The effect of three electrotherapeutic modalities upon peripheral nerve conduction and mechanical pain threshold


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Summary

The current study was designed to examine the neurophysiological and hypoalgesic effects of three types of electrical stimulation. Following approval by the University’s Research Ethical Committee, healthy volunteers (n = 40; 20 males and 20 females; age 20–40 years; mean age 26 ± 18 years) were recruited and screened for contraindications. Subjects were randomly allocated in equal numbers to the following groups: control, transcutaneous electrical nerve stimulation (TENS; 150 Hz, 125 μs), interferential therapy (IFT; 150 Hz, 125 μs) or action potential stimulation therapy (APS; 153 Hz, 6.4 ms). All treatments were applied under double-blind conditions for 15 min over the course of the median nerve in the subject’s right forearm. Antidromic median nerve compound action potentials (CAPs) were recorded pretreatment, immediately post-treatment (i.e. at 15 min) and then at 25, 35 and 45 min. Immediately following CAP recording, mechanical pain threshold (MPT) was recorded from two sites on the palmar surface of the right hand. Statistical analysis showed significant differences between groups for peak to peak amplitude (PPA) at 25, 35 and 45 min (Kruskal–Wallis: P = 0.01, 0.01 and 0.02). Mann–Whitney U-tests indicated a significant increase in PPA in the IFT group compared with all other groups at 25 and 35 min and compared with the TENS and APS groups at 45 min. No significant differences were found for the MPT data. This study has therefore demonstrated that none of the aforementioned modalities produced a significant hypoalgesic effect; however, IFT produced a significant change in PPA compared with TENS and APS.

Keywords: electrical current, experimental pain, nerve conduction, stimulation parameters.

Introduction

The use of electrical stimulation for pain relief dates back as far as the Egyptian Fifth Dynasty. In the 1960s, the publication of the pain gate theory (Melzack & Wall, 1965) acted as a ‘catalyst’ for electroanalgesia by providing the theoretical basis for the use of electrical currents for pain relief. Recent surveys have indicated the popularity of electrical currents in the treatment of pain of various aetiologies (Pope et al., 1995; Robertson & Spurritt, 1998). Transcutaneous electrical nerve stimulation (TENS), interferential therapy (IFT) and action potential stimulation (APS) therapy are examples of three different types of electrical currents currently used for pain relief in clinical practice. However, despite the popularity of such modalities, there is ongoing debate regarding their hypoalgesic and neurophysiological effects.
TENS has been extensively used in the management of pain for a wide variety of clinical conditions (Sjölund, 1988; Akyüz et al., 1995; Walsh, 1997); although the clinical success of TENS is documented, the associated neural mechanisms that modulate pain are not well understood (Johnson, 1998; McDowell et al., 1999). TENS and APS therapy are regarded as low frequency currents (<250 Hz) while IFT comprises two medium frequency currents (usually 4 kHz) one of which is amplitude modulated to produce a low frequency current (0–250 Hz). It is claimed that IFT has an advantage over other electrical currents in that its carrier frequency is associated with relatively lower skin resistance while still producing low frequency effects within the tissues (Kloth, 1987; Martin, 1996). Despite the increasing acceptance of this electrotherapeutic modality amongst clinicians (Lindsay et al., 1995; Pope et al., 1995; Robertson & Spurratt, 1998), literature reporting the efficacy of IFT is deficient, with several authors pointing to the scarcity of empirical evidence for this modality (Schmitz et al., 1997; Johnson, 1999; Palmer et al., 1999; Noble et al., 2000). APS therapy is a novel electrical stimulation device that delivers a monophasic exponential decaying waveform with a fixed frequency (153 Hz). This device was developed in the early 1990s in South Africa. At the present time there is an obvious scarcity of published literature on this form of electrical stimulation.

