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Effects of cranial transcutaneous electrical nerve stimulation in normal subjects at rest and during stress

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EFFECTS OF CRANIAL TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN NORMAL SUBJECTS AT REST AND DURING STRESS

by

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Abstract

EFFECTS OF CRANIAL TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN NORMAL SUBJECTS AT REST AND DURING STRESS

by

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The literature on the cranial application of transcutaneous electrical nerve stimulation (TENS) is reviewed. Three studies are reported which evaluate some physiological and psychological effects of cranial TENS of different frequencies, and investigate whether this treatment may be useful in the management of stress, offering improvements in experimental design and instrumentation over past cranial TENS research. In a pilot study, significant reductions in systolic and diastolic blood pressure and anxiety, but not in pulse rate, peripheral vascular tension or skeletal muscle activity, were observed in treatment-blind normal subjects after 30 minutes of sine-wave constant alternating current cranial TENS of 100 Hertz (Hz) frequency, as compared to a no treatment control. No placebo TENS effect was observed. In a second study, employing a double-blind procedure, significant reductions in systolic and diastolic blood pressure and pulse rate, but not in peripheral vascular tension or anxiety, were observed in normal subjects after 30 minutes of cranial

TENS of 100 Hz frequency, but not after cranial TENS of 5 Hz or 2000 Hz, as compared to a no treatment control. No placebo TENS effect was observed. In a third study, also double-blind, significant reductions in systolic blood pressure, pulse rate and anxiety, but not in diastolic blood pressure or peripheral vascular tension, were observed in normal subjects after 30 minutes of 100 Hz cranial TENS as compared to a no treatment control. No placebo TENS effect was observed. No significant group differences were observed in physiological or psychological response to 3 minutes of standardized experimental stress (mental arithmetic), which immediately followed the 30 minute treatment phase. Results are discussed in terms of the potential of cranial TENS for the management of stress.

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INTRODUCTION

The purpose of these studies is to investigate the effects of cranial transcutaneous electrical nerve stimulation (cranial TENS) on physiological and psychological measures in normal human subjects at rest and during mild psychological stress, offering improvements in experimental design and TENS instrumentation over past cranial TENS research, in order to assess the applicability of this technique to the management of stress.

Repeated or prolonged stress, common in this fast-paced society, can lead to pathologic nervous system activity resulting in a variety of disorders with a combined prevalence of over 30% in the U.S., consuming 10% of the gross national product (Ivancevich & Matteson, 1980). For example, chronic stress-induced autonomic nervous system hyperactivity (Cannon, 1953) can lead to hypertension (Forsman & Lindblad, 1983; Guyton, 1988; Reis, 1988) and myocardial necrosis (Rozanski et al., 1988; Selye, 1976); kidney changes (Evans et al., 1981; Folkow et al., 1977), resulting in hypertension (Selye, 1976) and renal damage (Cromin et al., 1978; Lohmeier et al., 1984); gastrointestinal difficulties such as ulcers (Backus & Dudley, 1977; Selye, 1976) and irritable bowel syndrome (Schuster, 1983); and vasomotor lability (Sokolov, 1963) resulting in migraine headache (Wolff, 1963) and disturbances of the peripheral blood supply (Taub & Stroebel, 1978). Somatic nervous system

hyperactivity from chronic stress (Jacobson, 1970) can lead to chronic muscular tension, which manifests as tension headache, bruxism, temporomandibular joint (TMJ) syndrome, chronic back pain and other musculoskeletal complaints (Basmajian, 1979). Additionally, prolonged stress can have psychologic sequelae such as anxiety (Gellhorn, 1969; Jacobson, 1970; Seligman, 1968), and can weaken the immune system (Dorian et al., 1982; Kiecolt-Glaser, et al., 1986; Linn et al., 1981; Locke et al., 1984), leaving the organism vulnerable to infection.

While pharmacologic treatments for stress-related disorders, such as the minor tranquilizers, are often habit-forming, or may have unpleasant side effects, behavioral interventions, such as training in self-executed relaxation, are hindered by anxiety (Carey & Burish, 1985), and can require months of practice before beneficial effects are observed. A fast-acting, non-addictive, non-aversive method for inducing nervous system relaxation might prove helpful in the management of stress-related disorders. This paper therefore reviews the literature on cranial TENS, and then describes a series of studies which investigate the ability of sine-wave constant alternating current cranial TENS to attenuate physiological and psychological arousal in normal human subjects at rest, and during experimental stress. If cranial TENS is shown to attenuate arousal under these conditions, this may suggest possible applications of this

technique to the management of real-life stress and its related disorders.

I. ORIGINS OF CRANIAL TENS

The application of transcutaneous electrical nerve stimulation (TENS) to the cranium for the treatment of anxiety-related disorders emerged in the 1950s in the Soviet Bloc literature as a technique involving the passage of pulsed direct current (DC) of low frequency (100 Hertz [Hz] or less) and intensity (less than 3 milliamperes [mA]) between electrodes placed on opposite poles of the cranium for the purpose of producing a normalizing and calming effect on the central nervous system. The treatment was called "electrosleep" owing to the observation that patients often fell asleep during treatment, and the belief that artificially induced sleep was responsible for the "restorative" effects of the treatment.

The idea of electrosleep began in the 1920s in Russia with Ivan Pavlov. His observations of dogs during investigations into the conditioned reflex led him to propose that sleep and internal inhibition were essentially the same process; that sleep was simply the spread of internal inhibition over the entire cortex, with later involvement of subcortical structures. Pavlov suggested that a monotonous rhythmical stimulus applied to an animal would produce internal inhibition and eventually sleep (Pavlov, 1927). Over the next forty years, many studies were reported from Eastern Bloc countries attesting to the efficacy of electrosleep in dealing with

various psychosomatic disturbances, neuroses and psychoses. Most of this research was presented at the International Symposia for Electrotherapeutic Sleep and Electroanesthesia held in Graz, Austria in 1966 and 1969 (Wageneder & Schuy, 1967; 1970). These reports were to be regarded with skepticism, however, owing to a lack of control procedures, follow-up data, reliable diagnostic criteria and outcome measures, and explanation of observed effects (Dodge, 1967; Iwanovsky & Dodge, 1968; Van Posnak, 1969; Von Richthofen & Mellor, 1979; Wageneder et al., 1969).

II. CLINICAL EVALUATION OF CRANIAL TENS IN THE U.S.

After the Graz symposia, Western researchers began to show an interest in electrosleep, changing its name to "cerebral electrotherapy" or "CET", owing to lack of evidence supporting its effectiveness as a sleep induction method (Frankel et al., 1973), and to reports suggesting that sleep is not a necessary component of the treatment (Wageneder et al., 1969; Tatsuno & Wageneder, 1970). From 1963 to 1976 a number of controlled and uncontrolled clinical studies were reported which supported three different conclusions: 1) cranial TENS is effective in reducing symptoms associated with spasticity, anxiety, insomnia and depression in clinical populations; 2) there are no appreciable effects of cranial TENS; and 3) any observed benefit of cranial TENS can be explained by suggestion or placebo effects. Although attempts were made to overcome the shortcomings of the Eastern Bloc research through the inclusion of double blind and placebo procedures, the results of these studies must also be interpreted with caution owing to the questionable success of these procedures, the subjective nature of the dependent measures, and the variability of the cranial TENS protocol and apparati.

Clinical Evaluation: Positive

U.S. reports apparently demonstrating measurable effects of cranial TENS began with Forster et al. (1963). These researchers were interested in controlling muscle

spasticity, a negative factor in rehabilitation. They administered cranial TENS to 17 patients suffering from a variety of disorders resulting from CNS trauma who ranged in age from 14-68 years, and to 6 healthy controls who ranged in age from 21-24 years. The cranial TENS current was passed from posterior to anterior electrodes in rectangular DC pulses of 20-40 Hz frequency and 0.5-0.8 mA intensity for an unspecified period of time. These authors reported observing reductions in muscle tension and spasticity, blood pressure, pulse rate and respiration, and concluded that cranial TENS might be a potentially valuable treatment in rehabilitation. The absence of subject-blind procedures, placebo and no-treatment control conditions, statistical analysis and standardization of treatment renders any conclusion tenuous, however.

Straus et al. (1964), in a double-blind study of 34 hospitalized patients complaining of insomnia and receiving medication, compared the effects of 1/2 hour of cranial TENS with 100 mg phenobarbital and a placebo cranial TENS condition (where the current was turned up until the subject reported a tingle, and then turned off). Cranial TENS was of posterior to anterior current flow in rectangular DC pulses of 30-40 Hz and an unspecified intensity. These authors reported that cranial TENS approached the effectiveness of phenobarbital, and was more effective than placebo, in inducing sleep. These results are questionable, however, since the dependent

measures, reported to be objective assessments of sleep onset, depth and duration, were simply nurses' ratings of sleep as determined by visual observation of the subjects. In fact, there was little concurrence between the nurses' evaluations of sleep and the subjective reports of the subjects, and there was no difference between the subjects' reports of sleep induction with active cranial TENS or with placebo cranial TENS. Additionally, it was not reported whether those receiving active cranial TENS felt any sensation from the stimulus. If no sensation was felt during placebo stimulation, while active stimulation caused a noticeable sensation, then it is possible that the patients receiving placebo were not convinced that they were receiving an effective treatment (other investigators [e.g., Frankel et al., 1973] have noted that patients generally have expectations as to what the electrical treatments should feel like), and may have conveyed this to whoever was carrying out the behavioral rating, invalidating both the placebo condition and the double-blind nature of the study. This was also a cross-over design, so that all subjects at one point in the study did become aware of any sensation associated with active treatment. The lack of statistical analysis and inter-subject variability in stimulation parameters and treatment course (ranging from 6-12 treatments) also make interpretation of results difficult.

In another double blind study, Rosenthal (1972)

administered either active or placebo (electrodes were not plugged into the machine) cranial TENS to 20 female and 2 male outpatients suffering from neurotic and personality disorders with prominent anxiety, depression and insomnia. Cranial TENS consisted of rectangular DC pulses of 100 Hz frequency and 0.5-1.2 mA intensity, passed from posterior to anterior electrodes in five consecutive daily 1/2 hour treatments. Ratings by an individual psychiatrist before and after treatment were reported to show significant reductions in anxiety and sleep disturbance, but not in depression, after active cranial TENS as compared to placebo. These results require cautious interpretation, however, owing to numerous shortcomings of the study. To begin with, an unspecified number of subjects continued to take a variety of medications (major and minor tranquilizers, antidepressants, sleeping medications) throughout the course of treatment. Also, as in Strauss et al. (1964), the double-blind nature of this study is invalidated by the fact that subjects in the active group felt a tingling at the electrodes during treatment, while those in the placebo group did not, possibly enabling subjects to discern which treatment condition they were experiencing. Additionally, results obtained from before and after observations by an individual rater on measures as loosely defined as "anxiety", "sleep disturbance" and "depression" do not lend themselves to quantitative analysis. Finally, These authors were unable to replicate

their own findings; when patients who were in the original placebo group were later administered active cranial TENS, they showed no response on any of the dependent measures.

