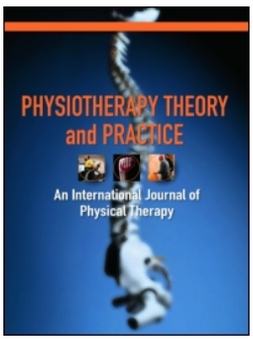

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Segmental and extrasegmental hypoalgesic effects of low-frequency pulsed current and modulated kilohertz-frequency currents in healthy subjects: randomized clinical trial

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ABSTRACT

Objective: To compare the segmental and extrasegmental hypoalgesic effects of TENS, IFC and Aussie current on pressure pain threshold (PPT) during and after stimulation in healthy subjects. The second objective was to compare the sensory comfort related to electrical stimulation.

Material and Methods: 120 healthy subjects were randomized in TENS, IFC, Aussie current or placebo groups. The electrical stimulation was administered on the forearm. The PPT was measured on the forearm (segmental measure) and on the lower leg (extrasegmental measure) by an algometer at baseline, during and after stimulation of the forearm, and the sensory comfort in relation to electrical stimulation was measured with a visual analogue scale. Statistical analysis was performed using linear mixed models for PPT analysis and one-way ANOVA for sensory comfort analysis.

Results: The TENS, IFC and Aussie current increased the segmental and extrasegmental PPTs during application of current compared to the placebo. The PPTs measures and sensory comfort were not significantly different between the TENS, IFC and Aussie current groups.

Conclusions: Segmental and extrasegmental hypoalgesic effects may be produced using TENS, IFC or Aussie currents in healthy subjects. Furthermore, all of them presented a similar sensory comfort.

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KEYWORDS
Pain; electric stimulation therapy; transcutaneous electrical nerve stimulation; pain threshold

Introduction

Electrical stimulation is used for various purposes, including muscle strengthening, pain control and edema control (Astokorki and Mauger, 2017). Currents most often used to achieve pain control are pulsed current, usually referred to as transcutaneous electrical nerve stimulation (TENS), amplitude modulated kilohertz-frequency current referred to as interferential current (IFC) (Beatti, Rayner, Souvlis, and Chipchase, 2010) and burst-modulated kilohertz-frequency current known as Aussie current (Ward, Oliver, and Buccella, 2006).

The majority of TENS units deliver symmetric or balanced asymmetric biphasic pulsed current (Alves-Guerreiro, Noble, Lowe, and Walsh, 2001; Johnson and Tabasam, 2003; Pantaleão et al., 2011). Pulse frequency usually is less than 200 Hz (Sluka, Bjordal, Marchand, and Rakel, 2013). Pulsed current of 10 Hz or less is known as low-frequency TENS and high-frequency TENS is defined as frequencies greater than 10 Hz to the maximum setting on the TENS device usually 150 Hz to 200 Hz (Johnson et al., 2017). A systematic review by Claydon and Chesterton (2011) concluded that high frequency (i.e. 10 to 200 Hz) and high intensity (i.e. strong and uncomfortable TENS, with muscle contraction) stimulation have stronger evidence of hypoalgesic efficacy in pressure pain models.

The interferential current (IFC) is composed of two independent medium frequency alternating currents with carrier frequencies ranging from 1 to 10 kHz, one current being set usually at a frequency of 4000 Hz and the other between 4001 Hz and 4250 Hz, producing an amplitude modulated sinusoidal wave at a frequency of 1–250 Hz. This frequency is also known as the beat frequency (Alves-Guerreiro, Noble, Lowe, and Walsh, 2001; Shanahan, Ward, and Robertson, 2006).

Ward and Lucas-Toumbourou (2007) developed a type of alternating current modulated in rectangular bursts of short duration (2–4 ms) with the aim of

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producing a current better suited for sensory and motor stimulation (Ward and Chuen, 2009). This type of current became known commercially as the Aussie current (Ward and Chuen, 2009; Ward, Lucas-Toumbourou, and McCarthy, 2009).

The hypoalgesic effects produced by electrical currents can be segmental (local) or extrasegmental (systemic). Segmental hypoalgesia is defined as a diminished pain at the treatment site or at spinal cord segment associated with the reported pain (Clark et al., 2011; Millan, Leboeuf-Yde, Budgell, and Amorim, 2012). Extrasegmental hypoalgesia occurs in remote areas, far from the site of application of therapy (Bialosky et al., 2009; Claydon, Chesterton, Barlas, and Sim, 2013; Millan, Leboeuf-Yde, Budgell, and Amorim, 2012).