Previous work at this centre has investigated the peripheral effects of electrical currents, e.g. TENS and H-wave therapy, by observing alterations in compound action potential (CAP) characteristics before and after the application of the treatment (McDowell et al., 1996; Walsh et al., 1995, 1998). In addition, mechanical pain threshold (MPT) recordings have been used successfully to assess the hypoalgesic effects associated with such neurophysiological changes (Walsh et al., 1995, 1998). An increase in negative peak latency (NPL) is an indicator of a decrease in the nerve conduction velocity and has been shown to highly correlate with changes in MPT (Walsh et al., 1995, 1998). Walsh et al. (1998) reported parameter-specific effects of TENS on conduction in the superficial radial nerve and on MPT recorded within the distribution of this nerve; an increase in NPL was associated with an increase in MPT. Other authors have similarly reported that TENS induced alterations in nerve conduction velocity (Campbell & Taub, 1973; Torebjörk & Hallin, 1974; Ignelzi et al., 1981; Sjölund, 1988), while Golding et al. (1986) and Cox et al. (1993) did not report any such significant changes. In contrast, few studies have examined the neurophysiological or hypoalgesic effects of IFT or APS.

As an extension of previous work, the current study was designed to compare the peripheral neurophysiological effects of three different electrical currents (TENS, IFT and APS) by recording nerve conduction in the median nerve; in addition, local hypoalgesic effects were assessed using MPT recorded within the distribution of the median nerve.

Methods

Following approval by the University of Ulster’s Research Ethical Committee, 40 healthy volunteers (n = 40; 20 males and 20 females; age 20–40 years; mean age 26–18 years) were recruited from the staff and students of the University, and screened for medical history or current signs/symptoms of neuromuscular disorders including peripheral neuropathy. The experimental procedure was explained to subjects who were then asked to sign a consent form and randomly assigned in equal numbers to one of four experimental groups: control; TENS (150 Hz); IFT (150 Hz); APS (153 Hz); n = 5 males and 5 females per group. Subjects remained supine for the duration of the experiment. The anterior surface of the right forearm and hand was prepared using alcohol, and the stimulation and recording sites at the elbow and second digit, respectively, were cleaned with a colloidal abrasive in order to decrease skin resistance. All data were recorded and statistically analysed by the primary investigator who was blind to the treatments applied by a second investigator.

Recording of compound action potentials

In order to record antidromic CAPs, a bipolar muscle stimulator was used to identify the right median nerve at the elbow. A monopolar muscle stimulator was further used to map the course of the nerve in the right forearm. A surface bar stimulation electrode was attached at the right elbow and two digital ring electrodes were attached to the second digit, with the
active electrode on the proximal phalanx, and the reference electrode 3 cm distally on the middle phalanx. An earth electrode was attached approximately 2 cm proximal to the treatment electrode immediately proximal to the wrist crease on the medial aspect of the forearm. All electrodes were connected to an electrophysiological stimulation and recording system (Mystro+, Medelec, Woking, UK). Standard settings were used to record CAPs on this system: 100 Hz–2 kHz bandwidth; 50–100 µV per division sensitivity and sweep duration of 10 ms. Figure 1 illustrates the attachment of electrodes.

The median nerve was stimulated supramaximally using 100 µs pulses, delivered at a frequency of 1 Hz. Averaged responses to a train of 16 pulses were recorded and stored digitally for subsequent analysis. Recordings were taken at 2-min intervals until three consecutive readings showed constant NPLs (variation less than ±0.01 ms). Once stabilized in this way, antidromic CAPs were recorded at 0, 15, 25, 35, 45 min.

Recording of mechanical pain threshold

In order to measure MPT, two recording points were marked on the palmar surface of the right hand as this represented an area innervated by the median nerve. A ruler was placed over the anterior aspect of the right forearm from the wrist crease along the middle of the second digit; the recording points were marked at 3 cm (proximal MPT recording site) and 4.5 cm (distal MPT recording site) distal to the wrist crease. MPT was measured using a handheld circular pressure algometer (Salter Abbey Weighing Machines Ltd, West Bromwich, UK) with a 0.9 cm diameter probe head. The head of the algometer was slowly lowered until it made contact with the skin at the recording site. Once in place, the pressure was further increased at a slow steady rate of ~5 N s⁻¹ until pain threshold was reached. Subjects were instructed to give a response of ‘pain or stop’ at the precise moment when the pressure sensation changed into a painful sensation, i.e. mechanical pain threshold. Two MPT measurements were obtained for each recording site at the same time points as the nerve conduction recordings. The MPT measurements always followed the same order, with the proximal point recorded first and the distal one recorded after. The mean score was used for the purpose of statistical analysis.