Weiss (1973) administered active cranial TENS (stimulus frequency and polarity not reported) and placebo TENS (the current was turned off after the initial tingle sensation) to 10 subjects (five per group), recruited through newspaper advertisements, in twenty-four daily 15 minute treatment sessions. Before and after sleep EEG recordings were reported to show a significant decline in sleep-onset latency, percentage of total bed time awake, and percentage of total time in stage 1 sleep after active cranial TENS and not after placebo, and that gains in the active cranial TENS group were maintained at a follow-up of two weeks. Again, the double blind nature of this study is questionable, since for active TENS the current was actually increased after the initial tingle, whereas for placebo the current was turned off only after the subjects had experienced a tingle, possibly allowing the placebo subjects to deduce that they were receiving no current. Further confounds might have arisen owing to the small sample employed, and the fact that before treatment, the placebo group scored higher on the Psychopathic Deviance, Schizophrenia and Mania scales of the Minnesota Multiphasic Personality Inventory (MMPI), as well as on two MMPI anxiety subscales, than did the active TENS group. The fact that the parameters of stimulation were

not included in the report would also hinder attempts at replication.

Another double-blind study was conducted by Feighner et al. (1973) on a predominantly female population of 23 outpatients with chronic psychiatric illness (of more than 2 years) with symptoms of anxiety, insomnia and depression predominating, who had been unresponsive to all previous treatments. This study was identical in design to the Rosenthal (1972) study described above, with the exception that these subjects were administered a treatment course of ten sessions instead of five, and the study included a six month follow-up. Results were reported, as in Rosenthal, to support the efficacy of cranial TENS in treating anxiety and insomnia, but contraindicating it in the management of depression. Unfortunately, these results are also suspect, owing to the same shortcomings of design as were found in the Rosenthal study. Additionally, not only were several depressive patients who showed "massive worsening" of symptoms during cranial TENS deleted from the statistical analysis, but all patients who showed improvement with active cranial TENS had completely relapsed in the first month following treatment, and did not respond to a further course of cranial TENS.

Smith and O'Neill (1975) administered cranial TENS in pulses of 100 Hz frequency and less than 1.5 mA intensity (the current bias and polarity of the stimulus were not stated), in 15 active or placebo treatments, to a

total of 47 inpatient male chronic alcoholics. This was a single-blind study, where, for the first time in the cranial TENS literature, an attempt was made to ensure that the subjects were blind to treatment by delivering the active cranial TENS at sub-threshold current levels. Symptom improvement was assessed by comparing pre- and post-treatment responses on the Profile of Mood States (POMS), a 65 item multiple choice questionnaire with 6 subscales indicating anxiety, depression, anger, vigor, fatigue and confusion. It was reported that the active cranial TENS group improved on more of the POMS subscales than did the placebo group, supporting the hypothesis that cranial TENS does exert therapeutic effects. Inspection of the data, however, reveals that the placebo group showed improvements equal to the active group on anxiety, depression, and total mood disturbance. Comparing subthreshold active cranial TENS to placebo cranial TENS was a significant improvement over previous designs; however, whether the active treatment was, in fact, subthreshold is questionable. The authors reported that cranial TENS was delivered in currents of less than 1.5 mA. Unless the patients were suffering from alcoholic neuropathy (which is not unlikely), they would be able to feel currents of more than 0.5 mA (Katims et al., 1986). It would also be difficult to generalize improvements on a simple self-rated mood questionnaire to status on the general clinical states of anxiety, insomnia and

depression. Finally, the lack of follow-up precludes any statement as to possible long-term treatment gains.

Ryan and Souheaver (1976; 1977) also reported reductions in anxiety levels in psychiatric inpatients suffering from "significant anxiety" after five daily treatments with cranial TENS at 100 Hz frequency and a "comfortable" intensity, but unspecified polarity, as compared to a placebo group. These results are again questionable owing to the fact that the subjects were not blind to the treatment (the active group had sensation of stimulus and the placebo group did not), and the only outcome measure used was a 20 item self-rated anxiety scale.

Clinical Evaluation: Negative

Reports apparently demonstrating the ineffectiveness of cranial TENS began with Frankel et al. (1973). These researchers administered 15 daily (except weekends) 45 minute treatments of cranial TENS at 100 Hz frequency, comfortable intensity and unspecified polarity, followed by one week of no treatment, followed by 15 more daily treatments of cranial TENS at 15 Hz frequency and comfortable intensity, to 17 outpatients suffering from chronic primary insomnia. No placebo or control conditions were included in the study. They reported observing no differences at either frequency between pre- and post-treatment sleep polygraph recordings, subjective sleep and mood questionnaires, and levels of 17-

hydroxycorticosteroids. They suggest that the more chronic a condition of insomnia becomes, the less likely it will be to respond to cranial TENS, citing reports of good response with conditions of six months' duration (Rosenthal, 1972), less positive response with conditions of 2 years' duration (Feighner et al., 1973), and no response in their own study of conditions of 20 years' duration. Rosenthal (1972), on the other hand, feels that the best results with cranial TENS occur when the anxiety is more chronic in nature rather than acute. While the exclusion of placebo or control groups was inelegant, the lack thereof, along with the apparent ineffectiveness of the treatment, might suggest that no placebo effect was observed in this study. This conclusion cannot be verified, however. Since no mention of the polarity of the stimulus was made, it is entirely possible that the treatment was administered with current flowing in a direction which would result in psychophysiological changes opposite to those expected (Becker, 1962; Redfearn et al., 1964).

Hearst et al., (1974), in a double-blind study, administered 5 daily 30 minute treatments of active or placebo cranial TENS of 100 Hz frequency (both posterior to anterior DC pulses and rectangular AC) and intensities in the 0.3 - 1.1 mA range, to 28 chronic psychiatric outpatients with prominent anxiety and depression, who maintained their customary medication throughout the course of treatment. The current intensities used are

normally felt as a tingle under the electrodes (Katims et al., 1986), but these authors reportedly masked this sensation through the use of tight headbands and electrode paste, resulting in the subjects being blind as to which treatment they were experiencing. No significant differences were noted between active and placebo cranial TENS on a self-rated symptom scale, and on global rating scales of sleep, anxiety, depression and overall status obtained from a psychiatric interview. While the effort to hide the treatment condition from the subjects was laudable, these results are difficult to interpret owing to the subjective nature of the dependent measures, and to the fact that there were more depressives in the active group than in the placebo group, which was comprised of predominantly hysterical patients. Other research has shown that cranial TENS is actually contraindicated in depression (Becker, 1962; Feighner et al., 1973; Redfearn et al., 1964; Rosenthal, 1972).

In another replication of Rosenthal (1972), but employing sub-threshold active cranial TENS, resulting in a true double blind procedure, Moore et al. (1975) administered active and placebo cranial TENS to 17 subjects of unspecified origin, who suffered from persistent anxiety and insomnia, with no evidence of psychosis, as determined by an unspecified diagnostic procedure. If the subjects were already on medication, this was maintained throughout the study. Their results

showed no significant pre- to post-treatment differences between active and placebo cranial TENS on a psychiatrist's ratings of anxiety, insomnia and depression using a 4 point scale of improvement, and on various self-rated mood inventories, or on subjects' self-report of anxiety and depression. The only significant difference between the groups was noted in the subjects' self-report of improvement in insomnia. These results are also difficult to interpret owing to the subjective nature of the dependent measures, and the fact that except for the frequency used (100 Hz), no description of the device or its electrical specifications, or of treatment current polarity, was included in the report. Additionally, although subjects do tend to habituate to very slight tingling sensations arising from an electrical stimulus, in this study, the "sub-threshold" active stimulation current was set at an average level of 0.5 mA. This current level does produce a tingling sensation in normal subjects (Katims et al., 1986), and was actually above these subjects' average initial threshold for cutaneous sensation (0.2 mA), while below the average current which was reported to be uncomfortable (0.7mA). It is therefore questionable whether the subjects were actually unable to discern a difference between the active and placebo treatments.

Clinical Evaluation: Placebo

Achte et al., (1968) assessed the effects of cranial

TENS of unspecified polarity on 24 predominantly female inpatient insomniacs via subjective opinions from the patients, nursing personnel, and a physician. Immediately following treatment, 83% of the patients were judged improved, but none achieved complete remission of insomnia or eliminated their dependence on sedative or hypnotic medication. Results of a two-month follow-up showed, however, that 67% had suffered complete relapse. The authors were unimpressed with these findings and concluded that the observed effects of cranial TENS were chiefly based on suggestion. Analysis of the methodology of this study, however, suggests that this conclusion might have been overly pessimistic. Their treatment protocol allowed for the number and duration of treatment sessions, as well as for the frequency and intensity of the treatment current, to vary according to what was reported by the subject to be most pleasurable. Thus, the number of treatment sessions varied from as few as 6 to as many as 29, and the duration of single sessions ranged from 30 minutes to two hours. Since all subjects did not receive the same amount of treatment, it is possible that those who received a lengthy course of cranial TENS responded favorably, while those given a short course of treatment made little or no progress. Because the number and duration of treatment sessions, as well as the electrical parameters of the treatment stimulus, were allowed to vary unsystematically across subjects, interpretation of these

results is difficult.

Tomsovic and Edwards (1973) administered 5 daily half hour active or placebo cranial TENS treatments, using rectangular AC waves of 100 Hz frequency, to 43 alcoholics who were 3 weeks into a 90-day treatment program. Results showed that, while approximately 75% of each group showed some level of improvement on ratings of anxiety, sleep disturbance, stomach disorders and headaches obtained by way of psychiatric interview, the improvements shown in the active cranial TENS group were not superior to those shown in the placebo group. These authors questioned whether cranial TENS is effective in reducing tension-related neurotic symptoms, suggesting that any observed effects of cranial TENS are attributable to suggestive aspects of the treatment situation. The use of self-report interview ratings as the sole measure of change, however, makes this study less than conclusive.