Segmental hypoalgesia of TENS, IFC, and Aussie current has been previously studied. Some studies in healthy subjects showed the segmental hypoalgesic effects (stimulation site) of different TENS parameters in relation to a control/placebo group (Chesterton et al., 2003; Claydon, Chesterton, Barlas, and Sim, 2008). Other studies concluded that there was no significant difference between TENS and IFC or between TENS and Aussie current at elevating pain thresholds (Cheing and Chan, 2009; Johnson and Tabasam, 2003; Ward, Lucas-Toumbourou, and McCarthy, 2009; Ward and Oliver, 2007). There was only one study that showed TENS was better than IFC at increasing the cold pain threshold (Shanahan, Ward, and Robertson, 2006). On the other hand, some clinical trials showed that IFC was better than TENS for pain relief treatment (Koca et al., 2014; Rajfur et al., 2017; Zeng et al., 2015). In a narrative review, Samuel and Maiya (2015) concluded that there is a plethora of evidence available to support the use of TENS and IFC of various frequencies for pain relief, and further research with more randomized controlled trials and studies with better methodological quality are warranted.

In contrast to segmental effects, the extrasegmental effects of TENS, IFC, and Aussie current have been much less studied. Chesterton et al. (2002) observed greater extrasegmental hypoalgesic effects of TENS compared to control or placebo groups in healthy subjects. Claydon, Chesterton, Barlas, and Sim (2008) found greater extrasegmental hypoalgesic effects only of TENS group compared to control group, but not in relation to placebo in healthy subjects. Thus, it can be observed from the literature that there is limited and equivocal evidence regarding the segmental and extrasegmental hypoalgesic effects produced by TENS, IFC or Aussie current in patients or healthy subjects. In addition, most studies do not investigate the extrasegmental effects between the electrical currents. Therefore, the aim of the present study was to compare the segmental (forearm) and extrasegmental (lower leg) hypoalgesic effects of TENS, IFC and Aussie current on pressure pain threshold during and after stimulation of the forearm and sensory comfort related to electrical stimulation in healthy subjects.

Methods

Study design and subjects

The present study was a randomized placebo-controlled clinical trial that followed the guidelines recommended by the Consolidated Standards of Reporting Trials (CONSORT). The study protocol has been published elsewhere (Rampazo Da Silva et al., 2018). The subjects and investigator 1 were blinded and the study was registered under No. NCT01950728 for Clinical trials (https://clinicaltrials.gov/). The study was approved by the Human Research Ethics Committee of the Federal University of São Carlos (UFSCar; CAAE: 67222317.0.0000). The study was carried out at the Federal University of São Carlos and the subjects were recruited through oral and virtual communication in the grounds of the university between September 2017 and July 2018. Eligibility criteria was previously described in detail (Rampazo Da Silva et al., 2018). Healthy subjects of both sexes, aged between 18 and 45 years and with no prior experience with electrical stimulation were eligible.

Calculation of sample size

The sample size was calculated considering a difference of 100 kPa between groups and standard deviation of 98 (Macedo et al., 2015) based on the PPT values evaluated with an algometer. At a significance level of 0.05 and power of 80%, it was calculated that a minimum of 22 subjects should be recruited per group (Minitab, v.17, software, State College, PA). Allowing for attrition, 30 subjects were recruited per group (120 in total).

Randomization and allocation concealment method

Subjects were stratified by sex to ensure equal numbers of women and men in each group and randomly allocated to 1 of 4 groups (n = 30 per group): 1) transcutaneous electrical nerve stimulation (TENS); 2) interferential current (IFC); 3) Aussie current; or 4) placebo group. The order of measurement of the PPT

between the upper and lower limbs were also randomized. An investigator uninvolved in data collection performed the online randomization (http://www.randomization.com/) and the allocation concealment method was performed with the use of opaque and sealed envelopes.

Subject preparation

Subjects signed consent forms after being familiarized with the study and screened for eligibility. Demographic data (i.e. age, sex, race, weight, and height) were collected and the subjects were asked to lie down on the table so that the dominant upper limb and ipsilateral leg could be cleaned with soap and water in the areas of electrode positioning and the algometry points were marked with a pen.

The first area of measurement of the PPT was marked on the dominant forearm (i.e. forearm extensor muscle). It was considered the segmental area because in this area, the electrical stimulation was applied. For this, a straight line was drawn between the lateral epicondyle of the elbow and the midpoint between the medial and lateral border of the wrist. The first electrode was positioned on the forearm at the elbow fold next to the lateral epicondyle and the second electrode was positioned 3 cm from the end of the first electrode on the previously drawn straight line (Figure 1). The measuring point of the algometer was exactly midway between the two electrodes (Chen and Johnson, 2009, 2010).