Temperature recording

Ambient and skin temperature were recorded concomitantly throughout the procedure at 1-min intervals. For this, one ambient probe and one skin thermistor (Grant Instruments, Cambridge, UK) were used. The latter was placed on the anterior aspect of the right forearm, attached directly to the skin overlying the mid-point between the elbow and the wrist. Both probes were connected to a Squirrel data logger (1250 series, Grant Instruments, Cambridge, UK). Both probes were sensitive to temperature changes of ±0.05°C. Shifts in ambient temperature of ≥0.5°C in any one experiment were defined as exclusion criteria for the study.

Treatment procedure

An Endomed 982 (Enraf Nonius, Delft, The Netherlands), a TENS 120Z unit (ITO, Tokyo, Japan) and an APS unit (APS Therapy, Dublin, Ireland) were used to deliver the three electrotherapeutic currents. In each case, the treatment currents were applied through two self-adhesive PALS neurostimulation electrodes (5 × 5 cm; Physio-Medical Services, Derbyshire, UK) placed 10 cm apart directly over the
course of the right median nerve. Prior to the commencement of the study, the parameters of the TENS unit were calibrated and the accuracy of the IFT and APS units were also checked using an oscilloscope (Gould Electronics, Essex, UK). Subjects were given a brief demonstration of the treatment they were randomly assigned to on their left forearm prior to the experiment. In addition, peripheral sensation was verified using a sharp/blunt test over the dermatome of the median nerve.

Four experimental groups were included in this study: control group; TENS group: asymmetrical biphasic waveform, with a frequency of 150 Hz and a pulse duration of 125 µs; IFT group: sinusoidal waveform, with a carrier frequency set at 4 kHz, a ‘beat’ frequency of 150 Hz and a pulse duration of 125 µs; APS group: monophasic exponential decaying waveform, this unit delivers a fixed frequency of 153 Hz and a fixed pulse duration of 6-4 ms.

Subjects in the control group received no active form of treatment, although the electrodes were attached. Treatment was applied for 15 min at an intensity that the subjects described as a ‘strong but comfortable’ sensation. All treatments were applied by a second investigator who was not involved in data collection. The blinding of the primary investigator, who collected and analysed the data, was maintained until after the data were statistically analysed; therefore double-blind conditions were fulfilled. Furthermore, the treatment units were hidden from the subjects’ view to counter any possible influence that the different appearance of the units may have. To counteract the accommodation effect induced by a constant form of electrical stimulation, all subjects were asked to report if the level of sensation had decreased at set time intervals (i.e. every 2 min); if sensation had decreased, the intensity was increased to return it to the original level.

Data analysis

For the purpose of statistical analysis, difference scores were calculated (i.e. the variation from baseline). These difference scores were calculated by taking the initial value as baseline and expressing subsequent values as differences from this, thus eliminating inter subject variability. In order to conduct the most appropriate statistical test, a Shapiro–Wilk test was performed in order to check data for normal distribution. This test compares baseline raw data against a normally distributed data set; therefore if the P-value was <0.05, then the data were significantly different from a normal population. When data were not normally distributed, non-parametric tests were used (Kruskal–Wallis and Mann–Whitney U-test). For normally distributed data, repeated measures analysis of variance (ANOVA) and post hoc tests were performed. Statistical analysis was carried out using the SPSS 9.0 software (SPSS Inc., Chicago, IL, USA).

Results

Negative peak latency (NPL)

Negative peak latency values were taken at the point of maximum negative peak amplitude from the stimulus artefact. In this study, the mean NPL recorded at 0 min (i.e. before electrical stimulation) was 6.59 ± 0.21 ms (mean ± SEM, n = 40). Analysis of baseline raw data showed no significance between groups (P ≥ 0.61, one factor ANOVA). Figure 2 shows NPL difference scores (mean ± SEM) plotted against time in minutes for all groups. At the 15-min point, i.e. after treatment application, the IFT group showed an increase in NPL, which reached a maximum at the 25-min point (increase of 0.05 ± 0.03 ms, mean ± SEM). The control, TENS and APS groups showed a steady decrease in NPL.