Astrup (1974) reported treatment outcome and long-term follow-up on a heterogeneous group of 51 psychotic and neurotic patients administered 10 to 15 half-hour treatments with cranial TENS of unspecified parameters. According to clinical observation, approximately two-thirds were improved following treatment, but long-term follow-up showed that only one subject maintained this status. This did not constitute a meaningful assessment of cranial TENS, however, owing to the questionable nature of the independent and dependent variables, and the fact that

the follow-up period was 12-18 years after treatment.

Marshall and Izard (1974), using an apparatus constructed by the first author, administered five daily active or placebo cranial TENS treatments to 40 psychiatric inpatients displaying predominantly depressive symptomatology. For active cranial TENS, rectangular DC pulses of 100 Hz frequency were passed from anterior to posterior electrodes, while for placebo cranial TENS, the same stimulus was passed between two anterior electrodes, with the posterior electrodes disconnected from the machine. The authors state that this arrangement made the active and placebo conditions indistinguishable. The dependent measures were patient and staff ratings on a pre-, post-treatment and one week follow-up basis on a depression inventory constructed by the second author. Results showed that all patients improved significantly following treatment, and that improvement with active cranial TENS was not significantly greater than that with placebo. One week follow-up also indicated similar results. It was concluded that improvements with cranial TENS were due to positive expectation. This interpretation is invalidated by the nature of the placebo treatment employed. The passage of current between two orbital electrodes does not rule out the possibility of CNS effects (Katims & Ng, 1985; Katims et al., 1986), and since both active and placebo groups showed significant improvement following treatment, it is possible that both

groups received active cranial TENS.

Passini and Watson (1976) administered 10 thirty-minute sessions of either active or placebo (the current was never turned on) cranial TENS, from posterior to anterior electrodes in rectangular DC pulses of 100 Hz frequency, to 60 inpatients suffering from various psychiatric disorders, with anxiety and depression present as determined by staff observations. The subjects were maintained on their medication (tranquilizers or antidepressants) throughout the course of treatment. Active and placebo cranial TENS were compared according to pre-to post-treatment improvement on brief mood inventories. Results were reported to show significant improvements in both groups on all criteria, with no significant differences between active and placebo cranial TENS; and that, in fact, the non-significant group differences in amount of change favored the placebo group rather than the active cranial TENS group on most of the measures. The authors state that these results contradict the view that cranial TENS has beneficial effects on anxiety and depression, and that any positive outcome with cranial TENS can be attributed to placebo effects. While these results are interesting, they cannot be viewed as unequivocal owing to the absence of a no-treatment control group against which to compare the observed improvement in the active and placebo groups, and to the subjective nature of the dependent measures.

The foregoing critique suggests that, while efforts to improve on Soviet research were laudable, the results of these studies may have been confounded by questionable double blind and placebo procedures, the almost exclusive use of subjective dependent measures, and variability in stimulation parameters, treatment protocol and equipment (no two American-made TENS devices seem to possess the same electrical characteristics [Brown, 1975]). In order for future clinical research to be valid and replicable, the methodology would have to include objective physiological dependent measures, use standardized instrumentation and procedure (electrode placement, polarity, frequency, current and waveform parameters, treatment course and duration), and establish experimentally identical active and placebo treatment procedures (except for the presence or absence of electric current), to ensure valid subject-blind and placebo conditions. U.S. researchers gave up on cranial TENS around 1976, however, assuming that the inconclusiveness in the existing literature was due to the questionable nature of the treatment itself, rather than to inadequacies in the research designs by which it was evaluated.

III. EXPERIMENTAL EVALUATION OF CRANIAL TENS IN THE U.S.

Experimental evaluation of cranial TENS addresses two questions: what happens to current passed between transcutaneous electrodes positioned at opposite poles on the cranium, and what effects, if any, does this current produce in the CNS.

Rush and Driscoll (1968), using a model of the human head consisting of a human half-skull suspended in an electrolytic tank, with components to mimic the conducting characteristics of the skin and scalp muscles, concluded that approximately 45% of a current in the cranial TENS intensity range, applied via anterior-posterior surface electrodes, passes through the brain itself.

Wageneder et al. (1969), reporting on their measurement of intracranial TENS current flow in the thalamus, lateral ventricle, frontal white matter and cortex of three patients undergoing stereotactic neurosurgical operations for parkinsonism, concluded that there was considerable (unspecified) current flow through the brain, predominantly in the frontal lobe, thalamus area and brain stem.

Dymond et al. (1975) administered anterior-posterior cranial TENS of 100 Hz frequency and intensities in the cranial TENS range (0.1-1.5 mA) to three patients with electrodes implanted in the amygdala and hippocampal formation (as part of a diagnostic procedure for temporal lobe epilepsy), and found that potential differences

between these electrodes supported the Rush and Driscoll (1968) estimate of 45% intracerebral current flow. It was also noted that with the application of a current of 1.0 mA intensity, electric field strengths around the implanted electrodes ranged from 6.4 mV/cm to 16.4 mV/cm, which values fall within the range of current densities necessary for minimal neural effect (Terzuolo & Bullock, 1956).

These studies suggest that approximately 45% of an applied cranial TENS current passes through the brain, and is of sufficient strength to modify ongoing neuronal activity; the question remaining is what effects might this current produce.

Becker (1962) suggested that the brain has a natural DC potential, that transcutaneous electrical stimulation can induce changes in the magnitude and polarity of this potential, and that these changes correspond to changes in the organism's state of consciousness. For example, by external manipulation of the electrical polarity of the brain, Becker reported inducing anesthesia and sleep in both reptiles and mammals (Becker, 1962). However, these reports were based on empirical observations rather than controlled investigations.

Iwanovsky and Dodge (1968) reported observing 60% reductions in EEG amplitude, without any significant change in frequency, in rabbits with cranial TENS of 100 Hz frequency and 0.2-0.3 mA intensity. Cox and Heath

(1975) also studied EEG changes with cranial TENS (100 Hz, 0.5 mA) in a depressive patient with anxiety predominating, prepared with deep and surface electrodes, who had failed to respond to other forms of treatment. In over 100 hours of previous recordings, only six minutes of alpha had been obtained. After one thirty minute active cranial TENS treatment, however, EEG recordings indicated a well-developed alpha rhythm over the occipital cortex, accompanied by feelings of drowsiness and relaxation. The next day, a control procedure was instituted which involved an identical treatment, but with no current delivered. Before and after placebo TENS EEG recordings failed to show the changes observed the previous day after active TENS. These results require cautious interpretation, however, owing to the fact that this was a study of only one patient who knew when the cranial TENS was active and when it was placebo.

Rosenthal (1973) administered five daily half-hour cranial TENS treatments, of posterior-to-anterior DC pulses of 100 Hz frequency and palpable intensity, to 41 patient and non-patient subjects, drawing serum prior to the first and fifth treatments. Significant increases in serum thyroxin levels were noted after four cranial TENS treatments, but these changes did not persist beyond the treatment period. In another study, Briones and Rosenthal (1973) administered cranial TENS, of the same parameters as Rosenthal (1973), to seven male patient and non-

patient subjects, and noted significant increases in 24-hour urinary free catecholamines, and non-significant increases in 17-ketosteroids, after five daily cranial TENS treatments (no follow-up was reported). Although it was not possible to state whether these effects were clinically significant, the authors suggested that they were evidence of stimulation of the hypothalamic-pituitary axis. Unfortunately, the absence of a control condition allows for the possibility that the results of these studies were due to factors other than the actual TENS current.

Kotter et al. (1975) monitored gastric acid secretion in 12 normal adult male subjects during active posterior-to-anterior DC cranial TENS of rectangular waveform at 100 Hz frequency and 1.0 mA intensity, during placebo TENS (current passed between the two frontal electrodes only), and during a control (no current) treatment. These authors reported observing significant reductions in basal and histamine-stimulated gastric acid secretion only during active cranial TENS, which changes did not persist beyond the treatment session. The authors concluded that these effects were evidence of possible inhibitory neurohumoral effects of cranial TENS.

Sine-Wave Constant Alternating Current (AC) Cranial TENS

Assuming that approximately 45% of an applied cranial TENS current flows intracranially, and is capable of affecting CNS activity, the question arises as to the

influence of the remaining 55% of the cranial TENS current, which must pass over the face and scalp, possibly exciting cranial nerve fibers innervating the area of stimulation, and exerting a nervous system effect via stimulation of the brainstem cell bodies of these nerves.

The hypothesis that the surface flow of cranial TENS current might affect brainstem cranial nerve cell bodies is supported by recent findings which suggest that even unilateral (no transcranial current flow) sine-wave cranial TENS is capable of modifying CNS activity. Katims and Ng (1985), using 2-deoxyglucose autoradiography to identify brain regions in the rat which increase their metabolic activity in response to sine-wave constant AC cranial TENS (electrodes were placed unilaterally on the ear), reported increases in metabolic activity in the C-1 dorsal horn, nuclei ambiguii, trigeminal nuclei, nucleus solitarius, reticular formation, median longitudinal fasciculi, vestibular nuclei, and the periaqueductal grey in rats receiving active cranial TENS of 5 Hz or 2000 Hz frequency and 0.25 mA intensity, and not in rats receiving sham stimulation.

In a human study, Katims et al. (1986) reported the evocation of three non-cutaneous cephalic sensations with sine-wave constant AC cranial TENS with electrodes placed either unilaterally or bilaterally on the cranium (1 cm anterior to the tragus of the ear) in 52 normal subjects. At frequencies ranging from 5 Hz - 19 Hz, all subjects

reported oscillopsia of approximately 2 of the arc of the visual field, which was not accompanied by retinal movement. Between 12 Hz and 80 Hz, all subjects reported flickering pale light in the periphery of the visual field, which was present with eyes open or closed. Between 60 Hz and 530 Hz, all subjects reported a non-auditory, non-aversive resonance, or vibratory, sensation that seemed to emanate from within the cranium in the occipital area. Only sine-wave stimulation was capable of evoking these three cephalic sensations at discrete frequencies; square-wave stimulation evoked all of the sensations together at frequencies between 5 Hz and 500 Hz, and rectangular-wave stimulation failed to evoke any of the sensations in 85% of the subjects (the remaining 15% reported only noticing the resonance sensation faintly). No differences were noted between the sensations evoked by unilateral (no transcranial current flow) and bilateral cranial TENS.

