

EVALUATION OF THE PAIN SUPPRESSIVE EFFECT OF DIFFERENT FREQUENCIES OF PERIPHERAL ELECTRICAL STIMULATION IN CHRONIC PAIN CONDITIONS

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The pain suppressive effect of low (2/s) and high (50-100/s) frequency electrical stimulation was studied in 12 patients with severe chronic pain in the back and/or the legs. All patients were subjected to a thorough physical examination before and 2-3 weeks after a series of stimulation sessions. The stimulation was applied via surface electrodes to areas both segmentally related and segmentally unrelated to the regions of chronic pain. Low frequency stimulation induced a partial pain relief in only one patient whereas stimulation with high frequency gave a suppression of pain in seven patients. The effect was short-lasting in most cases and the pain started to increase usually within 30 min. It is concluded that the observed pain suppression is not due to psychological factors but to more basic neurophysiological mechanisms. Augmentation of the effect after repeated stimulation sessions was not observed, neither was there any alteration in the neuro-orthopedic status nor any lasting pain relief in any patient.

Key words: pain; intractable pain; analgesia; electric stimulation; acupuncture

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The treatment of chronic pain conditions still constitutes a serious clinical problem since a causal therapy is often not available. In many cases the etiology of severe pain is difficult to understand largely because of our sparse knowledge of the basic mechanisms of pain itself. Methods involving electrical stimulation of peripheral structures have been reported to abolish or diminish the sensation of pain. *High frequency* stimulation (50-200/s) applied to painful areas or the corresponding afferent nerves seems to re-

lieve pain in certain cases (Wall & Sweet 1967, Meyer & Fields 1972). The contribution of "unspecific", psychological factors is difficult to evaluate but basic, physiological mechanisms interacting with the perception of pain are also supposed to be involved. Thus, stimulation of central nervous structures, such as the dorsal columns, via implanted electrodes has been tried in patients suffering from intractable chronic pain, with success in many cases (Shealy et al. 1970, Miles et al. 1974).

The interest in the pain suppressive effects of peripheral conditioning stimulation was reinforced by reports made by visitors to The People's Republic of China who claimed that *low frequency* electrical or mechanical stimulation may result in relief of acute pain also (Holmdahl 1973, Kerr 1973, Kaada et al. 1974). Electrical stimulation or manipulation of needles in various, often precisely defined, areas or points was said to suppress acute surgical pain totally or partially to the extent of allowing major surgery. This type of stimulation is supposed to suppress chronic pain also (Mann et al. 1973).

These clinical observations are of interest in relation to studies which have shown that low frequency (2/s) electrical conditioning stimulation results in an increase of the pain threshold in teeth (Andersson & Holmgren 1975, Andersson et al. 1975 a, b). During stimulation the pain threshold increased gradually and reached its maximum after 15–30 min with an average increase of two to three times the prestimulation control value. The pain threshold declined slowly to the control threshold in the post-conditioning period. Stimulation of the infra-orbital region changed the pain threshold similarly in both the upper and lower jaw and essentially the same results were obtained regardless of whether the electrical stimulation was given via needle or surface electrodes. High frequency stimulation (100/s) gave, however, only a transient increase of the pain threshold closely related to the stimulated afferent nerves (Andersson et al. 1975 b).

The aim of the present study was to compare the effects of low and high frequency stimulation in the same individuals, suffering from long-lasting severe pain, with regard to the following specific questions: Can pain relief be obtained? Is the effect segmentally related to the location of the conditioning stimulation? Do repeated sessions give any

“cumulative effects”? Do these types of stimulation give any serious adverse reactions in chronically ill patients?

MATERIALS AND METHODS

Subjects

Patients suffering from severe chronic back and/or leg pain were selected from the open ward of the Department of Orthopedic Surgery II at Sahlgren Hospital in Göteborg, without any primary regard as to the underlying cause of the pain. Twelve patients, seven women and five men, 37–73 years old, were asked to participate in the study and all accepted. The patients were informed individually of the general procedure and were told that the aim was to investigate if electrical stimulation could influence their pain but positive suggestions were avoided. The case history and actual pre-stimulation neuro-orthopedic status were thoroughly and independently investigated by two of the authors (G.H. and O.R.). They re-examined the patients 2–3 weeks after the last stimulation session. The underlying disorders varied considerably although no malignant diseases were represented. Only a few of the patients showed signs of neurological impairment. In nine of the patients one to three myelographies had been performed. In nine of the patients one or several operations aimed at relieving the pain disorder had been performed, including five explorations because of a suspected lumbar disc protrusion, of which only two could be verified. The posterior branches of sacral nerves had been resected in six patients. All patients had been treated with chemical analgesics and physiotherapy and in several cases nerve blockades by injection of local anesthetics had been tried, in particular as tests before nerve resections. In spite of these treatments a condition of chronic, severe pain persisted which usually had prevented the patients from doing ordinary work for some years.