The second area of PPT measurement was marked on the ipsilateral lower leg (i.e. tibialis anterior muscle) to the dominant arm, and it was considered the extrasegmental area because it is a distant area where the electrical stimulation was not applied (Figure 2). A tape measure was used to define the midpoint of the tibialis anterior muscle belly (Pelegrini, Venancio, and Liebano, 2012). After the positioning of the subject and the electrodes, investigator 1 opened the envelope to find out if the order of evaluation of the PPT with the algometer would start on the forearm or on the lower leg. Immediately after the PPT measurement, investigator 2 opened the envelope to determine which group that subject was assigned to and to initiate the treatment procedure with TENS, IFC, Aussie current or placebo.

Intervention groups

To deliver the TENS, IFC and Aussie current, the NEURODYN unit (IBRAMED®; Amparo, São Paulo, Brazil) and two standard square self-adhesive electrodes (5 x 5 cm) (ValuTrode®; Axelgaard, Fallbrook, CA) were used.

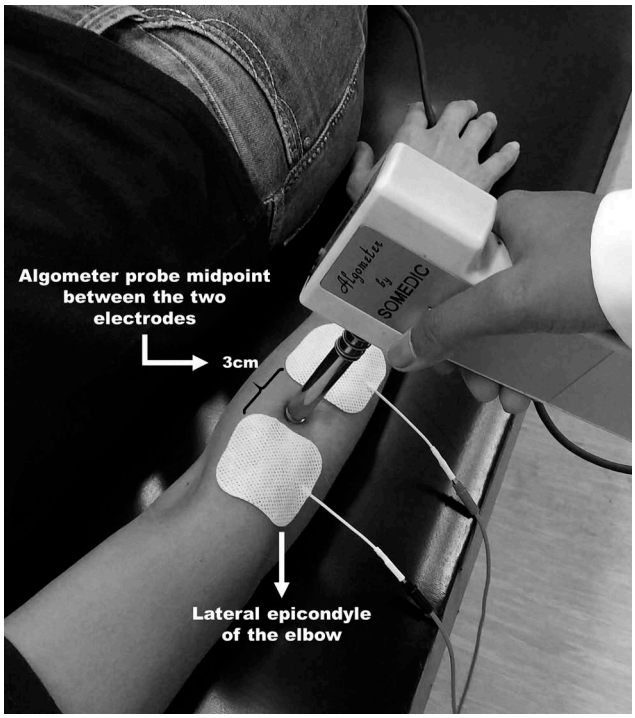

Figure 1. Positioning of electrodes and segmental PPT measurement on the forearm.

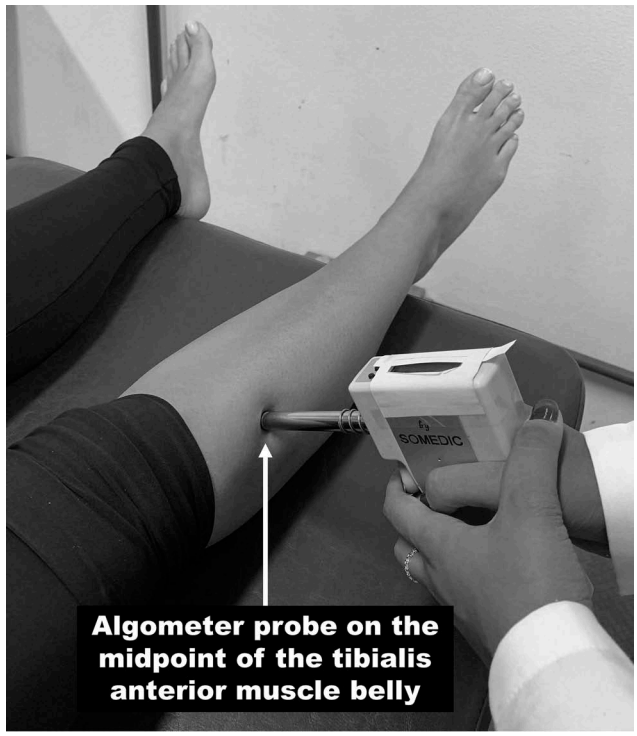

Figure 2. Extrasegmental PPT measurement on the lower leg.

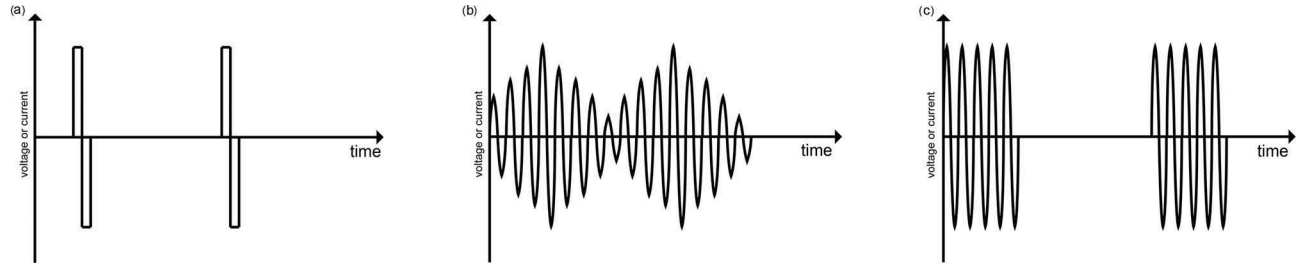

Figure 3. The 3 stimulus waveforms compared in the present study. A: symmetric biphasic pulsed current (Transcutaneous electrical nerve stimulation – TENS). B: sinusoidal amplitude modulated alternating current (Interferential current). C: burst-modulated alternating current with rectangular burst modulation (Aussie current).