Sine-wave constant AC cranial TENS provides three advantages over the traditional cranial TENS methodology, which for the most part employed square-wave DC of constant voltage. First, the frequency coding of the central nervous system for both communication and response to electrical stimulation is a well established fact in neuroscience (Stubbs, 1976). The sine wave is the fundamental component of all other waveforms, and has been demonstrated to have the greatest specificity in the

frequency-dependent excitation of specific sub-populations of nervous tissue located within a site receiving cutaneous electrical stimulation (Katims et al., 1986). A sine-wave cranial TENS stimulus would therefore be more neuro-specific, and possibly more effective, especially at lower (i.e. sub-threshold) intensities, than other waveforms in influencing CNS activity.

Secondly, since skin resistance/impedance to an applied current varies considerably according to in vivo physiological processes, the reproducible application of transcutaneous current has been difficult to achieve (Burton & Maurer, 1974; Butikofer & Lawrence, 1979; Mueller et al., 1952; Notermans, 1966). The use of constant current rather than constant voltage obviates this problem, ensuring the maintenance of a constant cranial TENS stimulus irrespective of changes in skin resistance/impedance. Constant voltage, on the other hand, allows the stimulus current to vary with changes in the resistance/impedance characteristics of a subject. Furthermore, it has been demonstrated that sensation of an electrical stimulus is proportional to current and not to voltage in humans (Tursky and Watson 1964).

Thirdly, AC stimulation has been shown to avoid certain complications which can arise with the use of polarizing DC current, such as electrical nerve fatigue and tissue damage (Lilly et al., 1955; Mihailovic & Delgado, 1956; Tanae et al., 1973).

STATEMENT OF PURPOSE

The evidence presented in the foregoing review of the experimental literature suggests that cranial TENS is capable of influencing the nervous system through the direct action of transcranial current flow, or by stimulation of brainstem cranial nerve cell bodies via surface fibers, and that sine-wave constant AC cranial TENS may offer advantages over past methodologies. The following studies are therefore designed for the purpose of measuring the effects of this new form of cranial TENS on the autonomic nervous system, as indicated by blood pressure, pulse rate, and peripheral vascular tension, on the somatic nervous system, as indicated by skeletal muscle activity, and on anxiety in normal human subjects at rest, and during standardized experimental stress. If cranial TENS is observed to attenuate arousal under these conditions, this may suggest possible applications of this technique to the management of stress-related disorders.

In these studies attempts were made to avoid some of the shortcomings of past research on cranial TENS through double-blinding, and evaluating objective physiological dependent measures as well as subjective ones.

IV. EXPERIMENT I (PILOT STUDY)

Effects of Cranial TENS in Normal Subjects at Rest

DESIGN

In a subject-blind protocol, thirty healthy volunteers received either active or placebo cranial TENS, or no treatment, for 30 minutes. Blood pressure, pulse rate, peripheral vascular tension, skeletal muscle activity and anxiety were measured before and after treatment.

MATERIALS AND METHODS

Subjects

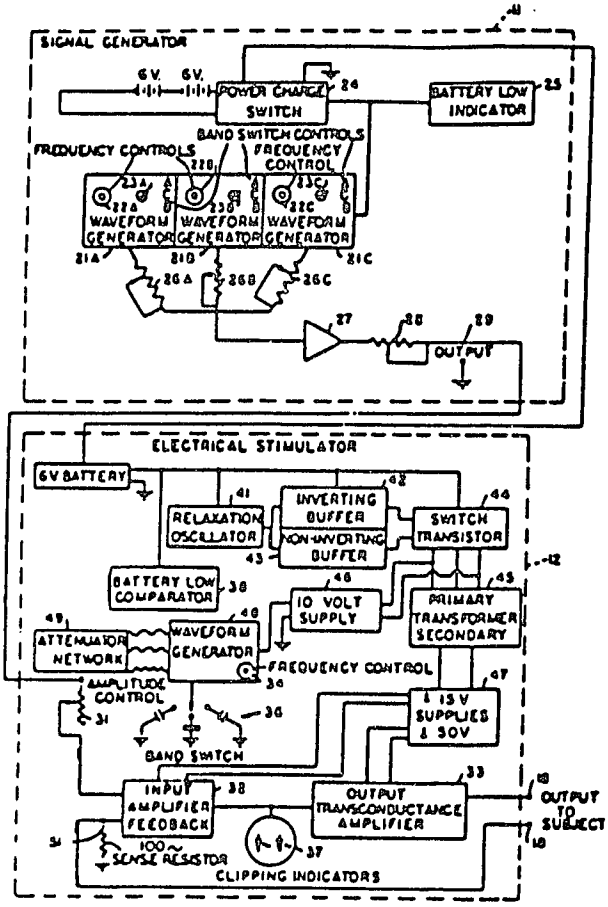
Thirty healthy volunteer subjects (13 male and 17 female) aged 18-30 years were tested. Informed consent was obtained from each subject under a protocol approved by the Investigational Review Board of Brooklyn College of the City University of New York (appendix A).

TENS apparatus

The Neurometer TENS stimulator (Neurotron, Inc., Baltimore, Md) is a portable battery-operated device which generates a sinusoid waveform stimulus of 0 - 5000 Hz frequency, calibrated to 0.5 Hz, and 0 mA - 10 mA intensity, calibrated to 5 microAmps (uA). One cm diameter cotton electrodes, moistened with water as a conducting medium, are held in place by clips to the anterior and posterior aspects of both earlobes. The following is a description of the device (Katims, 1985).

Referring to figure 1, signal generator [11] is a triple output signal generator used to send a large range

Figure 1.



of frequencies through electrical stimulator [12] to a pair of electrodes [18] placed on the skin of subjects. The signal generator [11] is composed of three waveform generators [21A, 21B, 21C], for sine, square and sawtooth output (only the sine wave output is used in the present study), each with its own frequency control [22A, 22B, 22C], and bandswitch control [23A, 23B, 23C]. Power is supplied to the waveform generators through a power charge switch [24] from two 6-volt batteries connected in series for a 12-volt power supply. A battery low indicator [25] indicates a need to recharge batteries, and is connected to

the power charge switch [24]. Current output controls from each of the waveform generators are illustrated as potentiometers [26A, 26B, 26C] and are connected to the output terminal [29] through an inverting amplifier [27] and a master current control, noted as a potentiometer [28]. The master control [28] regulates the over-all current output with a 10 mA maximum output current from the amplifier [27]. The waveform generators in the preamplifier have a 1.3 V peak signal. The signal generator's amplifier has a 10 mA/V transfer function when the amplifier's level control is at the full clockwise position.

The signal generator output terminal [29] is connected to the electrical stimulator [12], mainly using amplifier characteristics of the electrical stimulator. The signal from terminal [29] passes through a current amplitude control potentiometer [31], an input amplifier [32], and an output transconductance amplifier [33] to electrodes [18] contacting the subject. Transconductance amplifier [33] maintains constant current output despite fluctuations in the load.

The electrical stimulator [12] has a 6-volt battery supply. To this is connected a battery low comparator 38, used in conjunction with a diode reference (not shown) and a relaxation oscillator [41]. Most any DC input can be used but the battery connection illustrated is preferred. From the relaxation oscillator [41] a square wave output is buffered by an inverting buffer [42], and a non-inverting

buffer [43], with their complementary outputs driving a pair of power transistors [44], which chop the 6-volt battery voltage at a rate of several kilohertz, and drive a step-up transformer [45]. The induced voltage in the primary is full wave rectified to provide a + 10-volt supply [46]. The secondary drives a full wave doubler circuit that provides a +/- 50-volt supply [47].

The transformer [45] is used to match a high impedance load [the subject], and results in simple, safe low-voltage circuitry without having the transformer in the signal path, obviating problems such as distortions which are inherent to transformers (i.e. frequency-limiting effects and the fact that no DC current may pass through a transformer). The transformer is run at optimal frequency and only as a power supply, in order to produce the high voltage output and rectify it back to DC. Therefore, in this circuit, a low-voltage battery has been transformed into a high-voltage battery which powers a high-voltage circuit, namely the transconductance amplifier [33], which puts out a constant current independent of load impedance. Because it has been shown that sensation is proportional to current and not to power (Tursky & Watson, 1964), this type of constant current output prevents any problems concerning changing resistance of skin or electrode paste on neuron resting membrane potential. Therefore nothing inherently limits the bandwidth within the circuit.

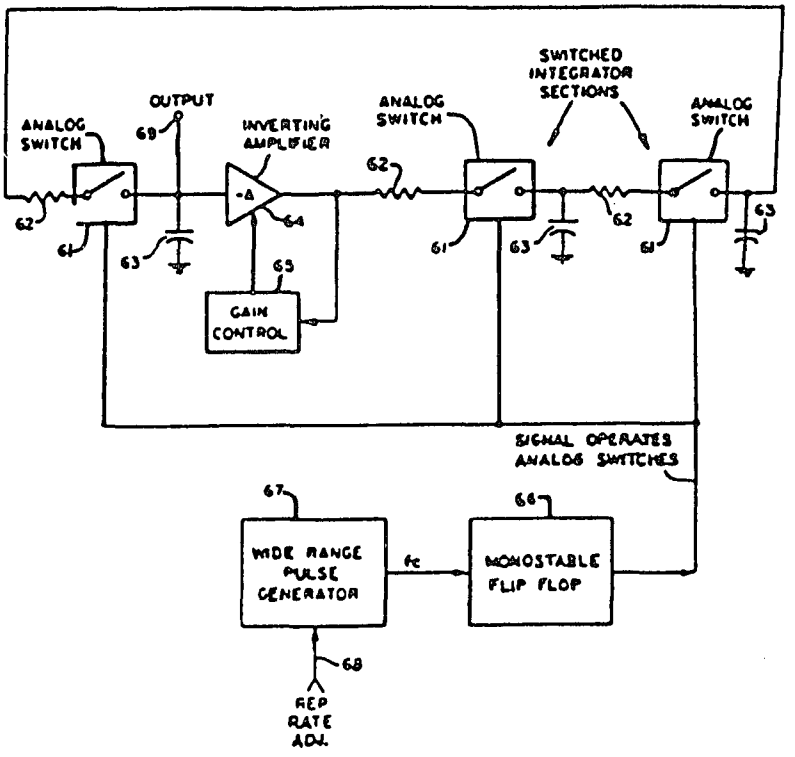
The 10 V supply [46] powers waveform generator [48].

The frequency is set by three hand switched capacitors [36] and the frequency control potentiometer [34]. Due to the different levels and output impedances of the outputs, compensating resistor networks [49] are included. The +/- 50 V supply [47] supplies power to high compliance transconductance amplifier [33]. A +/- 15-volt supply is provided by a zener regulated supply for operation of the input amplifier [32], which drives the transconductance output stage amplifier [33]. The load is driven in a floating configuration with the current sensed across a 100 Ohm resistor [51], which provides a 10 mA/V transfer function.

