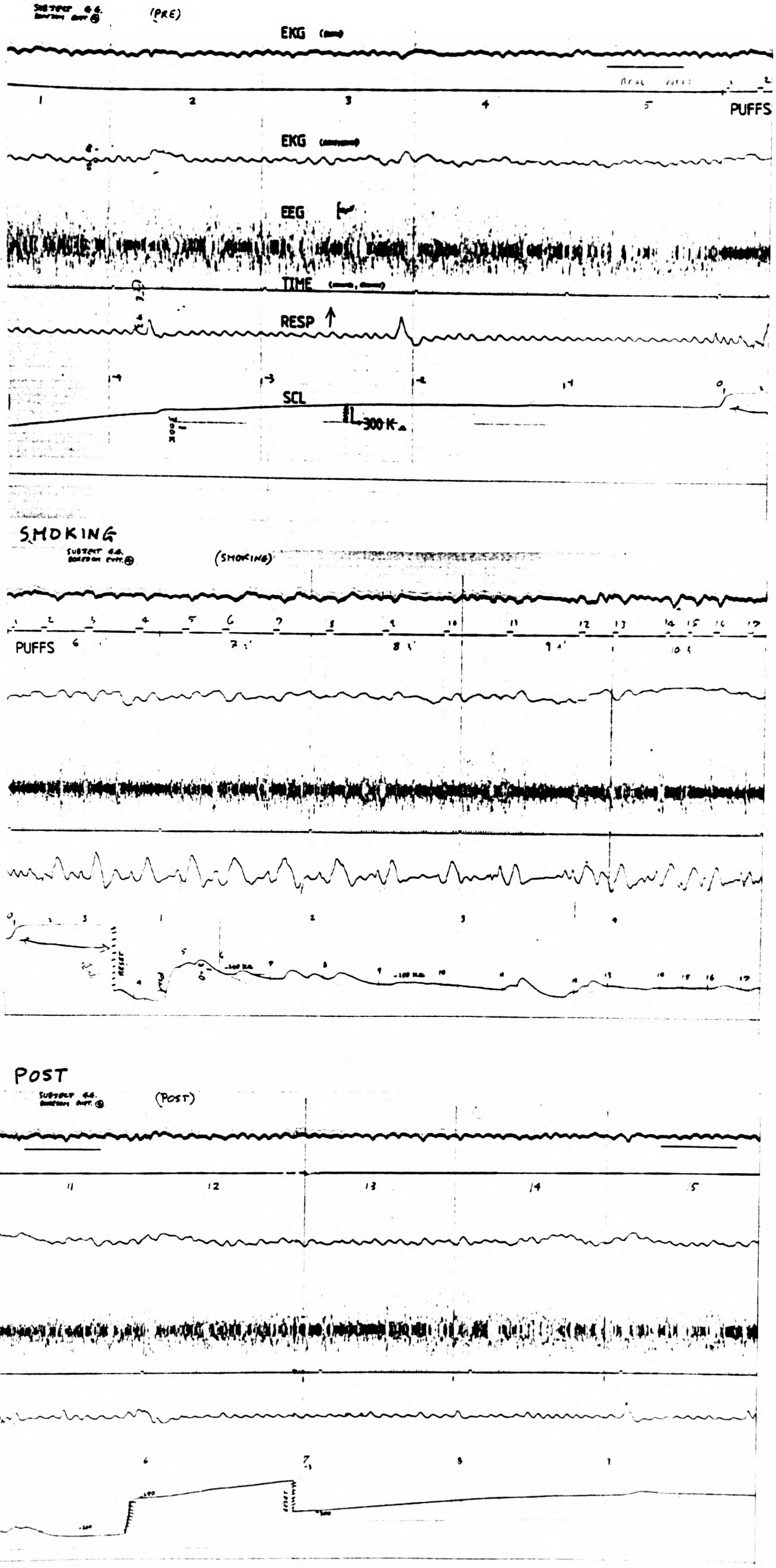


Figure 4: Subject G.G., Experiment 4, real smoking during 'boredom'. Response modalities and time period are marked on the figures.