The parameters used were: 1) TENS group: symmetric biphasic pulsed current (Figure 3a) with a frequency of 100 Hz and phase duration of 125 μs (pulse duration = 250 μs); 2) IFC group: sinusoidal amplitude modulated alternating current (Figure 3b) with a carrier frequency of 4 kHz, phase duration of 125 μs (pulse duration = 250 μs) and an amplitude modulated frequency (AMF) of 100 Hz; 3) Aussie current group: rectangular burst-modulated alternating current (Figure 3c) with carrier frequency of 4 kHz, phase duration of 125 μs (pulse duration = 250 μs), 4 ms burst duration and 100 Hz frequency. For all groups, the electrodes were positioned as described above, and the amplitude of TENS, IFC and Aussie current were increased until the subject reported strong but comfortable (including motor level stimulation) but no painful stimulation paraesthesia (Johnson and Tabasam, 2003; Liebano et al., 2013; Moran et al., 2011). The application of the current lasted for 30 minutes and at 4 minutes intervals, the subject was asked whether the current sensation had faded, and the pulse amplitude was increased until the subject again felt a strong but comfortable paraesthesia intensity level; and 4) Placebo group: the electrodes were positioned as previously described for 30 minutes and, every 4 minutes, investigator 2 questioned the subject regarding any possible discomfort and simulated the increase of current amplitude.

Outcomes and measures

PPT measures

Investigator 1 measured the PPT using a Somedic Type II pressure algometer (Somedic®, Hörby, Sweden), consisting of a circular rubber probe (1 cm^2). The algometer was calibrated prior to the start of the study by the manufacturer. The intra-rater reliability for the PPT measurement had already been estimated by calculating the intraclass correlation coefficients ($ICC_{2,3}$) for forearm (0.885; 95% CI 0.601 to 0.967) and for the lower leg (0.924; 95% IC 0.736 to 0.978). For this, a total of 13 healthy volunteers, uninvolved in the study, were recruited and evaluated on two occasions with a 48-hour interval between them (Cowan et al., 2009; Pantaleão et al., 2011).

During the study, investigator 1 was blinded to the division of the groups and the currents used. The device was covered during the PPT measures, so that investigator 1 did not know whether the TENS, IFC, Aussie current or placebo was applied. In the TENS, IFC and Aussie current groups, the amplitude of the current was reduced to the sensory threshold prior to the PPT measure by investigator 2 so that investigator 1 was also blinded to whether that subject belonged to any current group, since the increase in the amplitude could lead to muscle contraction. During the PPT measure, the circular algometer probe (1 cm^2 area) was applied perpendicular to the skin at a uniform and constant rate of 30 kPa/s (Figure 1). The subjects were instructed to close their eyes and to press the algometer sensor when the pressure sensation became painful. Each time (baseline, 15 minutes, 30 minutes, and 50 minutes), three measurements were collected with a 30 second interval between them, and the mean was used for data analysis. Subjects and investigator 1 were not permitted to see the algometer readings during measuring. All participants had three applications of the PPT measurement on their non-dominant upper limb to ensure that they understood the PPT concept prior to the data collection (Figure 1).

Sensory comfort

Sensory comfort in relation to electrical stimulation was measured post-stimulation with a 10 centimeter visual analogue scale (VAS) (Venancio et al., 2013) where the far left end indicated "more comfortable" and the far right end indicated "less comfortable" and the subject was asked to draw a perpendicular line on the VAS line.

Blinding assessment

Assessment of the effectiveness of blinding was performed after the conclusion of the fourth evaluation. Investigator 2 asked investigator 1 and the subjects: "Do you think that the application of electrical current was real, placebo or did not know?" Their responses were recorded and used to gauge the adequacy of subject and investigator blinding.

Statistical analysis

The characteristics of the participants were summarized using descriptive statistics. The averages of pressure pain threshold scores (baseline, 15, 30 and 50 minutes) were used to perform the statistical analysis. A natural logarithm transformation (log base 10) was applied to normalize the data. Therefore, the linear mixed models analysis (random intercepts and fixed coefficients), which incorporated terms for treatment, time, and treatment by time interactions was used to compare PPT scores between groups and one-way ANOVA was used to compare the sensory comfort between the active groups. The level of significance adopted was 5%. Data analysis were performed using the SPSS software (v.17; SPSS Inc; Chicago IL) by an investigator blinded to the division of the groups.