The sense resistor [51] is used since monitoring is done at the subject leads and not on the primary side of variable loss transformer [45].

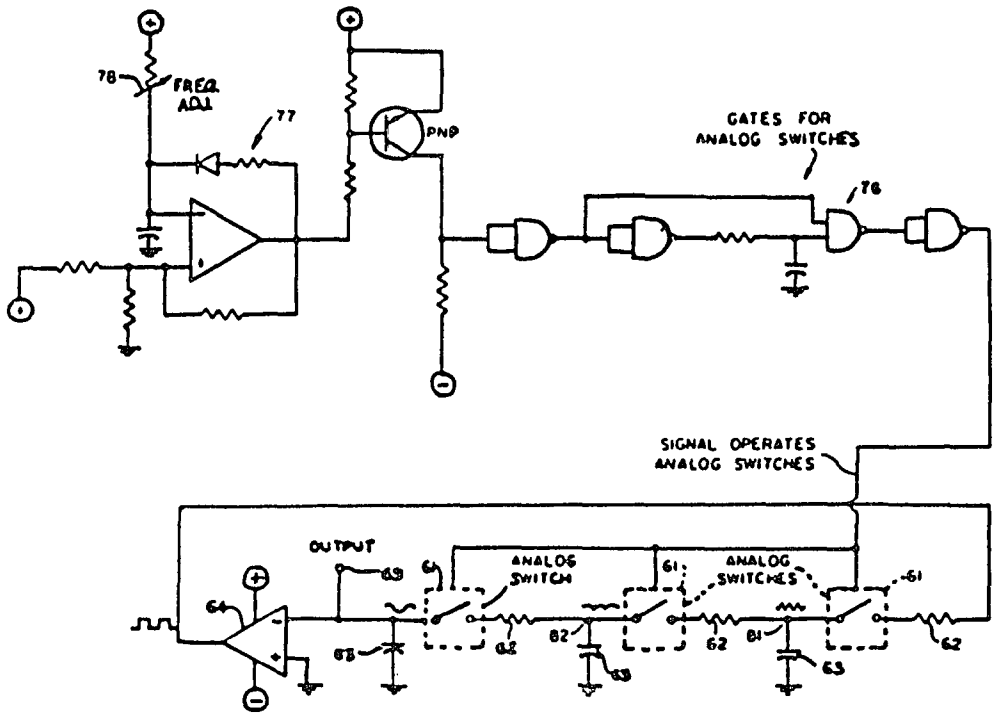
Referring to figure 2, three switched integrator sections are shown, each having an analog switch [61], a resistor [62], and a capacitor [63]. Three is the minimum number, although preferably more can be used which lowers the distortion from the amplifier [64] and the gain control [65]. The pulse generator [67], through monostable flip-flop [66] supplies the signal at the adjusted repetition rate of adjustment [68] to operate analog switches [61] which control the output at [69] through amplifier [64].

Figure 2.



Referring to figure 3, analog switches [61] are associated with their respective resistors [62] and capacitors [63] to form switched integrator sections with a signal from logic gates [76] operating analog switches [61]. A wide range pulse generator circuit [77] with frequency adjustment [78] feeds the pulses at adjusted frequency to gates [76]. Amplifier [64], in series with the switched integrator sections, conducts the signal to output [69] from whence output is fed through the stimulator apparatus which connects with the subject.

Figure 3.



Dependent measures

Blood pressure was measured in the brachial artery at the cardiac level by manual sphygmomanometry with subjects in a sitting position.

Pulse rate was measured by palpation of the radial artery at the wrist of the left hand for one minute.

Peripheral vascular tension was indicated by peripheral temperature (Freedman et al., 1988; Stallworth et al., 1981), obtained by thermography utilizing an Autogen 2000b Feedback Thermometer (Autogenic Systems, Chicago) with a 4mm diameter thermistor held in place by

surgical tape on the dorsal surface of the distal phalanx of the index finger of the left hand.

Skeletal muscle activity was quantified by electromyography (EMG) in the frontalis muscle, considered to be a reliable index of somatic activity (Budzynski & Stoyva, 1984; Hiebert, 1981; Lavallee et al., 1977; Reinking & Kohl, 1975). The EMG apparatus (Autogen 1700 Myograph Analyzer, Autogenic Systems, Chicago), employs 3 transcutaneous 1 cm diameter gold electrodes placed 2 cm apart in a line over the frontalis muscle, with standard electrode paste serving as a conducting medium. Baseline muscle tension levels were recorded from the electromyograph after surface myo-potential had stabilized within a 3 microvolt range for two minutes.

Anxiety was assessed by the Spielberger et al. (1970) State-Trait Anxiety Inventory, Form-1, which provides a quantitative index of subjective state anxiety in approximately five minutes.

Treatments

TENS treatment

Electrodes were placed as described above, with the TENS set at 100 Hz frequency and 0 mA intensity. The device was turned on, and the highest current level at which cutaneous or non-cutaneous sensations (Katims et al., 1986) were perceived 0% of the time (0% threshold) was determined. For 0% threshold determination a method of

limits with ascending and descending series was employed because of superior reliability and time-efficiency in cutaneous sensation threshold determination (Gerr & Letz, 1988; Kershaw, 1985; Muijser et al., 1986). With electrodes in place, the stimulator was turned on and the current intensity was increased from 0 mA at the rate of 20 uA per second until the subject reported a cutaneous or non-cutaneous sensation. A descending series followed the ascending series, and current values for the onset and offset of sensation were recorded. This cycle was replicated in five single-blind tests, with 0% threshold being defined as the highest current level at which sensation was reported 0% of the time (.15 - .35 mA, mean = .26 mA for these subjects). The procedure takes approximately 5 minutes. Once 0% thresholds were obtained, the TENS device was switched off and reset to 0 mA intensity. The subject was then informed that the treatment session was about to begin, and the stimulator was turned on with the current set at 50 uA below the subject's 0% threshold for active TENS, and set at 0 mA for placebo TENS, for the duration of the 30 minute treatment session. Since active TENS was delivered at current levels which were 50 uA below 0% threshold, subjects in the active and placebo TENS groups were blind to the treatment condition they were experiencing.

No treatment

Subjects in the no treatment control group were not

attached to the TENS device, and were asked to remain quietly in a sitting position for the duration of the session.

Experimental procedure

Subjects were randomly assigned to the active TENS, placebo TENS, or no treatment groups. All tests were conducted in a quiet room with no visual distractions. Subjects remained in a sitting position, and were asked not to talk, for the duration of the 30 minute treatment session. Subjects were asked to read and sign the informed consent form, which describes the experimental procedure. The dependent measures were obtained immediately before and after each test in the following order: anxiety, temperature, skeletal muscle activity, pulse rate and blood pressure.

RESULTS

One-way multivariate analysis of variance (MANOVA) indicated no significant group differences in baseline measures (Hotelling's T^2: df=12,42; F=1.36, p<.23). MANOVA did show significant group differences in pre- to post-treatment changes on the dependent variables (Hotelling's T^2: df=12,42; F=2.3, p<.02). Separate univariate ANOVAs were therefore performed on each of the six dependent variables in order to identify where there was significance. Where significance was found, Duncan's multiple range test was employed to identify which groups differed significantly.

Systolic blood pressure

One-way analysis of variance (ANOVA) (Table 1) revealed an effect which only achieved marginal significance (df=2,27; F=3.05, p<.06), but which was of sufficient magnitude to warrant a postiori comparisons among means. Duncan's test (Table 2) showed that active TENS differed significantly (p<.05) from both placebo TENS and no treatment, which did not differ significantly.

Table 1. Systolic Blood Pressure: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	2	294.87	147.43	3.05	.06
Within	27	1307.3	48.42		
Total	29	1602.17			

Table 2. Systolic Blood Pressure: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 Active TENS	Group 2 Placebo TENS	Group 3 No Treatment
mean	90.29	97.01	97.03
sd	6.18	7.22	7.38
Group 1			
Group 2	*		
Group 3	*		

Diastolic blood pressure

One-way ANOVA (Table 3) revealed a statistically significant effect (df=2,27; F=5.39, p<.01). Duncan's test (Table 4) showed that active TENS differed significantly (p<.05) from both placebo TENS and no treatment, which did not differ significantly.

Table 3. Diastolic Blood Pressure: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	2	350.6	175.3	5.39	.01**
Within	27	878.1	32.52		
Total	29	1228.7			

Table 4. Diastolic Blood Pressure: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 Active TENS	Group 2 Placebo TENS	Group 3 No Treatment
mean	91.07	97.84	98.82
sd	4.94	3.48	7.51
Group 1			
Group 2	*		
Group 3	*		

Pulse rate

One-way ANOVA (Table 5) revealed a statistically significant effect (df=2,27; F=3.5, p<.05). Duncan's test (Table 6) showed that active TENS differed significantly (p<.05) from placebo TENS, but not from no treatment. Placebo TENS and no treatment did not differ significantly.

Table 5. Pulse Rate: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	2	749.6	374.8	3.5	.05*
Within	27	2891.6	107.1		
Total	29	3641.2			

Table 6. Pulse Rate: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 Active TENS	Group 2 Placebo TENS	Group 3 No Treatment
mean	88.95	101.28	95.92
sd	5.28	16.38	4.85
Group 1			
Group 2	*		
Group 3			

Temperature

One-way ANOVA (Table 7) revealed a statistically significant effect (df=2,27; F=4.77, p<.02). Duncan's test (Table 8) showed that active TENS differed significantly (p<.05) from placebo TENS, but not from no treatment. Placebo TENS and no treatment did not differ significantly.

Table 7. Temperature: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	2	114.27	57.1	4.77	.02*
Within	27	323.0	11.96		
Total	29	437.2			

Table 8. Temperature: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 Active TENS	Group 2 Placebo TENS	Group 3 No Treatment
mean	104.28	99.45	101.13
sd	4.82	3.22	1.49
Group 1			
Group 2	*		
Group 3			

EMG

One-way ANOVA (Table 9) revealed no significant effect on this variable (df=2,27; F=.53, p<.59). Means and standard deviations are shown in Table 10.

Table 9. EMG: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	2	350.47	175.23	.53	.59
Within	27	8885.4	329.09		
Total	29	9235.87			

Table 10. EMG: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations

	Group 1 Active TENS	Group 2 Placebo TENS	Group 3 No Treatment
mean	67.67	76.13	71.03
sd	13.02	18.3	21.99

Anxiety

One-way ANOVA (Table 11) revealed a statistically significant effect (df=2,27; F=5.08, p<.01). Duncan's test (Table 12) showed that active TENS differed significantly (p<.05) from both placebo TENS and no treatment, which did not differ significantly.

