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Relief of Experimentally-Induced Pain by Stimulation at Acupuncture Loci: a Review

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24 recent studies on acupuncture analgesia for the relief of experimentally-induced pain are reviewed. Negative or equivocal results are reported in 7 of these. The remaining 17 (71%) report significant analgesic effects during manual or electrical stimulation (particularly at very low frequencies on the order of 2 Hz) at acupuncture loci. Many investigators note that the full analgesic effect is attained only after about 20 minutes of stimulation. Further investigation of the analgesic effects of stimulation at acupuncture loci, particularly the effect of very low frequency electrical stimulation, is fully warranted by these preliminary findings.

INTRODUCTION

There has been an immense resurgence of interest in acupuncture since its re-introduction to the West in 1972, resulting in many reports and evaluations of its effectiveness as well as textbooks describing its practical applications [1–9]. However, the practice of acupuncture is not the novelty it may now appear. It was first introduced to Western medical practice no later than the seventeenth century [10] and remained in occasional use throughout the nineteenth [11–13].

At first glance, the mere idea that pain can be alleviated by insertion and manipulation (whether by rotation or electrical stimulation) of a fine needle into some designated point on the surface of the skin is outrageous. But on second thought, this is no more unrealistic a concept than the rationale for the use of dorsal column stimulators for the relief of chronic intractable pain. The best argument for examining it more closely is that it does work.

Many explanations for the efficacy of acupuncture therapy have been proposed. Most predicate a mode of action related in some way to the nervous system [14–20] some postulating modified gate control theories [21–25]. Other hypotheses are based upon the physiological effects of histamine release at the needle insertion site [26], bioholographic information processing systems [27], or hypnosis [28–30], although differences have been reported between the effects of hypnosis and acupuncture analgesia [31,32]. It has been suggested that acupuncture may operate through a combination of several factors, including its effect on the nervous system and such psychophysiological effects as are associated with all treatment modalities [33–35].

Some investigators state that the acupuncture network has no relationship to the anatomy of the peripheral nervous system [36], but others have noted that many acupuncture loci correspond to concentrations of sensory receptors [37–39]. Levy and Matsumoto reported that an intact nervous system was a necessary prerequisite for effective acupuncture analgesia in rabbits [40].

The best results in acupuncture therapy are obtained when the patient experiences a feeling of "warmth" or "heaviness" (unlike paresthesia) upon manipulation of the needles. As a consequence, his cooperation is needed to assure optimal placement of

the needles. This leads to self-evident difficulties in the design of a truly double-blind study, although these might be partly countered by the use of electroacupuncture rather than the traditional manual stimulation [41,42]. It would seem, however, that the fundamental question of the physical reality of the acupuncture system and its mode of action should be studied before attempting an evaluation of its possible clinical applications.

While many of the early reports from the People's Republic of China were primarily anecdotal in nature, there is a growing literature concerning the analgesic effects of acupuncture treatment. Relief of pain in a clinical situation necessarily includes a major uncontrollable variable: the patient's own evaluation of the intensity of his pain. While this subjective factor is also present during an experimental procedure, the intensity of a painful stimulus can be measured and used in the data analysis. There exists the possibility that experimentally-induced pain, for which the subject is in some sense prepared, is not qualitatively equivalent to actual somatic pain, but the advantage of using a controlled stimulus outweighs the disadvantages of an artificial setting. We propose, therefore, to review the reported analgesic effects of stimulation at acupuncture loci on experimental pain thresholds.

THERMAL PAIN

Several reports have appeared on the effects of acupuncture stimulation on thermal pain thresholds in human subjects, generally measured with a Hardy-Wolf-Goodell dolorimeter [43].

Berlin et al. reported that 120 Hz electrical stimulation lasting for 20 minutes at two traditional acupuncture loci[1] (ho-ku, on the dorsum of the hand, and wai-kuan, on the distal forearm) was somewhat more effective in increasing endurance to a painful thermal stimulus on the forearm in 30 subjects than stimulation at non-acupuncture sites [44].