Results

A total of 201 subjects were assessed for eligibility, 81 were excluded and 120 were included and randomized into 4 groups with 30 each. One hundred percent of the included subjects completed the study (Figure 4). The demographics characteristics of the study subjects for each group are reported in Table 1.

Segmental pressure pain threshold

At 15 minutes, there were significant segmental hypoalgesic effects in the TENS (p = .016) interferential (p = .002) and Aussie groups (p = .026) compared to the placebo group. At 30 minutes, there were also significant segmental hypoalgesic effects in the TENS (p = .034), interferential (p < .001) and Aussie groups (p = .023) compared to the placebo group. Twenty minutes post-stimulation, there were no significant

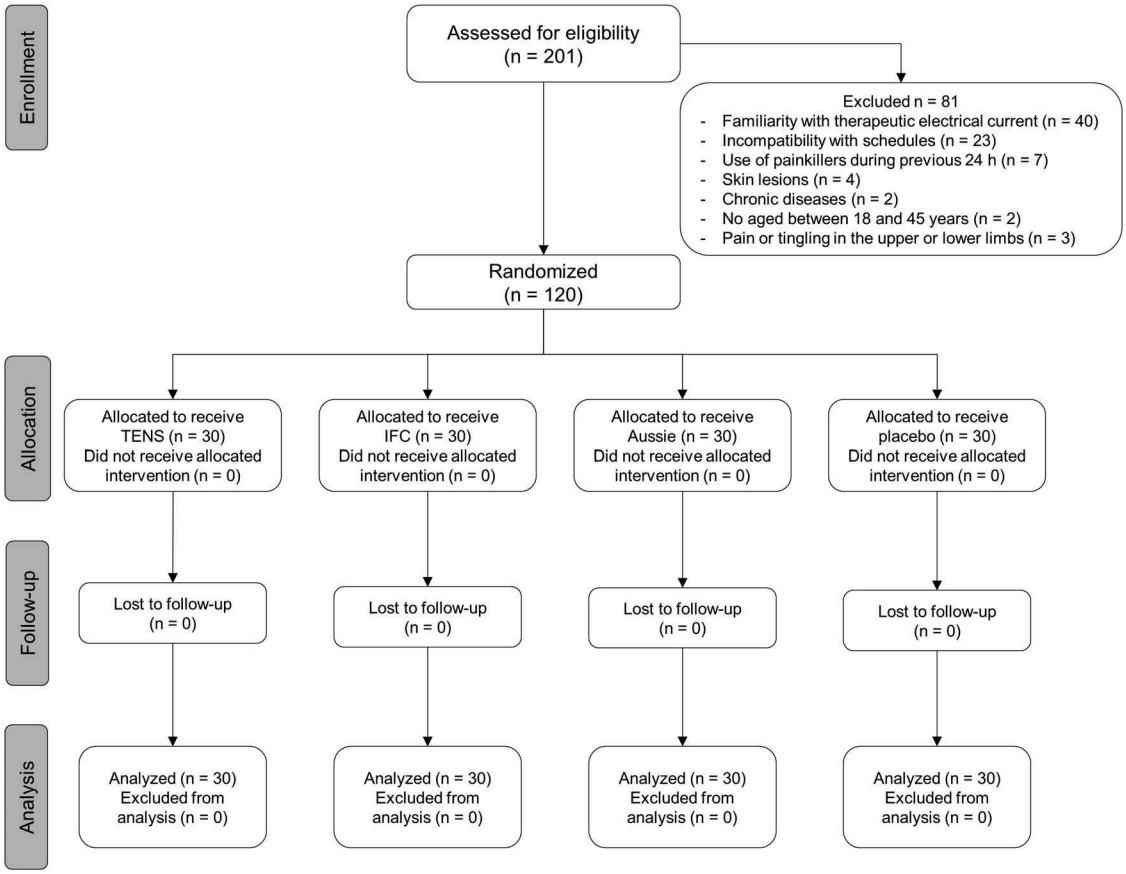

Figure 4. Study design and flow of subjects throughout the study.

Table 1. Demographics characteristics of the subjects for each group.

