

Influence of Transcutaneous Electrical Nerve Stimulation on Pain, Range of Motion, and Serum Cortisol Concentration in Females Experiencing Delayed Onset Muscle Soreness

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Abstract:

β -Endorphin (BEP) has been implicated in the analgesic response to transcutaneous electrical nerve stimulation (TENS). The anterior pituitary gland is a source of β -endorphin which shares the prohormone proopiomelanocortin (POMC) with adrenocorticotropin (ACTH). Current theory proposes that the stimulation-induced breakdown of POMC results in ACTH release with a subsequent elevation in blood cortisol levels. The purpose of this study was to determine the potential application and mechanism of TENS as an anti-inflammatory agent. Eight female subjects received low frequency, 300 μ sec pulse width TENS at four sites associated with relief of upper arm pain once when pain free and again while experiencing delayed onset muscle soreness (DOMS) of the elbow flexor muscle group. Blood samples were withdrawn 15 and 1 minute before and 1, 20, and 40 minutes after treatment. Serum was analyzed for cortisol by radioimmunoassay. TENS treatment failed to elevate serum cortisol concentration, but there was a significant reduction in perception of pain ($p < 0.05$) and an improvement in range of elbow extension ($p < 0.05$) when subjects were treated for DOMS. These results suggest that the anterior pituitary is not a source of BEP in TENS-induced analgesia.

Article:

The identification of endogenous opioids (17) and the isolation of β -endorphin (BEP) in the 1970s led to new models of stimulation-induced analgesia. Castel (5) proposed that transcutaneous electrical nerve stimulation (TENS) with selected parameters of low frequency and long pulse duration, would result in the release of BEP from the anterior pituitary gland. BEP shares the pro hormone proopiomelanocortin (POMC) with adrenocorticotropin (ACTH) (14, 20, 31) and ACTH subsequently stimulates the synthesis and release of cortisol from the adrenal cortex (15, 31).

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Cortisol is the most prevalent glucocorticoid in man (15). It stimulates gluconeogenesis, promotes glucose utilization, protein synthesis, fatty acid mobilization, and suppresses acute and chronic inflammatory responses (2). The purpose of this investigation was to measure serum cortisol concentrations in response to a 30-minute TENS treatment (pulse rate = 2/sec, pulse width = 300 μ sec, intensity adjusted to maximum tolerance) and to determine the potential application of TENS as an anti-inflammatory modality.

METHODS

Eight female subjects (age = 21.8 ± 1.9 years, height 166.1 ± 5.3 cm, weight = 58.1 ± 7.1 100 kg) were recruited to participate and gave their informed consent in compliance with the University of Virginia's Human Investigation Committee guidelines. None were currently participating in weight training programs or intercollegiate athletics. Each subject participated in an orientation session to become familiar with the investigation protocol and TENS.

To control for the diurnal variation in cortisol release, subjects were scheduled to return to the laboratory in pairs (two subjects each evening) at 1700 h. Following skin preparation, a heparinized needle (21 g) was inserted into the anticubital vein of the dominant arm. The subjects rested quietly or read for 30 minutes at which time a 5 ml sample was withdrawn. The skin was prepared and round, 10 mm diameter electrodes were placed at four sites (TH 14, LI 11, LI 13, LI 14) associated with pain control in the upper arm (33). The subjects rested for 15 minutes after the first sample, when a second 5 ml sample was withdrawn and the TENS treatment started. TENS was applied by a NeuroTech NT-16 (NeuroTech, North Andover, MA) stimulator set to deliver two pulses per second with a pulse width of 300 μ sec and the intensity adjusted to maximal tolerance for 30 minutes (5, 22). Blood samples were withdrawn 1, 20, and 40 minutes after treatment, while the subjects remained at rest. Serum was separated from the formed elements by centrifugation and frozen at -10°C .

Subjects returned 5 days after the first treatment session. A standard goniometer was used to assess elbow joint range of motion. All had normal elbow extension ($> -5^{\circ}$) bilaterally and denied having soreness in the upper arms before exercise. Delayed onset muscle soreness (DOMS) was induced in the elbow flexors through repeated eccentric muscle contractions. Each subject initially lowered a 25-lb dumbbell from full elbow flexion to complete extension over 3 sec. When subjects were unable to control the weight for the full 3 sec, the weight was decreased to 20 lbs. This process continued in 5-lb decrements until the subject could not control 5 lbs or had completed 40 repetitions with 5 lbs. Elbow flexion was done by laboratory personnel to avoid fatigue due to concentric lifting. Subjects were asked to refrain from using analgesic/anti-inflammatory medications, receiving physical therapy or participating in vigorous upper arm exercise for 48 hours.