Table 11. Anxiety: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	2	1290.47	645.23	5.08	.01**
Within	27	3430.5	127.06		
Total	29	4720.97			

Table 12. Anxiety: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 Active TENS	Group 2 Placebo TENS	Group 3 No Treatment
mean	79.44	94.6	91.88
sd	14.44	9.1	9.3
Group 1			
Group 2	*		
Group 3	*		

SUMMARY AND CONCLUSIONS

In this subject-blind pilot study, significant reductions in systolic and diastolic blood pressure and anxiety, but not in pulse rate, peripheral vascular tension or skeletal muscle activity, were observed subsequent to active sine-wave constant AC cranial TENS of 100 Hz frequency as compared to a no treatment control. No placebo TENS effect was observed on any measure.

These findings are consistent with previous reports of reductions in anxiety subsequent to cranial TENS, and fail to support theories that cranial TENS acts via placebo effects. The fact that post-treatment differences in pulse rate, peripheral vascular tension and skeletal muscle activity between active TENS and no treatment did not achieve significance might be due to the selection of normal, healthy volunteer subjects, resulting in baseline measures which were so close to optimal values as to preclude further change. This subject selection enhances the significance of the observed cranial TENS effect on blood pressure and anxiety measures. The observation of significant post-treatment differences in pulse rate and peripheral vascular tension between active and placebo TENS, but not between active TENS and no treatment, suggests that the cranial TENS procedure itself may be anxiety-provoking, resulting in tension when there is no current to attenuate treatment-related arousal.

While the results of this study must be interpreted

with caution, owing to the fact that it was a single-blind study with a relatively small number of subjects, the significant reductions in blood pressure and anxiety observed after 30 minutes of 100 Hz sine-wave constant AC cranial TENS, as compared to both placebo TENS and no treatment, may suggest possible applications of this technique in the management of stress. Exploring this possibility, the following two double-blind studies attempt to determine the optimal frequency parameters of stimulation for nervous system relaxation, and then examine the influence of cranial TENS of optimal frequency on physiological and psychological measures during standardized experimental stress in normal subjects.

In the second study (experiment II), 90 healthy volunteers received active TENS of 5, 100 or 2000 Hz frequency, placebo TENS or no treatment, for 30 minutes. Blood pressure, pulse rate, peripheral vascular tension and anxiety were measured before and after treatment. The 5 Hz and 2000 Hz stimulation frequencies were selected for comparison to the 100 Hz frequency based on previous evidence that sine-wave cranial TENS at these frequencies causes frequency-dependent changes in CNS activity. Katims & Ng (1985) observed increases in glucose metabolism in the C-1 dorsal horn, nuclei ambiguii, trigeminal nuclei, nucleus solitarius, reticular formation, median longitudinal fasciculi, vestibular nuclei, and the periaqueductal grey, in rats after cranial TENS of both 5

Hz and 2000 Hz (but not after sham stimulation), with 5 Hz causing greater metabolic increases in the region of the nuclei ambiguii and trigeminal nuclei, and 2000 Hz causing greater metabolic increases in the region of the nucleus solitarius and the vestibular nuclei.

V. Experiment II

Effects of Different Frequencies of Cranial TENS in Normal Subjects at Rest

DESIGN

In a double-blind protocol, 90 healthy volunteers received active TENS of 5, 100 or 2000 Hz frequency, placebo TENS or no treatment, for 30 minutes. Blood pressure, pulse rate, peripheral vascular tension and anxiety were measured before and after treatment.

MATERIALS AND METHODS

Subjects

Ninety healthy volunteer subjects (20 male and 70 female) aged 18-25 years were tested. This sample size was computed following the method of Kirk (1968) for alpha = .05 and power = .80. Informed consent was obtained from each subject under a protocol approved by the Investigational Review Board of Brooklyn College of the City University of New York (appendix A).

TENS Apparatus

As in experiment I.

Dependent Measures

Blood pressure. As in experiment I.

Pulse rate. As in experiment I.

Peripheral vascular tension. As in experiment I.

Anxiety. As in experiment I.

Treatments.

TENS treatment

Four different TENS groups were administered active TENS of low (5 Hz), medium (100 Hz) or high (2000 Hz) frequency, or placebo TENS, for 30 minutes. TENS treatments were administered as described in experiment I, except that after 0% threshold had been determined (.12 - .39 mA, mean = .24 mA for these subjects), a confederate set a switch on the TENS device in a predetermined way according to subject number. The position of this switch determined whether treatment was active or placebo, and remained unknown to the experimenter to ensure the double-blind nature of the study.

No treatment

As in experiment I.

Experimental procedure

As in experiment I.

RESULTS

One-way MANOVA indicated no significant group differences in baseline measures (Hotelling's T^2: df=20,318; F=.68, p<.84). MANOVA did show significant group differences in pre- to post-treatment changes on the dependent variables taken collectively (Hotelling's T^2: df=20,318; F=4.87, p<.01). Separate univariate ANOVAs were therefore performed on each of the five dependent variables in order to identify where there was significance. Where significance was found, Duncan's

multiple range test was employed to identify which groups differed significantly.

Systolic blood pressure

One-way ANOVA (Table 13) revealed a statistically significant effect (df=4,85; F=7.86, p<.01). Duncan's test (Table 14) showed that active 100 Hz TENS differed significantly (p<.05) from 5 Hz TENS, 2000 Hz TENS, placebo TENS and no treatment. No other group differences were observed.

Table 13. Systolic Blood Pressure: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	942.27	235.57	7.86	.01**
Within	85	2547.72	29.97		
Total	89	3489.98			

Table 14. Systolic Blood Pressure: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Res lts of Duncan's Test (* = Significant Difference at p<. 5)

	Group 1 5 Hz TENS	Group 2 100 Hz TENS	Group 3 2000 Hz TENS	Group 4 Placebo TENS	Group 5 No Treatment
mean	96.4	90.57	100.05	97.19	98.53
sd	6.14	7.58	4.16	4.26	4.38
Group 1		*			
Group 2					
Group 3		*			
Group 4		*			
Group 5		*			

Diastolic blood pressure

One-way ANOVA (Table 15) revealed a statistically significant effect (df=4,85; F=7.51, p<.01). Duncan's test (Table 16) showed that active 100 Hz TENS differed significantly (p<.05) from 5 Hz TENS, 2000 Hz TENS, placebo TENS and no treatment. No other group differences were observed.

Table 15. Diastolic Blood Pressure: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	1110.52	277.63	7.51	.01**
Within	85	3144.07	36.99		
Total	89	4254.57			

Table 16. Diastolic Blood Pressure: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 5 Hz TENS	Group 2 100 Hz TENS	Group 3 2000 Hz TENS	Group 4 Placebo TENS	Group 5 No Treatment
mean	96.46	90.40	99.4	99.06	99.8
sd	6.91	4.75	5.67	7.74	4.75
Group 1		*			
Group 2					
Group 3		*			
Group 4		*			
Group 5		*			

Pulse rate

One-way ANOVA (Table 17) revealed a statistically significant effect (df=4,85; F=11.05 p<.01). Duncan's test (Table 18) showed that active 100 Hz TENS differed significantly (p<.05) from 5 Hz TENS, 2000 Hz TENS, placebo TENS and no treatment, and that 5 Hz TENS differed significantly (p<.05) from placebo TENS. No other group differences were observed.

Table 17. Pulse Rate: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	1582.38	395.59	11.05	.01**
Within	85	3043.03	35.8		
Total	89	4625.41			

Table 18. Pulse Rate: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1 5 Hz TENS	Group 2 100 Hz TENS	Group 3 2000 Hz TENS	Group 4 Placebo TENS	Group 5 No Treatment
mean	97.3	89.22	97.88	101.71	99.07
sd	4.21	6.13	5.87	7.92	5.17
Group 1		*			
Group 2					
Group 3		*			
Group 4	*	*			
Group 5		*			

Temperature

One-way ANOVA (Table 19) revealed no significant effect on this variable (df=4,85; F=1.59, p<.18). Means and standard deviations are shown in Table 20.

Table 19. Temperature: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	72.21	18.05	1.59	.18
Within	85	964.47	11.34		
Total	89	1036.68			

Table 20. Temperature: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations

	Group 1 5 Hz TENS	Group 2 100 Hz TENS	Group 3 2000 Hz TENS	Group 4 Placebo TENS	Group 5 No Treatment
mean	100.73	103.22	102.03	101.28	101.01
sd	2.4	4.8	4.1	2.91	1.64

Anxiety

One-way ANOVA (Table 21) revealed no significant effect on this variable (df=4,85; F=2.03, p<.10). Means and standard deviations are shown in Table 22.

Table 21. Anxiety: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	2051.29	512.82	2.03	.10
Within	85	21455.91	252.42		
Total	89	23507.2			

Table 22. Anxiety: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations

	Group 1 5 Hz TENS	Group 2 100 Hz TENS	Group 3 2000 Hz TENS	Group 4 Placebo TENS	Group 5 No Treatment
mean	84.8	79.18	84.4	89.54	93.16
sd	18.49	12.93	11.11	14.77	20.28

SUMMARY AND CONCLUSIONS

In this double-blind study, significant reductions in systolic and diastolic blood pressure and pulse rate, but not in peripheral vascular tension or anxiety, were observed subsequent to 100 Hz cranial TENS, but not after 5 Hz TENS or 2000 Hz TENS, as compared to a no treatment control. No placebo TENS effect was observed on any measure. These findings are consistent with those of experiment I, with the exception that in this study no group differences were observed on changes in peripheral

vascular tension and anxiety. The observed reductions in cardiovascular activity after 100 Hz cranial TENS and not after 5 Hz or 2000 Hz TENS is consistent with previous findings of frequency-dependent effects of sine-wave constant AC cranial TENS (Katims et al., 1986), and provides further evidence for the frequency coding of the central nervous system for response to electrical stimulation (Stubbs, 1976).