	Groups			
Characteristics	TENS (n = 30)	IFC (n = 30)	Aussie (n = 30)	Placebo (n = 30)
Sex n (%)				
Male	15 (50%)	15 (50%)	15 (50%)	15 (50%)
Female	15 (50%)	15 (50%)	15 (50%)	15 (50%)
Age, years (Mean ± SD)	23.10 ± 4.67	23.66 ± 4.62	24.03 ± 4.29	22.83 ± 5.11
BMI, Kg/m^2 (Mean ± SD)	23.30 ± 4.40	23.49 ± 3.66	24.59 ± 4.25	23.37 ± 3.74
Ethnicity n (%)				
Caucasian	16 (53.3%)	20 (66.7%)	20 (66.7%)	22 (73.3%)
Others	14 (46.7%)	10 (33.3%)	10 (33.3%)	6 (26.6%)
Education n (%)				
High school or less	0 (0%)	1 (3.3%)	1 (3.3%)	0 (0%)
Some college or above	30 (100%)	29 (96.7%)	29 (96.7%)	30 (100%)
Dominance upper limb n (%)				
Right	28 (93.7%)	29 (96.7%)	29 (96.7%)	29 (96.7%)
Left	2 (6.7%)	1 (3.3%)	1 (3.3%)	1 (3.3%)

TENS: transcutaneous electrical nerve stimulation. IFC: interferential current. BMI: body mass index. SD: standard deviation.

segmental hypoalgesic effects between groups (TENS vs placebo group (p = .657), IFC vs placebo group (p = .265) Aussie vs placebo group (p = .780)). There was no significant difference between active electrical current groups for all time periods: at 15 minutes, at 30 minutes and twenty minutes post-stimulation (TENS vs IFC group (p = .510, 0.167 and 0.119 for all time points respectively); TENS vs Aussie group (p = .849, 0.879 and 0.470 for all time periods respectively); Aussie vs IFC group (p = .396, 0.219 and 0.403 for all time periods, respectively)). Segmental PPT measures (kPa) for all time periods, for each group are reported in Table 2.

Extrasegmental pressure pain threshold

At 15 minutes, there were significant extrasegmental hypoalgesic effects in the TENS (p = .008) interferential (p = .004) and Aussie groups (p = .010) compared to the placebo group. At 30 minutes, there were also significant extrasegmental hypoalgesic effects in the TENS (p = .001), interferential (p = .009) and Aussie groups (p = .006) compared to the placebo group. Twenty minutes after current application, there were significant extrasegmental hypoalgesic effects in the TENS (p = .018), interferential (p = .034) and Aussie groups (p = .030) compared to the placebo group. Similar to the segmental data, there was no significant difference between active electrical current groups for all time periods. Extrasegmental PPT measures (kPa) for all time periods for each group are reported in Table 2.

Sensory comfort

According to sensory comfort, there was no significant difference between the TENS, interferential current and Aussie current (p = .825). The mean values ± SEM were 3.25 ± 0.33 for the TENS group, 2.99 ± 0.38 for the IFC group and 3.30 ± 0.35 for the Aussie group.

Table 2. Between-group differences at 15 minutes and 30 minutes stimulating and 20 minutes follow up.

	Stimulating				Monitoring	
	15 minutes		30 minutes		Follow up of 20 minutes	
Between groups comparison	AMD (95% CI)	p-value	AMD (95% CI)	p-value	AMD (95% CI)	p-value
Segmental PPT measures						
TENS *vs* Placebo	0.06 (0.012 to 0.115)	**0.02**	0.05 (0.004 to 0.107)	**0.03**	−0.01 (−0.063 to 0.039)	0.66
IFC *vs* Placebo	0.08 (0.029 to 0.132)	**< 0.01**	0.09 (0.040 to 0.143)	**< 0.01**	0.02 (−0.022 to 0.080)	0.26
Aussie *vs* Placebo	0.05 (0.007 to 0.110)	**0.02**	0.06 (0.008 to 0.111)	**0.02**	0.00 (−0.044 to 0.059)	0.78
TENS *vs* IFC	−0.02 (−0.068 to 0.034)	0.51	−0.03 (−0.087 to 0.015)	0.17	−0.04 (−0.092 to 0.010)	0.12
TENS *vs* Aussie	0.00 (−0.056 to 0.046)	0.85	−0.00 (−0.047 to 0.055)	0.88	−0.2 (−0.032 to 0.070)	0.47
IFC *vs* Aussie	0.02 (−0.293 to 0.073)	0.40	0.03 (−0.193 to 0.083)	0.22	0.02 (−0.029 to 0.073)	0.40
Extrasegmental PPT measures						
TENS *vs* Placebo	0.06 (0.016 to 0.110)	**< 0.01**	0.08 (0.036 to 0.129)	**< 0.01**	0.06 (0.009 to 0.103)	**0.02**
IFC *vs* Placebo	0.07 (0.021 to 0.115)	**< 0.01**	0.06 (0.016 to 0.109)	**< 0.01**	0.05 (0.003 to 0.097)	**0.03**
Aussie *vs* Placebo	0.06 (0.015 to 0.108)	**0.01**	0.06 (0.019 to 0.113)	**< 0.01**	0.05 (0.005 to 0.098)	**0.03**
TENS *vs* IFC	0.00 (−0.051 to 0.042)	0.845	0.02 (−0.026 to 0.066)	0.402	0.00 (−0.040 to 0.052)	0.80
TENS *vs* Aussie	0.00 (−0.045 to 0.048)	0.944	0.01 (−0.030 to 0.063)	0.485	0.00 (−0.042 to 0.051)	0.84
IFC *vs* Aussie	0.00 (−0.040 to 0.053)	0.80	−0.00 (−0.050 to 0.043)	0.89	−0.00 (−0.048 to 0.045)	0.95