Stimulation procedures

The stimulation sessions were performed at the Department of Physiology and started within one week of the orthopedic examinations. The stimulation was performed by two of the authors (S.A. or E.H.) or by an assistant under their direct supervision. The same type of transcutaneous stimulator was used as in previous studies (Andersson et al. 1975 a), i.e. a square wave stimulator with several transformer isolated outputs giving pulses of 0.2 ms duration. The stimulation was applied via surface elec-

trodes with a contact area of about 4 cm². Repeated stimulation sessions were performed with intervals of one or a few days. In the first eight patients the low frequency stimulation (2/s) was presented in the first sessions and high frequency stimulation in the later sessions; in the last four patients this order was reversed. In the same session either low or high frequency stimulation was performed although different high frequencies (50–100/s) were often tried. Each stimulation session lasted for about 1 hour including a short pre-stimulation interview. The patients were free to use their ordinary analgesics on the days between the sessions but were asked not to take any drugs during the hours prior to the stimulation to avoid an interactive effect between stimulation and drugs.

Low frequency stimulation was usually performed with 2–4 pairs of electrodes. The stimulation was applied to areas segmentally related as well as unrelated to the region of pain. Thus, in patients with low back pain radiating into one leg, electrodes were applied to the paravertebral lumbar region and to the painful leg but also to the other leg and to the hands. The electrodes were placed over large nerves such as the sciatic, femoral and peroneal nerves and also in areas overlying large muscle bellies. The intensity of the stimulation was increased gradually during the session and adjusted to the maximum level which the patient could accept with regard to the discomfort from the heating sensations and muscle twitches produced.

During high frequency stimulation the electrodes were usually placed over the painful areas or over peripheral nerve trunks innervating such areas. The intensity was gradually increased to the level just below that tolerated by the patient. The stimulation induced a sensation of intense vibration or paresthesia, and fasciculations or tetanic contraction of muscles were frequently observed. If pain relief was obtained the intensity was kept constant or slightly reduced during the stimulation period which lasted about 15 min.

Personality tests

All patients were tested with standardized personality inventories. The psychasthenic-sthenic (validity) and hysterical-nonhysterical (solidity) character variance was evaluated with the MNT-scale (Marke & Nyman 1958) and the characters of neuroticism and extra-introversion with the Swedish form of Eysenck Personality Inventory (Bederoff-Petersson et al. 1971).

Evaluation and scoring of effects

Since pain is a subjectively experienced phenomenon the main estimation of the effect of the electrical stimulation had to be made by the patients and reported to the investigators. In addition the patient's behavior including body movements and facial expressions were observed and related to the verbal reports. No physical examinations were performed in connection with the stimulation sessions. The effects of conditioning stimulation, summarized in Tables 1 and 2, were scored as follows:

Degree of pain relief was noted as no effect – weak – fair – good – very good, where “very good” corresponds to a complete abolition of pain. *Distribution of effect* was noted as “partial” if the pain was relieved from some parts of the painful area and as “general” if the pain was relieved in the whole region. *Post-stimulation duration* indicates the period between the discontinuation of the stimulation and the start of pain increase after a pain reduction. *Reproducibility* indicates similarity in effects at repeated sessions. *Adverse effects* notes all disturbances reported by the patient as due to the stimulation.

These aspects of the effects and the results of the physical re-examination were summarized as the *Evaluated effect*, which was ranged as no effect – weak – fair – good – very good. “Weak” indicates the report of minor changes such as “pleasant warmth” although the effect on the pain as such was very uncertain. “Very good” indicates a total pain abolition of a general distribution and with a post-stimulation duration of at least 1 hour. “Good” indicates a substantial pain relief although either a subtotal abolition, a partial distribution of the effect or a short post-stimulation duration did not justify the score “very good”. “Fair” denotes a significant, although less strong and often variable effect.