Croze et al. studied the effect of manual stimulation at acupuncture and non-acupuncture loci on burning pain thresholds. Steel needles were inserted into loci shou-san-li (near the knee) and zu-san-li (on the volar surface of the forearm) and rotated for 3–10 seconds every 2 minutes for a total of 40 minutes. The non-acupuncture sites were treated similarly. In 4 out of 8 subjects, acupuncture treatment had no effect. In other 4 subjects, there was a significant increase in pain threshold during stimulation at the acupuncture loci, reaching a maximum analgesic effect some 20 minutes after onset of stimulation. There was a smaller increase for nearby non-acupuncture loci, but no increase during stimulation at distant non-acupuncture

[1]There is no universal agreement on nomenclature for the acupuncture loci. Some investigators use the traditional Chinese names, while others follow the system used by Mann [6], denoting the loci by their relative positions on the various meridians. Thus the ho-ku locus, on the dorsum of the hand, is also called Li-4, as it is the fourth most distal locus on the Li (large intestine) meridian. In each case, we have attempted to follow the terminology used by the authors.

Results of experimental studies (only those reports in which the nature of the acupuncture stimulus used was noted are included). The efficacy of very low frequency (2 Hz) electrical stimulation at the ho-ku point (Li-4) in producing dental analgesia is demonstrated in several reports [57,58,60,64], although higher frequency stimulation induced sufficient analgesia to permit tooth extraction in one case [62]. It appears that low frequency electrical stimulation is generally more effective than either manual or high (on the order of 100 Hz) frequency stimulation. Not enough information is presently available about the detailed stimulus characteristics (pulse shape, duration, and polarity; duration of treatment, etc.) to determine the most effective electrical stimulus parameters.

[2]A total of six subjects were tested in this study. One received electrical stimulation and three manual stimulation at the ho-ku locus. For the other two subjects, an acupuncture needle was placed at the ho-ku locus and left *in situ* throughout the experiment. Significant analgesia was obtained for only one subject, but it is not noted which of these three treatments

Table I

Reference	Pain Stimulus	Acupuncture Stimulus	Number of Subjects	Results[3]	Comments
66	Immersion in ice water (hand)	Electrical - DC	30	+	
46	Thermal - (neck and chest)	Electrical - 3 Hz at Li-4, GB-21, TB-8, and Li-14	4	-	
48	Thermal (various locations)	Electrical - 2.5 Hz	12	+	
55	Thermal (back of hand)	Electrical - 2 Hz at various hand and arm points	8	+	
57	Dental pulp tester	Electrical - 2 Hz at Li-4 (ho-ku)	30	+	Total duration of the test was 60 min; the full analgesic effect was attained after 20 min.
58	Dental pulp tester	Electrical - 2 Hz at Li-4	34	+	
60	Dental pulp tester	Electrical - 2 Hz at Li-4	30	+	20 min. induction time for full effect
64	Dental pulp tester	Electrical - 2 Hz at Li-4	42	+	
65	Electrical stimulus	Electrical - 3-10 Hz	108	+	
58	Dental pulp tester	Electrical - 10 Hz	34	±	Some analgesic effect effect was noted, but electrical stimulation at 10 Hz was not as effective as 2 Hz
61[2]	Dental pulp tester	Electrical - 30 Hz at Li-4	1	?	
63	Dental pulp tester	Electrical - 5 Hz	12	-	
44	Thermal (forearm)	Electrical - 100 Hz at ho-ku and wai-kuan points	30	+	Electrical stimulation at real acupuncture points is more effective than at placebo points in inducing analgesia
53	Thermal	Electrical - 88 Hz	12	-	The authors ascribed the observed analgesic effect to purely subjective factors
58	Dental pulp tester	Electrical - 100 Hz	34	-	An analgesic effect of very short duration was observed
62	Dental - for tooth extraction	Electrical - 180 Hz at Li-4 and St-44	1	+	The subject remained sensitive to pressure and heat but not pain; the analgesic effect persisted for 12 hours
45	Thermal (thenar eminence)	Manual - 2 Hz at shou-san-li and zu-san-li	8	±	A significant analgesic effect was observed in 4 of 8 subjects
61[2]	Dental pulp tester	Manual at Li-4	3	?	
70	Ischemic pain	Manual - 2 Hz	25	+	Stimulation at real acupuncture points is more effective than control stimulation
72	Electrical stimulus	Manual - 2 Hz at Li-4 and EH-6	12	+	Stimulation at real points is more effective than placebo stimulation
73	Electrical - near supraorbital nerve	Manual at Li-4 and other points	14	-	
61[2]	Dental pulp tester	Acupuncture needles placed at Li-4	2	?	
69	pain, touch, and vibration	Needles in situ at acupuncture and other knee points	40	+	

was effective.