Figure 2 Summary of negative peak latency (NPL) differences plotted against time for each of the experimental groups (mean ± SEM; n = 10 each group).
throughout the experimental period. Repeated measures analysis of variance did not demonstrate any significant difference between groups (P = 0.102) or an interactive effect (P = 0.41). However, there was a significant difference over time (P = 0.001).

Positive peak latency (PPL)

In this study, the mean PPL recorded at 0 min was 7.58 ± 0.26 ms (mean ± SEM, n = 40). Analysis of baseline raw data showed no significance between groups (P = 0.5, one factor ANOVA). After treatment application, the IFT group showed an increase in PPL, which reached a maximum at the 35-min point. The control, TENS and APS groups showed a reduction in the PPL values throughout the experimental procedure. Repeated measures analysis of variance (ANOVA) showed no differences between groups (P = 0.131), over time (P = 0.26), nor a significant interactive effect (P = 0.268).

Peak to peak duration (PPD)

In this study, the mean PPD recorded at 0 min was 0.98 ± 0.06 ms (mean ± SEM, n = 40). Analysis of baseline raw data showed no significance between groups (P = 0.19, one factor ANOVA). The results show a small variation between groups, although at 35 min there was a sharp increase in the values for the IFT group, which dropped substantially at 45 min towards baseline values. Kruskal–Wallis test showed no significant differences between groups at any of the time points (P ≥ 0.43).

Peak to peak amplitude (PPA)

In this study, the mean PPA recorded at 0 min was 15.26 μV (mean ± SEM, n = 40). Analysis of baseline raw data showed no significance between groups (P = 0.4, one factor ANOVA). PPA difference scores are presented in Fig. 3. The values recorded for the IFT group showed a steady rise that peaked at 35 min (increase of +5.56 ± 1.62 μV, mean ± SEM). The TENS group showed a dramatic increase at 15 min (increase of +8.3 ± +2.5 μV, mean ± SEM), followed by a decrease that reached values close to the baseline by the end of the experimental period. In the APS and control groups, a decrease in PPA values was observed. Kruskal–Wallis test showed that there were significant differences between groups at 25 min (P = 0.01), 35 min (P = 0.01) and 45 min (P = 0.02). Mann–Whitney U-tests showed that the IFT group was significantly different from all other experimental groups at 25 and 35 min, and at 45 min the IFT group was significantly different to the APS and TENS groups but not to the control group.

Mechanical pain threshold (MPT)

The mean scores of all mechanical pain threshold values recorded from both sites (proximal and distal) were used for statistical analysis. In this study, the mean overall mechanical pain threshold recorded at 0 min was 38.87 ± 3.71 N (mean ± SEM, n = 40). Analysis of baseline mean raw data showed no significance between groups (P = 0.56, one factor ANOVA). Mean mechanical pain threshold difference scores are presented in Fig. 4. All values above baseline represent an increase in mechanical pain threshold, i.e. a hypoalgesic effect. The values recorded for the IFT group demonstrated a slight increase immediately after treatment (i.e. 15 min). However, the values drop off below baseline for the rest of the experimental period. The control, APS and TENS groups showed a consistent decrease in the values recorded throughout the experimental period. Kruskal–Wallis test showed no significant differences between groups at any of the time points (P ≥ 0.32).
Ambient and skin temperature

Analysis of baseline raw skin temperature data showed no significance between groups \((P = 0.22, \text{one factor ANOVA})\). There was a significant difference between groups for baseline raw ambient temperature data \((P = 0.01, \text{one factor ANOVA})\). However, an ambient temperature variation of \(\pm 5^\circ\text{C}\) for any individual subject was defined as exclusion criteria for the study. In this study, the mean ambient temperature recorded at 0 min was 25.86 ± 0.38°C and at 45 min it had increased to 25.96 ± 0.36°C \((\text{mean} \pm \text{SEM}, n = 40)\). Repeated measures analysis of variance showed no difference between groups \((P = 0.068)\), over time \((P = 0.834)\), nor a significant interactive effect \((P = 0.592)\). The mean skin temperature recorded at 0 min was 32.4 ± 0.3°C and at 45 min it had increased to 32.7 ± 0.33°C \((\text{mean} \pm \text{SEM}, n = 40)\). Repeated measures analysis of variance for skin temperature data showed no significant differences between groups \((P = 0.19)\), nor an interactive effect \((P = 0.108)\); however, there was a significant effect over time \((P = 0.012)\).