RESULTS

Effects of low frequency (2/s) stimulation

The results obtained with conditioning stimulation of 2/s are summarized in Table 1. All patients were stimulated at several, usually 3–12, sessions. The pain relief obtained using this frequency was reported to be weak or non-existent in all cases except one. During the stimulation some patients experienced “a pleasant sensation” or “a pleasant distraction”

Table 1. Effect of 2 Hz conditioning

Subj. no.	Number of sessions	Degree of pain relief	Distribution of effect	Post-stimulation duration
1.	23	weak	partial	~ ½ day
2.	12	weak	partial	~ ½ hour
3.	11	weak	partial	~ ¼-½ hour
4.	11	weak	probably general	1-2 hours
5.	5	weak	probably general	~ ¼-½ hour
6.	3	none	—	—
7.	6	weak	probably general	¼ hour
8.	5	none	—	—
9.	4	weak	partial	—
10.	1	none	—	—
11.	2	good	partial	~ 2 hours
12.	3	weak	general	0

either at the electrode sites or more generally. Although the patients often interpreted this type of sensation as a "weak" pain relief when it first was experienced, it became apparent after repeated stimulation sessions, when the patients looked more critically away from the distraction produced by stimulation as such, that the underlying pain sensation was unchanged. No tendency to a cumulative effect appeared at repeated stimulation sessions. No serious adverse effects appeared during the stimulation sessions or were reported to have appeared in the intersessional days.

An important adverse effect, which to some extent restricted the applicability of the method in these patients, however, was the tendency for increased local tenderness when the stimulation was applied to the painful areas. During stimulation the intensity was increased to the level which the subject could just tolerate and efforts were made to increase the intensity successively. It was only possible in exceptional cases to reach intensities corresponding to those required to induce a pain threshold increase in healthy subjects (Andersson et al. 1975 b, Holmgren 1975) when the stimulation

Table 2. Effect of 50-100 Hz conditioning

Subj. no.	Number of sessions	Degree of pain relief	Distribution of effect	Post-stimulation duration
1.	3	good	partial	0-few min
2.	7	good - very good	general	few min
3.	3	none	—	—
4.	5	weak	probably general	0
5.	4	fair	partial - general	few min - ½ hour
6.	3	none	—	—
7.	4	good	partial - general	few min - 1 hour
8.	3	weak	probably partial	0
9.	8	very good	partial	few min
10.	7	very good	general	2-8 hours
11.	4	good	partial	few min - ½ hour
12.	6	weak	general	0

stimulation on severe, chronic pain

Reproducibility	Cumulative tendency	Adverse effects	Evaluated effect
yes	none	Followed by tiredness.	weak
yes ²	none	Followed by tiredness, dry mouth.	weak
yes	none	Followed by slight myalgia.	weak
yes	none	Followed by tiredness and slight incoordination in hands.	weak
yes	none	Sometimes followed by increased pain.	weak
yes	none	Local tenderness.	none
yes	none	Often followed by pain increase.	weak
yes	none	None	none
weak	none	None	weak
?	?	Followed by beating sensation in legs.	none ?
yes	none	Occasional muscle spasms.	good
yes	none	None	weak

was applied in or close to regions of pain. It was, however, often possible to stimulate with higher intensities in segmentally unrelated areas (for example bilaterally in the hands in cases of low back pain). No additional pain blocking effect could be obtained by such non-segmental stimulation. Only in one case (No. 11) was a more substantial pain relief found by the 2/s stimulation. In this patient the experience of a dull, intense pain in the legs and the intense hyperesthesia around skin scars became markedly depressed a few minutes after the start of the conditioning stimulation

and during a post-stimulation period of about 2 hours. These effects were well reproducible even during repeated stimulations performed by the patient himself at home.

In summary: In this series of patients with severe chronic pain 2/s conditioning stimulation induced obvious effects on the pain in only one out of 12 subjects.

Effects of high frequency (50-100/s) stimulation

The effect of high frequency stimulation is summarized in Table 2. All pa-

stimulation on severe, chronic pain.