[3]+: significant analgesic effect; —: no significant effect which could be attributed to acupuncture; ± : equivocal results (these are described under "comments"); ? : results not given.

loci [45].

In a study of pain perception and galvanic skin resistance in 4 subjects, Day et al. found that electroacupuncture (0.2 msec unidirectional pulses, frequency 3 Hz) lasting for 60 minutes had no effect on either parameter [46].

Haider et al. studied the effect of electrical stimulation at acupuncture loci (including Li-14 on the upper arm and P-6 on the distal forearm) and non-acupuncture areas on thermal pain in 16 subjects. The stimulation was applied for a total of 20 minutes. They reported that both treatments increased pain thresholds, but the former was more effective [47]. Stewart et al. used low frequency (2.5 Hz) electrical stimulation at acupuncture and placebo loci and found a significant increase in thermal pain thresholds for the former [48].

Some investigators have utilized signal detection theory as a means to separate the objective (measured intensity of the painful stimulus) from the subjective (the patient's report of his sensation) effects by measuring the discriminability of the sensation [49,50]. In theory, effective analgesia reduces the subject's ability to discriminate between varying stimulus intensities. It has been suggested, however, that signal detection analysis may not be entirely applicable to studies of acupuncture or indeed any form of analgesia. In particular, it can measure only differential, not absolute pain sensitivity [51]. Furthermore, it is logically possible that true analgesia could result only in reduced absolute sensitivity to pain, with no accompanying decrease in differential sensitivity [52].

Clark and Yang used signal detection theory in the analysis of thermal pain thresholds on 12 subjects during 88 Hz electrical stimulation at acupuncture loci. They reported that the experimental pain threshold was increased during treatment (which lasted for 15–20 minutes), but concluded that the effect was purely subjective in nature [53]. The methodology of this study has been criticized on the grounds outlined above [51,52,54].

Lloyd et al. analyzed thermal pain thresholds on the dorsum of the hand during 2 Hz electrical stimulation at two acupuncture loci, one on the hand and one near the elbow. Signal detection analysis of the results indicated that acupuncture treatment increased pain thresholds in a total of 8 subjects [55].

DENTAL PAIN

As Brennan and Bowman have noted, stimulation of tooth pulp, whether electrical, mechanical, or thermal, produces a relatively pure pain sensation. In addition, the stimulus can be accurately controlled and measured. The pain threshold, while varying considerably between subjects, is highly reproducible for each individual [56].

Several studies have been conducted on the effects of stimulation at acupuncture loci for the relief of dental pain, notably by Andersson et al. In a preliminary report, they stated that electrical stimulation at point Li-4 (dorsum of the hand) and other points in the area of the infra-orbital nerve significantly increased pain thresholds in 30 subjects. The analgesic effect reached a maximum about 30 minutes after the onset of stimulation, slowly declining over 30 minutes upon cessation [57]. Surface electrodes were more effective than subcutaneous electrodes, and low frequency constant current stimulation (2 Hz) was more effective than higher frequencies (10 Hz, 100 Hz) in inducing analgesia [58]. Omura [59] has also noted that longer-lasting effects are obtained with very low frequency electrical stimulation. Further tests showed that a fairly strong stimulus was needed for any significant increase in pain threshold [60].

Brennan and Veldhuis, in a pilot study on 5 subjects, found that a degree of analgesia sufficient to permit dental procedures was achieved in only 1 subject. Both

manual and 30 Hz electrical stimulation at the ho-ku locus were used, but it was not noted which of these was successful [61]. On the other hand, Bresler reported that 180 Hz electrical stimulation at acupuncture loci Li-4 and St-44 (dorsum of the foot) produced sufficient analgesia after 30 minutes to permit the subjects to undergo tooth extraction [62]. Only pain thresholds were affected; the teeth remained sensitive to heat, cold, and pressure, and the unattached gingiva were sensitive to painful stimuli [62].