The results of experiments I and II seem to indicate that 30 minutes of 100 Hz cranial TENS has the effect of reducing cardiovascular activity, and perhaps anxiety. The following study was therefore designed to answer three questions. Can 100 Hz cranial TENS attenuate the physiological and psychological response of normal subjects to standardized stress (mental arithmetic)? Are the effects of cranial TENS immediate, or is a certain amount of stimulation necessary before effects are observed? Do the effects of cranial TENS last after the current has been turned off? These questions were dealt with by comparing the response to experimental stress of four different TENS groups with that of a no treatment control group. One TENS group received active TENS of 100 Hz frequency during a 30 minute treatment phase, as well as during a 3 minute stress phase which followed immediately after the treatment phase. A second TENS group received active TENS during treatment followed by placebo TENS during stress. A third TENS group received placebo TENS

during both treatment and stress, and a fourth TENS group received placebo TENS during treatment followed by active TENS during stress. TENS groups 2 (active TENS during treatment followed by placebo TENS during stress) and 4 (placebo TENS during treatment followed by active TENS during stress) were included in the design in order to determine whether the effects of cranial TENS persist after the current has been discontinued, and whether cranial TENS can produce an immediate effect without the initial 30 minute treatment, respectively.

VI. Experiment III

Effects of Cranial TENS in Normal Subjects at Rest and During Standardized Experimental Stress

DESIGN

In a double-blind protocol, 90 healthy volunteers received active cranial TENS of 100 Hz frequency, placebo TENS or no treatment, for 30 minutes, immediately followed by 3 minutes of standardized mental stress (mental arithmetic). Blood pressure, pulse rate, peripheral vascular tension and anxiety were measured before and after treatment, and before and after stress.

MATERIALS AND METHODS

Subjects

Ninety healthy volunteer subjects (26 male and 64 female) aged 18-25 years were tested. This sample size was computed following the method of Kirk (1968) for alpha = .05 and power = .80. Informed consent was obtained from each subject under a protocol approved by the Investigational Review Board of Brooklyn College of the City University of New York (appendix B).

TENS Apparatus

As in experiment I.

Dependent Measures

Blood pressure. As in experiment I.

Pulse rate. As in experiment I.

Peripheral vascular tension. As in experiment I.

Anxiety. As in experiment I.

Treatments.

TENS treatment

All TENS treatments were administered as described in experiment II, employing a stimulation frequency of 100 Hz (0% thresholds for these subjects were .15 - .29 mA). Four different TENS groups were administered active and/or placebo TENS in a 33 minute procedure:

Group 1 - active TENS during a 30 minute treatment phase followed by active TENS during a 3 minute stress phase which immediately followed the treatment phase;

Group 2 - active TENS during treatment followed by placebo TENS during stress;

Group 3 - placebo TENS during treatment followed by placebo TENS during stress;

Group 4 - placebo TENS during treatment followed by active TENS during stress.

TENS groups 2 (active TENS for 30 minutes followed by placebo TENS during the 3 minute stress period) and 4 (placebo TENS for 30 minutes followed by active TENS during the 3 minute stress period) were included in the design in order to determine whether the effects of cranial TENS persist after the current has been discontinued, and whether cranial TENS can produce an immediate effect on stress, without the 30 minute pre-stress treatment. At the beginning and at the end of the 30 minute treatment phase (before the experimental stress procedure), a confederate set a switch on the TENS device

in a predetermined way according to subject number. The position of this switch determined whether treatment was active or placebo, and remained unknown to the experimenter to ensure the double-blind nature of the study.

No treatment

Subjects in this group (Group 5) were administered no treatment during the 33 minute procedure.

Experimental Stress Condition

Standardized laboratory stress was accomplished using a mental arithmetic task, for which the subject is instructed to subtract consecutive serial 17s from 4300 aloud as fast as possible without making mistakes. If a mistake is made, the subject must go back to the last correct answer and begin again. This procedure has been demonstrated to cause increases in blood pressure and heart rate, as well as increases in subjective estimates of psychological distress (Arnetz & Fjellner, 1986; Kemmer et al., 1986; Sleight et al., 1978).

Experimental procedure

Subjects were randomly assigned to the five groups, 18 per group. All tests were conducted in a quiet room with no visual distractions with subjects in a sitting position. The session began with the subject being asked to read and sign the informed consent form, which describes the experimental procedure. Following a ten minute adaptation period the dependent measures were

obtained (anxiety, temperature, pulse rate, blood pressure - approximately 5 minutes). 0% threshold was then obtained (.11 - .41 mA, mean = .30 mA for these subjects), and treatment was administered as described above. At the end of 30 minutes the dependent measures were again taken, followed by administration of the mental arithmetic procedure for 3 minutes. The dependent measures were taken a final time at termination of the mental arithmetic procedure while treatment remained active.

RESULTS

A. PRE- TO POST-30 MINUTE TREATMENT

One-way MANOVA indicated no significant group differences in baseline measures (Hotelling's T^2: df=20,318; F=1.38, p<.12). MANOVA did show significant group differences in pre- to post-treatment changes on the dependent variables taken collectively (Hotelling's T^2: df=20,318; F=3.36, p<.01). Separate univariate ANOVAs were therefore performed on each of the five dependent variables in order to identify where there was significance. Where significance was found, Duncan's multiple range test was employed to identify which groups differed significantly.

Systolic blood pressure

One-way ANOVA (Table 23) revealed a statistically significant effect (df=2,87; F=9.2, p<.01). Duncan's test (Table 24) showed that active TENS differed significantly (p<.05) from placebo TENS (with the exception of group 1 vs. group 4) and no treatment. Placebo TENS and no treatment did not differ.

Table 23. Systolic Blood Pressure: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	618.27	154.57	5.24	.01**
Within	85	2509.33	29.52		
Total	89	3127.6			

Table 24. Systolic Blood Pressure: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1	Group 2	Group 3	Group 4	Group 5
Treat.	Active	Active	Placebo	Placebo	No
Stress	Active	Placebo	Placebo	Active	Treatment
mean	93.33	90.83	97.39	96.06	97.72
sd	5.99	5.08	6.32	5.45	4.03
Group					
Group 2					
Group 3	*	*			
Group 4		*			
Group 5	*	*			

Diastolic blood pressure

One-way ANOVA (Table 25) revealed a statistically significant effect (df=4,85; F=3.31, p<.01). Duncan's test (Table 26) showed that active TENS differed significantly (p<.05) from placebo TENS (with the exception of group 1 vs. group 4), but not from no treatment. Placebo TENS and no treatment did not differ.

Table 25. Diastolic: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	757.89	189.47	3.31	.01**
Within	85	4864.33	57.23		
Total	89	5622.22			

Table 26. Diastolic Blood Pressure: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1	Group 2	Group 3	Group 4	Group 5
Treat.	Active	Active	Placebo	Placebo	No
Stress	Active	Placebo	Placebo	Active	Treatment
mean	92.56	90.11	98.17	96.78	95.17
sd	9.13	9.15	7.46	5.28	5.96
Group 1					
Group 2					
Group 3	*	*			
Group 4		*			
Group 5					

Pulse rate

One-way ANOVA (Table 27) revealed a statistically significant effect (df=4,85; F=2.58, p<.05). Duncan's test (Table 28) showed that active TENS differed significantly (p<.05) from no treatment, but not from placebo TENS. Placebo TENS and no treatment did not differ.

Table 27. Pulse Rate: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	821.04	205.26	2.58	.05*
Within	85	6765.44	79.59		
Total	89	7586.49			

Table 28. Pulse Rate: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1	Group 2	Group 3	Group 4	Group 5
Treat.	Active	Active	Placebo	Placebo	No
Stress	Active	Placebo	Placebo	Active	Treatment
mean	92.89	92.83	97.22	97.89	100.61
sd	8.72	8.95	13.23	5.78	5.78
Group 1					
Group 2					
Group 3					
Group 4					
Group 5	*	*			

Temperature

One-way ANOVA (Table 29) revealed no significant effect on this variable (df=4,85; F=.62, p<.65). Means and standard deviations are shown in Table 30.

Table 29. Temperature: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	43.33	10.83	.62	.65
Within	85	1489.56	17.52		
Total	89	1532.89			

Table 30. Temperature: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations.

	Group 1	Group 2	Group 3	Group 4	Group 5
Treat.	Active	Active	Placebo	Placebo	No
Stress	Active	Placebo	Placebo	Active	Treatment
mean	100.72	100.39	100.61	102.22	101.61
sd	4.07	6.31	2.2	3.39	3.87

Anxiety

One-way ANOVA (Table 31) revealed a statistically significant effect (df=4,85; F=7.74, p<.01). Duncan's test (Table 32) showed that active TENS differed significantly (p<.05) from placebo TENS and no treatment, which did not differ significantly.

Table 31. Anxiety: Univariate ANOVA Summary

Source	DF	SS	MS	F	P
Between	4	3477.4	894.35	7.74	.01**
Within	85	9823.89	115.58		
Total	89	13401.29			

Table 32. Anxiety: Post-treatment Group Means (as percentage of pre-treatment) and Standard Deviations; Results of Duncan's Test (* = Significant Difference at p<.05)

	Group 1	Group 2	Group 3	Group 4	Group 5
Treat. Stress	Active Active	Active Placebo	Placebo Placebo	Placebo Active	No Treatment
mean	80.28	84.11	96.11	94.72	93.22
sd	12.51	12.19	8.74	11.31	8.27
Group 1					
Group 2					
Group 3	*	*			
Group 4	*	*			
Group 5	*	*			

B. PRE- TO POST-STRESS

Correlated T tests indicated that the stress procedure was successful in bringing about significant increases in systolic blood pressure (df=17; t=4.22, p<.01), diastolic blood pressure (df=17; t=3.5, p<.01) and anxiety (df=17; t=6.78, p<.01), but not in pulse rate (df=17; t=.54) or temperature (df=17; t=1.38, p<.1) in the no treatment control group. One-way MANOVA revealed no significant group differences in physiological or psychological response to stress (Hotelling's T^2: df=20,318; F=1.25, p<.21). Group means and standard deviations are shown in Table 33.

Table 33. Post-stress Group Means (as percentage of pre-stress) and Standard Deviations. SYS = Systolic Blood Pressure; DIA = Diastolic Blood Pressure; PUL = Pulse Rate; TEMP = Temperature; ANX = Anxiety

		Group 1	Group 2	Group 3	Group 4	Group 5
Treatment		Active	Active	Placebo	Placebo	No
Stress		Active	Placebo	Placebo	Active	Treat.
SYS	mean	103.56	107.44	102.0	101.56	104.33
	sd	5.51	8.71	8.85	6.91	4.5
DIA	mean	104.11	112.89	103.78	102.61	105.94
	sd	8.64	10.19	10.09	7.06	7.14
PUL	mean	100.33	106.44	101.33	103.56	98.94
	sd	8.87	8.92	7.41	10.81	10.16
TEMP	mean	98.28	99.28	99.39	99.5	99.17
	sd	3.74	1.9	2.52	2.55	2.43
ANX	mean	114.28	127.94	119.44	120.67	126.44
	sd	13.89	26.29	31.87	21.24	19.66

SUMMARY AND CONCLUSIONS

In this double-blind study, significant reductions in systolic blood pressure, pulse rate and anxiety, but not in diastolic blood pressure or peripheral vascular tension, were observed in normal subjects subsequent to 30 minutes of 100 Hz sine-wave constant AC cranial TENS as compared to a no treatment control. Significant reductions in diastolic blood pressure were also observed after active TENS as compared to placebo TENS. No placebo TENS effect was observed on any measure. No significant group differences were observed in physiological or psychological response to experimental stress.