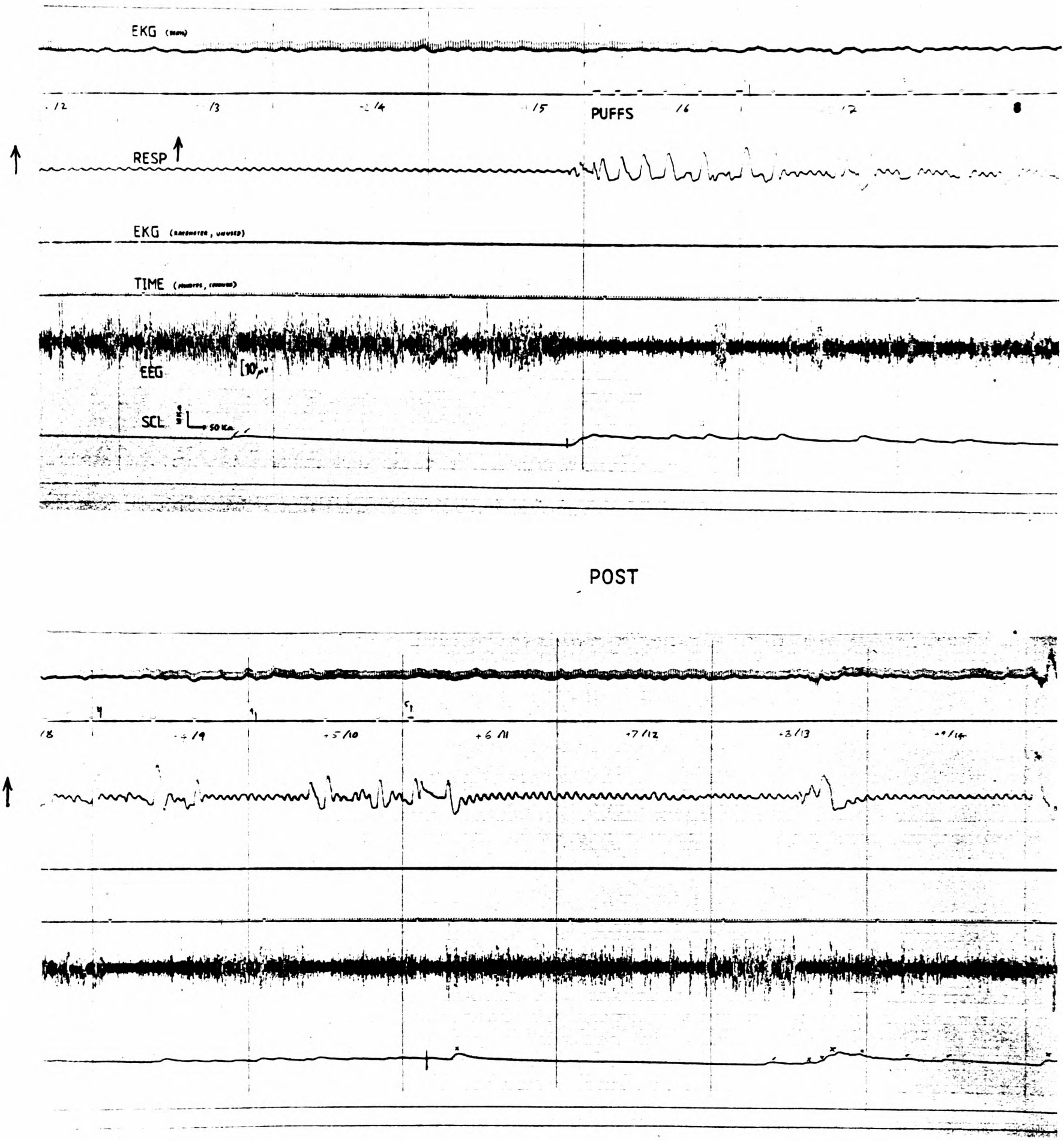


Figure 5: Subject J.D., Experiment 5, smoking a 20% holder during sensory isolation. Response modalities are labelled on the figures, time period immediately above.