PPT = pressure pain threshold; AMD = adjusted mean difference; CI = Confidence interval; vs = versus TENS = transcutaneous electrical nerve stimulation; IFC = Interferential current; Bold numbers represent significant p value. Data are transformed with log base 10.

Blinding assessment

Investigator 1 correctly identified that subjects received active electrical stimulation in 30% of the cases (27 to 90). He/she also identified that subjects received placebo application of electrical current in 10% (3/30). The rate of blinding in the placebo group was different than chance, indicating successful investigator 1 blinding in this group (Chi-square test, $p < .0001$).

In the placebo group, 13 of 30 subjects correctly identified that they received placebo application of electrical current, 7 thought they received real application of electrical current and 10 did not know. The rate of blinding in the placebo group was no different than chance indicating successful subjects blinding (Chi-square test, $p = .4066$).

Discussion

The aim of the present study was to compare the segmental (forearm) and extrasegmental (lower leg) hypoalgesic effects of TENS, IFC and Aussie current on pressure pain threshold and sensory comfort related to electrical stimulation in healthy subjects. For this, in our randomized placebo-controlled trial, the subjects had no prior experience with electrical stimulation, and they received only one type of electrical current (TENS, IFC or Aussie current), in contrast to other studies that used a cross-over design (Ward, Lucas-Toumbourou, and McCarthy, 2009; Ward, Oliver, and Buccella, 2006). However, we consider that it was important because we had a placebo group and we did not want to compromise the blinding of subjects.

We showed that the TENS (symmetric biphasic pulsed current), IFC and Aussie current have greater segmental hypoalgesic effects when compared to the placebo group during stimulation in healthy subjects. Segmental hypoalgesic effects were not significantly different between active electrical currents.

Some studies have demonstrated that TENS produced higher hypoalgesic effects when compared to the control and/or placebo group during stimulation (Chesterton et al., 2002, 2003; Çıtak Karakaya et al., 2014; Claydon, Chesterton, Barlas, and Sim, 2008) or after stimulation in healthy subjects (Chesterton et al., 2003; Çıtak Karakaya et al., 2014; Claydon, Chesterton, Barlas, and Sim, 2008). These findings differ from our results which did not show the hypoalgesic effects after the stimulation. However, Claydon, Chesterton, Barlas, and Sim (2008) and Chesterton et al. (2003) stimulated the segmental and extrasegmental areas and we only stimulated the segmental area.

Similar to our findings, Johnson and Tabasam (2002) concluded that IFC produced significantly greater analgesia than the placebo group and previous studies failed to identify a difference in the analgesic effects of TENS and IFC in relationship to cold-induced pain, mechanical pain threshold, heat pain threshold and ischemic pain (Alves-Guerreiro, Noble, Lowe, and Walsh, 2001; Cheing and Hui-Chan, 2003; Johnson and Tabasam, 1999, 2003).

In contrast to our results, Shanahan, Ward, and Robertson (2006) concluded that TENS was more effective than IFC at increasing cold pain thresholds in healthy subjects. It is noteworthy that the experimentally induced pain was a different kind than that used in the present study (i.e. ischemic versus mechanical pressure) and this may account for the differences between the observed results.

There are few studies comparing pulsed current to Aussie current. These studies concluded that pulsed current and burst-modulated kilohertz-frequency current appear to be equally effective at elevating the cold pain threshold during stimulation (Ward, Lucas-Toumbourou, and McCarthy, 2009; Ward and Oliver, 2007). Ward, Lucas-Toumbourou, and McCarthy (2009) found that once the electrical stimulation was switched off, thresholds returned close to baseline (Ward, 2009). Our findings are consistent with these authors.

We have not found many studies assessing the extrasegmental hypoalgesic effects of electrical currents. In our findings, TENS, IFC and Aussie current have also presented extrasegmental hypoalgesic effects compared to the placebo group during stimulation in healthy subjects and moreover, this effect was maintained for 20 minutes after stimulation. Chesterton et al. (2002) showed that TENS produced an extrasegmental hypoalgesic effect during the stimulation and was sustained for 30 min after stimulation in healthy subjects, however, different from our parameters, they used low frequency TENS (4 Hz). In contrast, Claydon, Chesterton, Barlas, and Sim (2008) did not show extrasegmental hypoalgesic effects of TENS compared to the placebo group, nevertheless, an extrasegmental hypoalgesic effect was found compared to the control group. Extrasegmental hypoalgesic effects suggest some form of systemic response in line with an endogenous opioid response (Chesterton et al., 2002) and clinically, this is very relevant, because we can consider the use of electrical currents for pain relief in patients with chronic widespread muscle pain (Dailey et al., 2013).