Forty-eight hours after the exercise bout subjects returned for a second treatment session. The session was identical to the first except that elbow extension was assessed with a standard goniometer and perceived pain was assessed with the pain scale described by Talag (30) (Fig. 1). Blood samples were withdrawn at these times. Subjects were also questioned regarding their compliance with our instructions. All subjects denied using medications, receiving therapy, or engaging in upper body exercises since the experimental exercise bout.

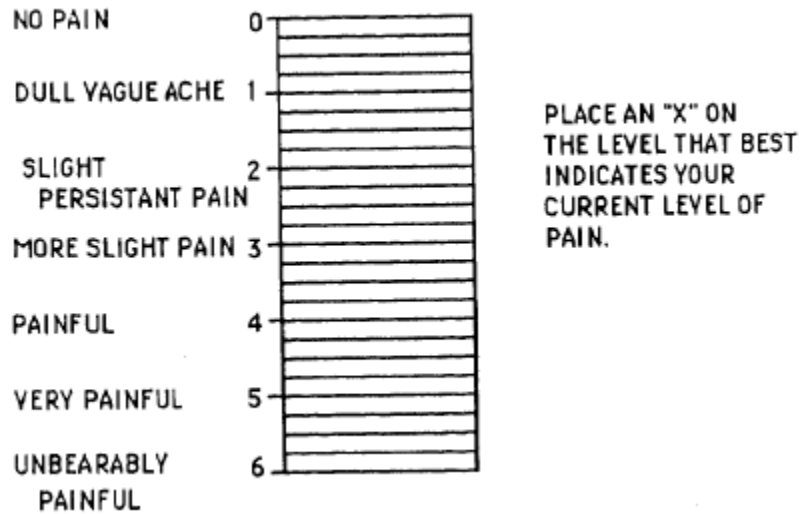


Figure 1: Pain scale described by Talag (30).

Serum samples were analyzed by a solid phase cortisol radioimmunoassay (Cort-A-Count Cortisol, Diagnostic Products Corp., Los Angeles, CA) in a single assay run. Intraassay variability was less than 11% in the range tested.

RESULTS

Serum cortisol concentration did not rise following low frequency, long pulse width TENS (Table 1). Only one subject had post-treatment cortisol concentrations above her pre-treatment level. This elevation was small (188 nmo1/1 at 1, 103 nmol/I at 20, and 52.4 nmo1/1 at 40 minutes after treatment) and occurred only in the pain free state. Five subjects had cortisol levels elevated above normal values for the time of day during the first treatment session. Four had similar levels during their second treatment.

There was a significant decrease in perceived pain following treatment when subjects were experiencing DOMS [$F(4,28) = 4.10, p = 0.01$] (Table 2). There was also a significant increase in elbow extension after treatment (Table 3) [$F(2,28) = 10.82, p < 0.01$]. Post hoc Tukey tests revealed that elbow extension immediately following treatment was significantly greater ($p < 0.05$) than at baseline and that at 20 and 40 minutes after treatment elbow extension was significantly greater ($p < 0.05$) than before treatment.

DISCUSSION

We found that TENS treatment decreased perceived pain and increased elbow extension range of motion, but that cortisol levels did not rise. These data are not consistent with the hypothesis that low frequency, long pulse width TENS-induced analgesia is mediated by BEP released from the anterior pituitary gland.