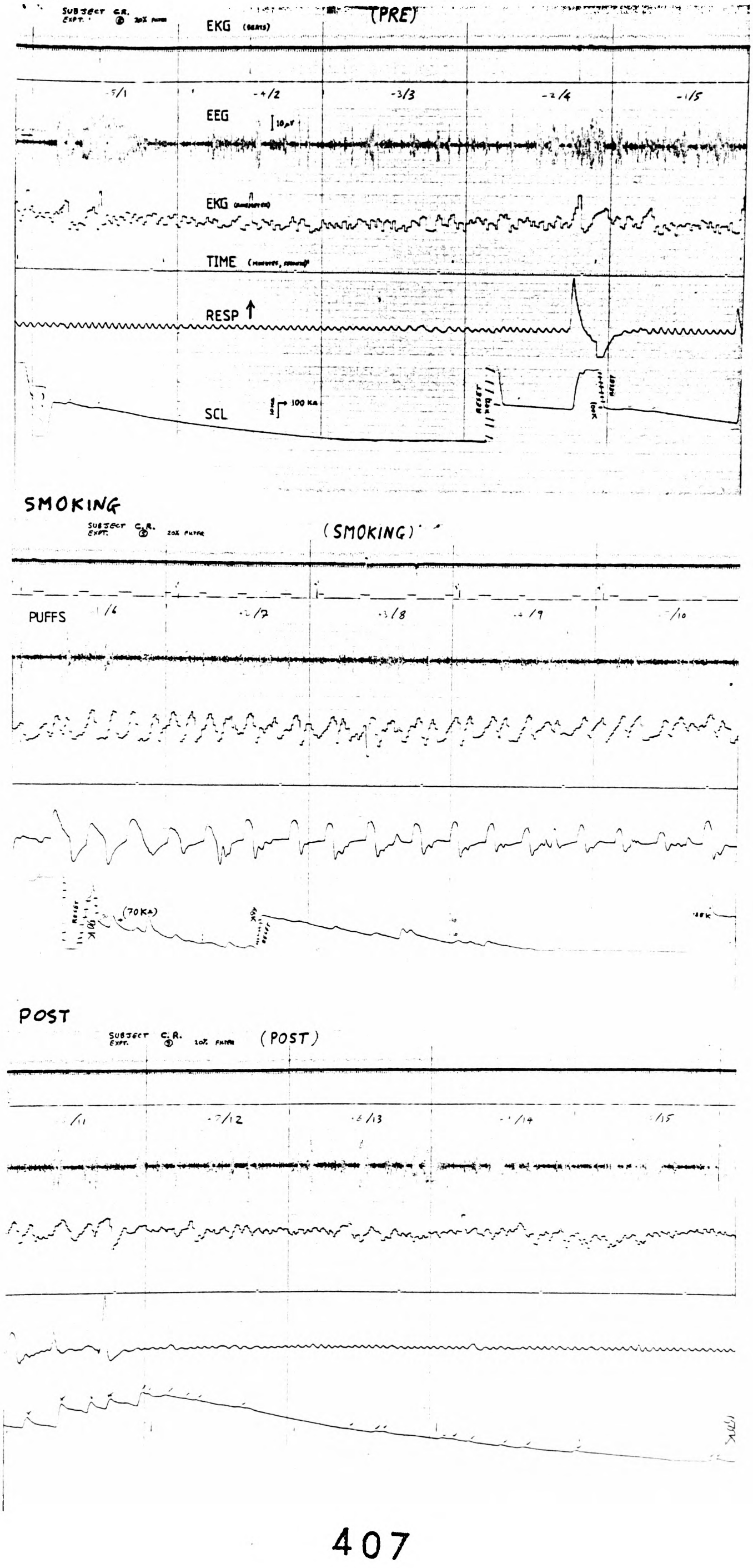


Figure 6: Subject C.R., Experiment 5, smoking a 20% delivery holder during sensory isolation. Response modalities and time period are labelled on the figures.