Stich, in a study on 12 subjects, compared the effects of 5 Hz electrical stimulation at acupuncture loci, morphine, and local anesthetics (such as novocaine) on dental pain thresholds. He reported that only the latter resulted in any significant increase in pain threshold [63]. Chapman et al. compared 33% nitrous oxide inhalation with 2 Hz electrical stimulating lasting for 20 minutes at locus Li-4 for the relief of dental pain in 42 subjects. Signal detection analysis was used in an attempt to separate the subjective from the objective variables. The results indicated that both treatments produced increases in response bias as well as reduced pain sensitivity [64].

Umlauf compared the effect of both manual and electrical stimulation (about 3–10 Hz) at acupuncture loci to placebo in 108 subjects. Both treatments induced a significant analgesic effect after 15 minutes of stimulation [65].

OTHER STUDIES

Anderson et al. reported that DC electrical stimulation for 15 minutes at acupuncture loci Li-5, Li-11, Si-5, and Si-8 on the forearm reduced sensitivity to pain due to immersion of the hand in ice water, but stimulation at non-acupuncture sites or control conditions had no effect. There were 10 subjects in each treatment group [66].

Baum tested the effects of stimulation at acupuncture and non-acupuncture loci on a painful sensation (pressure on the throat), and found no differences between the two treatments in 11 of 15 subjects [67]. Lynn and Perl studied the effects of electrical stimulation on pinch pain thresholds in 18 volunteers, and found elevated pain thresholds during treatment [68]. Man and Barager reported that insertion of needles into several acupuncture sites near the knee resulted in a marked decrease in pain sensitivity, while similar treatment at non-acupuncture points had no demonstrable effect. A total of 40 subjects were tested [69].

Smith et al. compared the effects of morphine, placebo, and manual stimulation at acupuncture loci for the relief of ischemic pain. Treatment at the acupuncture loci was consistently more effective than treatment at non-acupuncture sites or placebo, and as effective as morphine except for pain rated as "unbearable" by the 25 subjects [70,71].

Stacher et al. tested 12 subjects, and found that manual stimulation at loci Li-4 and H-6 (ventral wrist) for 16 minutes reduced pain due to electrical stimulation in the region of the thyroid. Stimulation at non-acupuncture points had a lesser effect [72]. Li et al. studied pain due to electrical stimulation near the the supraorbital nerve during hypnosis, manual stimulation (lasting for about 30 minutes) at several hand and foot loci, and control conditions in 14 volunteer subjects. The experimental pain threshold was increased under hypnosis, but not significantly increased during either real or placebo acupuncture [73]. Saletu examined pain due to electrical stimulation at the wrist during hypnosis, real and placebo acupuncture, morphine and ketamine analgesia, and control conditions. Stimulation at non-acupuncture loci had no effect, but all of the other treatment modalities yielded significant increases in experimental pain thresholds. EEG recordings from subjects under hypnosis showed increases in the slow beta and decreases in the alpha and beta waves. Stimulation at acupuncture loci had the opposite effect on the EEG [32].

CONCLUSION

Of a total of 24 studies on acupuncture analgesia for the relief of experimentally-induced pain, 3 reported unequivocally negative results. Of these, two utilized low frequency electrical stimulation [46, 63] and one used manual stimulation [73]. An additional 4 studies had equivocal results: Baum reported that acupuncture was not effective in relieving pain for 11 of 15 subjects [67]; Brennan and Veldhuis found that effective dental analgesia could be produced in only 1 out of a total of 5 subjects [61]; Croze et al. found that manual stimulation at traditional acupuncture loci significantly increased thermal pain thresholds in 4 out of 8 subjects [45]; Clark and Yang reported increased pain thresholds in 12 subjects during acupuncture treatment, but concluded that the effect was purely subjective [53].

The remaining 17 reports demonstrated significant analgesic effects during electrical or manual stimulation at acupuncture loci. In only 2 studies were successful results achieved with electrical stimulation of frequencies on the order of 100 Hz [44, 62]. Most utilized manual stimulation [45,65,70–72], DC electrical stimulation [66], or very low frequency AC stimulation (on the order of 2 Hz [48,55,57,58, 60,64]. An induction time of about 20 minutes for full analgesia was noted by several investigators [45,57,58,60,62].

Further investigation of the analgesic effects of stimulation at acupuncture loci, particularly through manual or very low frequency electrical stimulation, appears to be justified by the preliminary findings. In our opinion, carefully controlled studies under laboratory conditions hold the most promise for elucidating the effects and physiological mechanisms of acupuncture analgesia, and would be indispensable in evaluating its possible clinical applications.

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