Discussion

Although the clinical efficacy of some forms of electrical stimulation has been reported, their physiological basis remains controversial \((\text{Akyüz et al.}, 1995)\). The inconsistency of the peripheral neurophysiological effects of electrical stimulation has been emphasized in the literature \((\text{Cox et al.}, 1993; \text{McDowell et al.}, 1999)\). Therefore, the aim of the current study was to examine the effect of three electrotherapeutic modalities (IFT, TENS and APS) upon nerve conduction in the human median nerve and on mechanical pain threshold within the area of distribution of this nerve. In the present study, only one form of electrical stimulation showed a statistically significant difference in any of the CAP measurements, i.e. the IFT group showed a significant increase in PPA.

Peak to peak amplitude data for the IFT group revealed significant differences from all other experimental groups at 25 and 35 min, and from the APS and TENS groups at 45 min. As PPA is an expression of the estimate of the number of fibres recruited \((\text{Ma & Liveson, 1988; Stalberg & Erdem, 2000})\), the results obtained for the IFT group, may be related to the characteristics of this type of current. The ability to recruit and excite certain nerve fibre populations, as well as the ‘timing’ for the occurrence of these phenomena (during treatment or immediately after) may be specifically related to the carrier frequency and waveform. Further studies using microneurographic techniques would be needed to determine if the observed changes in PPA were related to specific types of nerve fibres.

There were no significant changes for any of the other CAP characteristics in the current study. Belcher \((1974)\) carried out an uncontrolled study to assess the effects of IFT \((0–100\text{ Hz}; \text{suction at }0.1\text{ kp cm}^{-2}; 15\text{ min})\) upon nerve conduction velocity of the human median and ulnar nerves, concluding that there were no significant changes in nerve conduction velocities. However, previous work at this centre has reported a significant increase in NPL in the superficial radial nerve following the application of TENS \((110\text{ Hz}, 200\text{ }\mu\text{s})\) for 15 min \((\text{Walsh et al.}, 1998)\); the variation in stimulation parameters in the current study may provide some explanation for this difference.

Pain threshold recordings have been used to study both local and central changes induced by electrical stimulation \((\text{Walsh et al.}, 1998); \text{Zoppi et al. (1981)}\) and Marchand \textit{et al.} (1991) both reported changes in a...
range of sensory thresholds after the application of TENS (50–100 Hz). In addition, Ward & Robertson (1998) showed that manipulating the frequency of alternating currents over a wide range of 1–35 kHz (amplitude modulated at 50 Hz) produced clear separation of sensory, motor and pain thresholds. They found that the three thresholds decreased as frequency increased up to 10 kHz; above 10 kHz, the thresholds increased again. Findings from the current study showed a marginal hypoalgesic effect in the IFT group (values raised immediately after treatment, i.e. 15 min) associated with an increase of NPL. MPT values then decreased after the treatment period.

Walsh et al. (1998) have demonstrated a correlation between an increase in NPL, an indicator of a decrease in the nerve conduction velocity, with an increase in MPT. However, MPT values only increased during the TENS application and showed a decrease following the treatment period, similar to the findings of the current study. This would suggest a short-lasting effect on MPT. These findings are also in accordance with previous studies conducted by Johnson & Wilson (1997) and Tabasam & Johnson (1999) who reported significant increases in ice pain thresholds after the application of IFT. The MPT values obtained for the TENS group showed a decrease throughout the 45-min period, indicating a non-hypoalgesic effect, which agreed with the results of Golding et al. (1986) and Cox et al. (1993), but contradicts previous work carried out by this research group (Walsh et al., 1995, 1998). However, the frequency and pulse duration used in the present study were slightly different than the parameters used in previous studies, which may account for the difference of the results recorded.

In conclusion, the current study has demonstrated that according to the parameters used in this investigation TENS, IFT and APS did not show a significant hypoalgesic effect. However, IFT produced a significant change in PPA compared with TENS and APS. These findings suggest that further research is warranted to assess the peripheral effects of these electrical currents.

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References