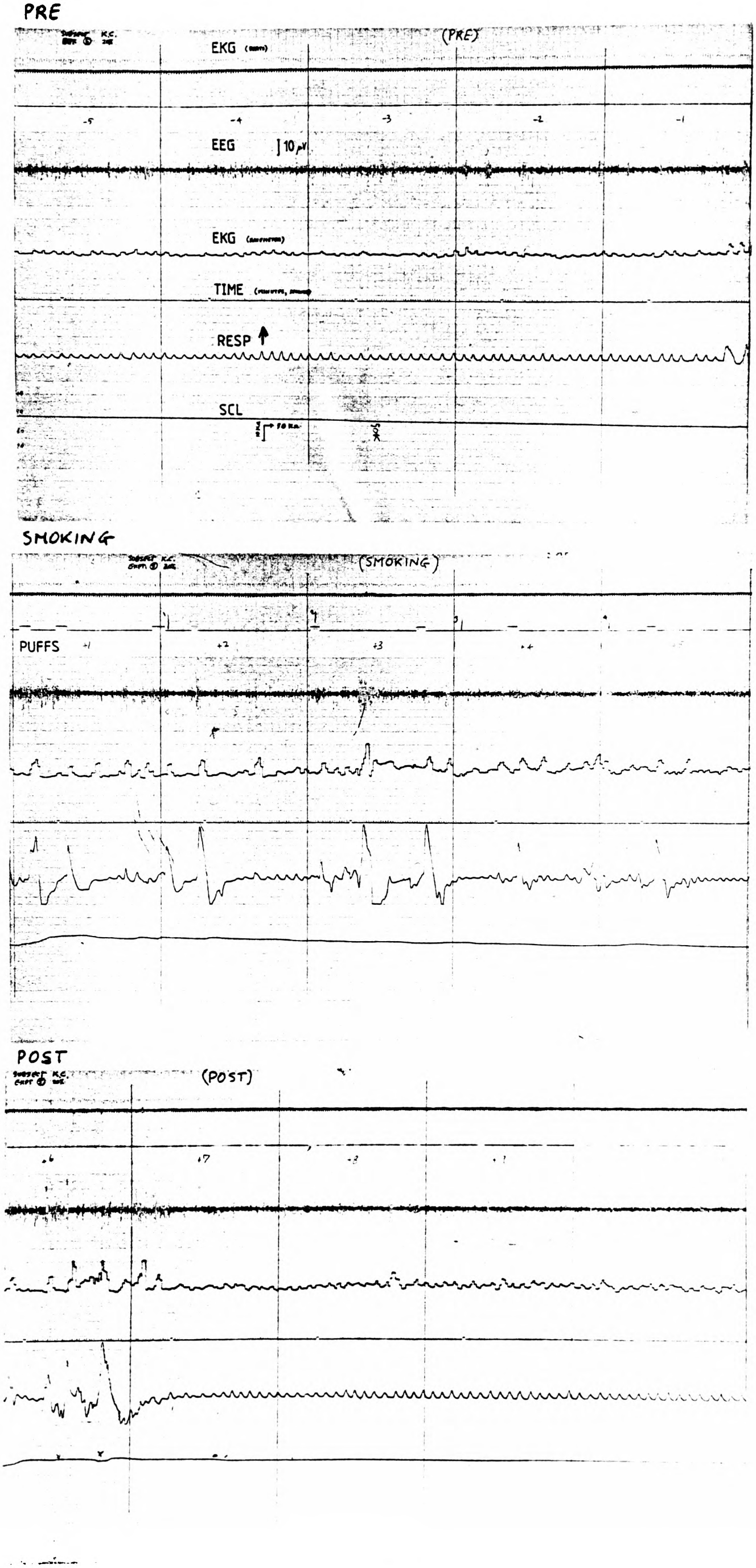


Figure 7: Subject K.C., Experiment 5, smoking a 20% delivery holder during sensory isolation. Response modalities and time period are labelled on the figures.

APPENDIX B : Valium and Smoking Study.

(Work carried out with R. Stepney
at the Clinical Psychopharmacology Unit,
Newcastle upon Tyne.)

THE EFFECTS OF SHORT-TERM DIAZEPAM ADMINISTRATION ON SOCIAL DRUG USE

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The effects of short-term diazepam administration on social drug use

Summary

Consumption of cigarettes, tea and coffee was studied over a four day period in smokers given diazepam and placebo. Over the period of diazepam administration tea and cigarette consumption remained unaltered. There was some evidence, however, that coffee consumption increased and that smokers adjusted their nicotine extraction from cigarettes to obtain a stimulant dose.