TABLE 1: Serum cortisol levels (mol/l) before and after treatment in a pain free condition and during delayed onset muscle soreness

(DOMS) (mean ± SD)

	15 min before	1 non before	1 min after	20 min after	40 min after
Pain free	749 ± 370	701 ± 398	646 ± 387	621 ± 434	540 ± 353
With DOMS	551 ± 342	573 ± 426	504 ± 345	462 ± 306	404 ± 261

The failure to elevate serum cortisol concentration in our subjects indicates that neither PMOC nor ACTH were released from the anterior pituitary. The results suggest that the treatment effects were not due to a release of BEP from the anterior pituitary. These findings are in agreement with previous studies that reported TENS analgesia was not reversed by naloxone hydrochloride (1, 7, 13, 24, 25, 32), although none used stimulation parameters identical to ours. Our results do not rule out BEP as an active agent in TENS induced analgesia. However, if BEP is an active agent in TENS-induced analgesia, the source is probably within the brain since BEP does not easily cross the blood-brain barrier (3, 31).

A previous study reported that TENS treatment altered perceived pain in subjects following DOMS, but did not significantly alter elbow extension (11). That study employed a bipolar electrode placement over the site of greatest tenderness and the musculotendinous junction of the biceps with large (250 sq cm) electrodes. In this study, the stimulation of acupuncture sites with smaller electrodes yielded different results. This conflict is not easily explained, but is suggestive of multiple analgesic mechanisms as proposed by others (8) and illustrates the need for continued search for the mechanism(s) of TENS-induced analgesia.

TABLE 2: Perceived pain in the upper arm as measured by the Talag pain scale at each measurement time (mean ± SD)

15 min before	1 min before	1 min after	20 min after	40 min after
3.5 ± .9	3.5 ± .9	2.6 ± 1.1*	2.6 ± 1.1*	2.6 ± .9*

* Post-treatment measures were different ($p < 0.05$) than the pre-treatment measures.

Several investigators have implicated endogenous opioids in electro-acupuncture (EA) and TENS induced analgesia using naloxone hydrochloride challenge studies (6, 16, 23, 26, 28), and direct measurement of BEP levels in plasma (12, 21) and cerebrospinal fluid (10, 27, 29). In 1979 Castel (5) proposed that the anterior pituitary gland was an important source of BEP in low frequency, long pulse width TENS induced analgesia. Elevated levels of ACTH in man (21) and cortisol in horses (4, 9) and rabbits (18, 19) have been reported following low frequency EA.

The elevation of ACTH and cortisol concentrations in animals following EA may represent a generalized stress response rather than a specific response to electrotherapy (7). Animal subjects are unable to anticipate the experimental treatment and would respond to the stress of EA only after the initiation of treatment. The subjects in this study were aware of the experimental procedure and the discomfort of venipuncture and low frequency, long pulse width TENS. The experimental procedure and treatment may have represented a stressor sufficient to elicit an elevation in ACTH and cortisol concentrations for some subjects. Physical and psychological stressors have been reported to elevate blood cortisol levels 20-fold (15); however, the cortisol levels were within 5-fold of normal values in all subjects. In nearly one-half of the trials (7 out of 16) serum cortisol levels were within normal limits for the time of day.

A control group was not employed because we could not justify inducing soreness simply to document the normal course of DOMS in a study directed at measuring blood cortisol responses. Previous work reported that DOMS increases for about 48 hours, decreases slightly (<0.25 on the pain scale) between 48 and 72 hours, and gradually disappears over 5-7 days (30). Other factors, such as a placebo response or the passage of time, cannot be ruled out as contributing to the decrease in pain and increase in elbow extension. We believe that the decrease in reported pain and increase in elbow extension following TENS while subjects had DOMS was primarily due to the TENS treatment.

TABLE 3: Elbow extension (degrees) at each measurement time (mean \pm SD)

15 min before	1 non before	1 min after	20 min after	40 min after
-20.9 \pm 12.7	-19.75 \pm 12.8	-11.5 \pm 10.5*	-8.1 \pm 8.0r	-8.1 \pm 7.8t

* Significantly different from 15 minutes before treatment measure.

t Significantly different < 0.05) from both pre-treatment measures.

CONCLUSION

The low frequency, long pulse duration TENS treatment applied in this study resulted in decreased perceived pain and increased elbow extension range of motion but did not increase serum cortisol concentration. These data do not support TENS as an anti-inflammatory agent. Furthermore, these data are not consistent with the hypothesis that low frequency, long pulse duration TENS-induced analgesia is mediated by BEP released from the anterior pituitary gland. These results do not rule out BEP as an active agent in low frequency, long pulse width TENS-induced analgesia. However, if BEP is active in TENS-induced analgesia, the source is probably within the blood brain barrier.

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