It is important to emphasize that clinically, segmental hypoalgesic effects produced by electrical currents were observed in patients with: chronic low back pain

(Ebadi et al., 2018); temporomandibular disorders (de Lima Ferreira et al., 2017); and cervical myofascial pain (Hou et al., 2002; Rodríguez-Fernández, Garrido-Santofimia, Güeita-Rodríguez, and Fernández-de-Las-Peñas, 2011). Segmental and extrasegmental hypoalgesic effects have been observed in patients with chronic nonspecific low back pain and fibromyalgia (Corrêa et al., 2016; Dailey et al., 2013). Dailey et al. (2013) observed that application of TENS in cervical or lumbar area produced segmental (on spine location of TENS application) and extrasegmental (on the leg outside the site of TENS application) hypoalgesic effects suggesting widespread effects of TENS. Therefore, extrasegmental hypoalgesic effects can be important for treatment of patients with widespread pain.

TENS and IFC are likely to stimulate similar afferent fibers (Cheing and Hui-Chan, 2003). Since both are electrical stimulations applied to the skin, it is likely that their analgesic mechanisms are similar, probably involving the gate control theory and the endogenous descending pain inhibitory system (Cheing and Hui-Chan, 2003). Therefore, we discussed that the segmental hypoalgesic effects during stimulation of TENS, IFC and Aussie current could be explained by gate control theory, activating endogenous inhibitory mechanisms in the central nervous system involving opioid, gamma-aminobutyric acid (GABA), and muscarinic receptors (DeSantana et al., 2008; Johnson, Paley, Howe, and Sluka, 2015; Vance, Dailey, Rakel, and Sluka, 2014). In relation to the extrasegmental hyapoalgesic effect during and after stimulation, it could be explained by release of different endogenous opioids at the level of the spinal cord and the rostral ventral medulla (DeSantana et al., 2008; Liebano et al., 2011). Specifically TENS with frequencies usually greater than 50 Hz, activate δ-opioid receptors (Chandran and Sluka, 2003; Sluka et al., 1999).

In the present study, there was no significant difference in relation to sensory comfort between active electrical current groups. Until now, we have not found a study that has compared sensory comfort between these 3 types of analgesic electrical currents (TENS, IFC and Aussie current). We have found only one study that compared the comfort between Aussie current and TENS in healthy subjects and different from our results, they concluded that the Aussie current was more comfortable (Ward, Lucas-Toumbourou, and McCarthy, 2009). Another study also assessed comfort between 4 electrical stimulations: Russian current, Aussie current, and 2 conventional monophasic PCs (Ward, Oliver, and Buccella, 2006). They found that the AC stimuli (Russian and Aussie currents) were more comfortable than the 2 PC stimuli (Ward, Oliver, and Buccella, 2006). However, in these previous studies, the same subjects received the currents and the subjects rated the Aussie as more comfortable compared to the pulsed current. In the present study, the subjects with no prior experience with electrical stimulation received only one type of electrical stimulation (TENS, IFC or Aussie current). This means that the subjects could not compare, for example, if the TENS was more comfortable than the IFC or Aussie current because they did not receive the application of these currents. It may justify the absence of significance in relation to sensory comfort between the types of electrical currents. The carrier frequency of IFC used in the present study was considered one of the more comfortable carrier frequencies in the study of Venancio et al. (2013), who concluded that the frequencies of 4 kHz, 8 kHz and 10 kHz have been found to be more comfortable compared to the frequencies of 1 kHz and 2 kHz in healthy subjects.

In the present study, we have found statistically significant differences between the active electrical currents groups and the placebo group in relation to segmental and extrasegmental hypoalgesic effects. However, there was no difference between electrical currents. The findings of the present study could only be considered for healthy subjects with mechanically induced pain. We discuss the extrasegmental hypoalgesic effect produced by analgesic electrical currents can be very significant in patients with widespread pain. Nevertheless, we could not directly translate our findings to the clinic because the characteristics of the clinical population may differ from healthy subjects. Therefore, studies comparing the analgesic effects of these electrical currents for clinical pain conditions should be performed.

Conclusion

Segmental and extrasegmental hypoalgesic effects may be achieved using transcutaneous electrical nerve stimulation, interferential or Aussie current in healthy subjects. There was no difference between them. Furthermore, all of them presented a similar sensory comfort.

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Disclosure of Interest

The authors report no conflict of interest.

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