Introduction

Habits involving consumption of the commonly available social drugs are inter-related. For example, smokers drink more alcohol and coffee than non-smokers.[1] The relationship, however, is not straightforward. Thus, whilst rate of smoking under controlled conditions increases in response to increased alcohol administration,[2] nicotine intake increases in response to caffeine deprivation.[3] This complicated inter-relationship suggests that the consumption of social drugs may be regulated by a desire to obtain a balance between their stimulant and depressant effects. Nevertheless, a strictly pharmacological interpretation of social drug use is complicated by the probable importance of social, oral-manipulative and taste factors. It is therefore of interest to consider whether a depressant drug (diazepam) independent of such a complicated context of administration, produces any compensatory changes in social drug use.

Subjects and Method

Fifteen volunteer subjects (3M, 12F; aged 19-44 years), all regular inhaling smokers of 10 - 30 cigarettes per day, participated in the experiment. Subjects acted as their own controls, taking either 2 (8 subjects) or 3 (7 subjects) 5 mg capsules of diazepam per day and

equivalent placebo over 2 day periods in a balanced, crossover, double-blind experimental design spanning 10 days. The drug or placebo was taken on days 2 and 3, and 8 and 9. Days 1, 4, 7 and 10 were treated as control days and days 5 and 6 (the weekend) ignored. Subjects were asked, and agreed, to abstain from alcohol for the period of the experiment. On each day subjects collected the butts from all cigarettes smoked and carefully noted the number of cups of tea and coffee consumed. To take account of changes in the intensity with which cigarettes were smoked, the daily butt collections of 7 subjects were assayed for nicotine and an average figure for nicotine-in-tip (which is proportional to the nicotine dose delivered to the smoker) was calculated.

Results

Data for subjects taking 10 and 15 mg diazepam per day was pooled. The drug effect was defined as the difference between control and drug days , and compared with the difference between control and placebo days (Table I). Differences of borderline significance emerged in respect of coffee, combined tea and coffee consumption and butt length.

Discussion

The dose of diazepam used was calculated to produce mild drowsiness and this was confirmed by subjective report. There is evidence that caffeine and the nicotine derived from cigarettes may be used to manipulate arousal[4,5] and specifically, that smoking can counteract the impairment in performance caused by alcohol.[6]

Nicotine has biphasic stimulant and depressant properties depending on rate of dosage[4] (stimulant effects at low dosage, depressant at higher dosage).Thus one would predict that as well as increasing coffee consumption the smoker will attempt to obtain a smaller dose of nicotine in

the face of lowered arousal.

The results of the present experiment would suggest that a small compensatory increase in caffeine consumption together with a reduction in the amount of each cigarette smoked are the initial reactions to a diazepam-induced lowering of arousal.

Table I. Consumption of cigarettes, tea and coffee with diazepam and placebo

Condition	Diazepam			Placebo			difference (diazepam-control	difference (placebo-control	p
	$\bar{x}$ control days	$\bar{x}$ drug days	p	$\bar{x}$ control days	$\bar{x}$ drug days	p			
Cigarette consumption/ day	14.7	15.1	ns	14.8	15.1	ns	0.40	0.27	ns
Butt length mm	7.65	8.15	ns	8.44	8.17	ns	0.50	-0.27	.07
Butt nicotine mg	0.70	0.68	ns*	0.70	0.69	ns*	-0.03	-0.01	ns*
Coffee consumption cups/day	2.7	3.0	.15	2.6	2.5	ns	0.30	-0.07	.17
Tea consumption cups/day	3.87	3.83	ns	4.13	4.40	ns	0.03	0.27	ns
Combined tea and coffee consumption, cups/day	6.57	6.83	.09	6.70	6.90	ns	0.33	0.20	ns

STATISTICS: T-TEST: 2-TAILED, D.F. = 14, *D.F. = 6

References

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STATISTICAL ADDENDUM

The statistics employed for data analysis of the experiments presented in this thesis have had as their primary objective the demonstration of specific effects of cigarette smoking on a variety of psychophysiological measures.

In some cases n-way ANOVA could have been employed as opposed to the use of a battery of statistical tests making specific comparisons between means and variances (i.e. Sign Test, Wilcoxon Matched-Pairs Test, Kruskal-Wallis 1-way ANOVA, Mann-Whitney "U" Test, T-test, F ratio).

However, all means and S.D.s analysed in these ways have been carefully examined and in no case would an n-way ANOVA have produced different conclusions of a statistically significant nature.