These results are consistent with those of the first two studies in demonstrating reductions in cardiovascular activity and anxiety after 30 minutes of 100 Hz cranial TENS. However, of the questions posed at the outset of this study (whether cranial TENS can attenuate the physiological and psychological response of normal subjects to mental stress, whether cranial TENS effects on stress are immediate, and whether the effects of cranial TENS last after the current has been turned off) only question 1 can be answered. MANOVA revealed no significant group differences in physiological or psychological response to mental stress.

VII. DISCUSSION

A review of the experimental literature suggested that cranial TENS is capable of influencing the central nervous system through the direct action of transcranial current flow, or by stimulation of brainstem cranial nerve cell bodies via surface fibers, and that sine-wave constant AC stimulation may offer advantages over other methodologies. However, a review of the clinical literature showed that previous reports claiming a) effectiveness of cranial TENS, b) ineffectiveness of cranial TENS, or c) that any cranial TENS effects are due to placebo, were inconclusive owing to methodological shortcomings, including questionable double-blind and placebo procedures, the exclusive use of subjective dependent measures, and variability in cranial TENS protocol and apparatus. The present studies attempted to eliminate some of these difficulties through the administration of active TENS at sub-threshold current levels, ensuring an effective double-blind, the inclusion of no treatment control conditions for comparison purposes, and the inclusion of objective physiological dependent measures.

The results of these studies suggest that 30 minutes of sine-wave constant AC cranial TENS of 100 Hz frequency can bring about reductions in blood pressure, pulse rate and anxiety in normal subjects at rest, while no such effects are observed after 5 Hz or 2000 Hz TENS, and that these effects are not due to placebo. They also indicate,

however, that cranial TENS is unable to alter the physiological and psychological response to mental stress.

While these results are of limited generalizeability owing to the relatively small samples used and fact that the subjects were all healthy volunteer college students between the ages of 18 and 30, they are consistent with previous reports of reductions in anxiety subsequent to cranial TENS, and fail to support theories that the effects of cranial TENS are due to placebo. These findings also provide further demonstration of the frequency coding of the central nervous system for response to electrical stimulation (Stubbs, 1976), and frequency-dependent effects of sine-wave constant AC stimulation (Katims & Ng, 1985; Katims et al., 1986).

Although the mechanism of action of cranial TENS has yet to be elucidated, it has been demonstrated that a cranial TENS current passes both transcranially and over the surface of the cranium, possibly influencing cortical and sub-cortical structures and brainstem cell bodies of cranial nerves. This current may produce a variety of effects, including the release of endorphins (Ng et al., 1975; Pert et al., 1981; Salar et al., 1981; Sjolund & Erikson, 1976), cortical inhibition via gate control mechanisms (McKenzie et al., 1971; Melzack, 1975), and parasympathetic autonomic nervous system dominance via stimulation of the vagus nerve (Toriyama, 1975).

Cranial TENS with the present electrode placement

might affect the 5th (trigeminal), 7th (facial), 9th (glossopharyngeal) and 10th (vagus) cranial nerves. The trigeminal (5th) nerve provides sensory innervation for the skin of the face and forehead, the mucous membranes of the nose, the nasal sinuses and the oral cavity, the teeth, and portions of the cranial dura and external auditory meatus. The facial (7th) nerve innervates the facial muscles. The glossopharyngeal (9th) nerve provides sensory innervation for the mucous membranes of the posterior third of the tongue, the tonsil, the posterior wall of the upper pharynx, and the Eustachian tube. The vagus (10th) nerve provides sensory innervation for the posterior wall of the external auditory meatus and parts of the auricle, the pharynx, larynx, trachea, and esophagus.

The cell bodies of the primary sensory fibers of the trigeminal (5th) nerve are located within the midbrain in the trigeminal nucleus. Stimulation of the trigeminal nucleus and its sensory fibers has been demonstrated to induce electrocortical activity (Fields et al., 1975). Additionally, both the putative neurotransmitters, Substance P and Enkephalin, which have been postulated to be involved in limbic emotional brain functions, have been found in neurons within this nucleus (Hokfelt et al., 1977). Stimulation of the trigeminal nucleus may therefore account for some of the effects of cranial TENS observed in these studies.

Brainstem nuclei which have intimate neuronal connections with the trigeminal nucleus, and have (in rats) been demonstrated to increase their metabolic activity in response to sine-wave cranial TENS (Katims & Ng, 1985) include the nucleus ambiguus, which contains some of the cell bodies of the 9th and 10th cranial nerves, the nucleus solitarius, which receives fibers from both the 7th and 9th cranial nerves, and the nucleus gigantocellularis, which is comprised of the pontine portion of the reticular formation, whose primary role is the regulation of electrocortical activity. Cranial TENS may therefore indirectly influence the trigeminal nucleus via stimulation of these other brainstem nuclei.

Stimulation of the brainstem cell bodies of cranial nerves might also result in the changes observed in these studies via electrotonic interactions with the surrounding central gray region, which contains among the densest concentrations of enkephalins within the brain (Belluzzi & Stein, 1977), stimulation of which has been demonstrated to produce analgesia in humans (Richardson & Akil, 1977).

Direct stimulation of the 9th (glossopharyngeal) and 10th (vagus) cranial nerves might explain the cardiovascular effects of cranial TENS observed in these studies via the carotid sinus reflex, which causes a reduction in heart rate and arterial pressure when these nerves are stimulated.

While the effects of cranial TENS in normal subjects

at rest observed in these studies are interesting, and call for further exploration into the mechanism of action of cranial TENS, the fact that cranial TENS was not shown to influence subjects' physiological or psychological arousal in response to stress suggests that the effects of this technique may not be sufficiently robust to be useful in clinical cases where there is acute psychological stress at the time of treatment. Whether cranial TENS can be of benefit in cases where psychological stress is not a factor is a question left to future clinical trials.

Appendix A

CLINICAL INVESTIGATION CONSENT FORM
Brooklyn College of the City University of New York

Title of Research Project: "Effects of Cranial Transcutaneous Electrical Nerve Stimulation on Physiological and Psychological Measures"

Explanation of Project:

You have agreed to participate in a study which tests the effects of electrical stimulation on physiological and psychological measures. You will have electrodes placed on both your earlobes, and levels of electricity too weak for you to feel will be applied for 30 minutes. Your blood pressure, pulse rate, skin temperature and level of anxiety will be measured at intervals during the experiment.

There are no known risks or benefits associated with the electrical stimulation that you will receive in this study. Electrical stimulation is routinely employed in medicine for the relief from pain, but little is known about its effects on physiological and psychological measures. You are free to withdraw from the research study at any time. Medical attention will be available during the test, and in the event that you believe participation in this research has led to injury, you may contact Dr. C.T.Lee at 718-780-5601 to identify the medical resources which are available to you and to assist you in obtaining the appropriate medical care.

Please indicate by your signature below that the research procedures have been explained to your satisfaction, and that you consent to participate in this study.

_____
Signature of Subject

_____
Signature of Witness

_____
Date

CLINICAL INVESTIGATION CONSENT FORM
Brooklyn College of the City University of New York

Title of Research Project: "Effects of Relaxation on Physiological and Psychological Measures"

Explanation of Project:

You have agreed to participate in a study which tests the effects of relaxation on physiological and psychological measures. You will be asked to sit quietly for 30 minutes. Your blood pressure, pulse rate, skin temperature and level of anxiety will be measured at intervals during the experiment.

You are free to withdraw from the research study at any time. Medical attention will be available during the test, and in the event that you believe participation in this research has led to injury, you may contact Dr. C.T.Lee at 718-780-5601 to identify the medical resources which are available to you and to assist you in obtaining the appropriate medical care.

Please indicate by your signature below that the research procedures have been explained to your satisfaction, and that you consent to participate in this study.

_____
Signature of Subject

_____
Signature of Witness

_____
Date

Appendix B

CLINICAL INVESTIGATION CONSENT FORM
Brooklyn College of the City University of New York

Title of Research Project: "Cranial Transcutaneous Electrical Nerve Stimulation and Response to Experimental Stress"

Explanation of Project:

You have agreed to participate in a study which measures the effects of electrical stimulation on your response to stress. You will have electrodes placed on both your earlobes, and levels of electricity too weak for you to feel will be applied for 30 minutes. During the test, you will be asked to perform a mental arithmetic task for five minutes. Your blood pressure, pulse rate, skin temperature and level of anxiety will be measured at intervals during the experiment.

There are no known risks or benefits associated with the electrical stimulation that you will receive in this study. Electrical stimulation is routinely employed in medicine for the relief from pain, but little is known about its potential for the treatment of stress. You are free to withdraw from the research study at any time. Medical attention will be available during the test, and in the event that you believe participation in this research has led to injury, you may contact Dr. C.T.Lee at 718-780-5601 to identify the medical resources which are available to you and to assist you in obtaining the appropriate medical care.

Please indicate by your signature below that the research procedures have been explained to your satisfaction, and that you consent to participate in this study.

_____
Signature of Subject

_____
Signature of Witness

_____
Date

CLINICAL INVESTIGATION CONSENT FORM
Brooklyn College of the City University of New York

Title of Research Project: "Relaxation and Response to Experimental Stress"

Explanation of Project:

You have agreed to participate in a study which measures the effects of relaxation on your response to stress. You will be asked to sit quietly for 35 minutes. During the test, you will be asked to perform a mental arithmetic task for five minutes. Your blood pressure, pulse rate, skin temperature and level of anxiety will be measured at intervals during the experiment.

You are free to withdraw from the research study at any time. Medical attention will be available during the test, and in the event that you believe participation in this research has led to injury, you may contact Dr. C.T.Lee at 718-780-5601 to identify the medical resources which are available to you and to assist you in obtaining the appropriate medical care.

Please indicate by your signature below that the research procedures have been explained to your satisfaction, and that you consent to participate in this study.

_____
Signature of Subject

_____
Signature of Witness

_____
Date

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