Reproducibility	Cumulative tendency	Adverse effects	Evaluated effect
yes	none	None	good
yes	none	Followed by weak paresthesia.	good
yes	none	Followed by slight local back tenderness.	none
yes	none	Unpleasant vibratory sensation.	weak
variable	none	100 Hz "tearing".	fair
yes	none	Sometimes followed by increased pain.	none
yes	none	Occasional radiating pain.	good
yes	none	None	weak
yes	none	None	good
yes	none	Occasional muscle spasms.	very good
yes	none	Occasionally pain switched to opposite leg.	good
yes	none	None	weak

tients were stimulated at several (3–8) sessions, and the conditioning stimulation was often repeated several times during each session sometimes with different frequencies within the high frequency range. The effect of high frequency stimulation on the pain was quite different as compared to that of a frequency of 2/s. A marked pain relief was achieved in seven of the patients within one or a few minutes when stimulation was applied to the painful areas or to areas overlying nerves innervating the regions of pain. Three patients experienced, at repeated sessions, a total suppression of a very intense pain. Within minutes after the onset of the stimulation, the perception of pain was abolished and the patients could lie quietly with a relaxed facial expression, only experiencing the buzzing sensation of the stimulation. In four patients a “fair” to “good” pain relief was achieved, i.e. depression of the pain was judged as significant although not total. The distribution of the pain relief was closely related to the region innervated by the stimulated nerves. In patients with a wide distribution of pain it was often difficult to suppress the pain in the entire painful area. In five patients the pain was not influenced by the high frequency conditioning stimulation, although the stimulation procedure was the same as in the responsive patients. The post-stimulation duration of the effect varied between individuals but the effect persisted after stimulation in all responsive subjects. In three patients the after-effect varied between a few minutes and 30 to 60 min and in one subject it lasted several hours. The reproducibility of the pain-relieving effects was good. Any cumulative tendencies such as increasing pain suppression or more long-lasting effects were not observed. Most stimulations were performed with 50/s or 100/s. These frequencies essentially induced the same subjective sensations

and pain relief. In some patients 10/s and 25/s were also used. The pain relief given by these frequencies was reported to be less than with the higher frequencies.

No serious adverse effects were reported. Occasionally, increased, short-lasting, radiating pain was evoked by the stimulation. Some patients with pronounced pre-stimulation tenderness or muscle rigidity reported a slightly increased tenderness and rigidity during the post-stimulation periods, although pain relief was reported during the stimulation. In no case did such symptoms last until the next day.

In summary: High frequency segmental stimulation induced pain relief in seven out of 12 patients with severe chronic pain.

Relation between pain relieving effects and psychological factors

No obvious relation was found between the pain relief during the high frequency conditioning stimulation and any of the personality traits tested. The small number of patients does not allow a statistical evaluation. It should, however, be mentioned that a subgroup of four patients characterized by subvalidity, corresponding to a psychasthenic personality, in combination with a relatively high degree of suggestibility (subsolidity) did not differ with regard to pain relief from the test group as an entity.

Orthopedic re-examinations

At the interview and physical examination 2–3 weeks after the last stimulation session, the patients gave essentially the same report on the subjective sensation and the effect on the perception of pain as reported during the stimulation sessions. In no case was there any lasting improvement of the basic pain condition, neither was any alteration of the neuro-orthopedic status observed.

Table 3. Effect of electrical conditioning stimulation on severe, chronic pain.

No.	Subject		Stim. freq., 2 Hz				Stim. freq., 50-100 Hz			
	Sex	Age (years)	non-exist. or weak	fair	good	very good	non-exist. or weak	fair	good	very good
1	♀	63	×						×	
2	♀	45	×						×	
3	♂	45	×				×			
4	♀	46	×				×			
5	♀	51	×					×		
6	♀	39	×				×			
7	♂	48	×						×	
8	♀	53	×				×			
9	♀	37	×						×	
10	♂	58	×						×	
11	♂	59			×				×	
12	♂	73	×				×			

DISCUSSION

The effects of stimulation with low and high frequencies are summarized in Table 3. The reports of "a feeling of warmth" or "pleasant sensation" should be considered as a distraction which also became evident to the patients after repeated sessions. Such distractory phenomena are indicated as "no effect" in Table 3. No serious adverse effects of either low or high frequency stimulation were reported, neither did the physical re-examination disclose any impairment or improvement of the neuro-orthopedic status. Some patients complained of slight disturbances such as tiredness, myalgia or increased tenderness, but some of these effects may have been due to traveling to the laboratory rather than to the stimulation itself.

The results show that the possibility of suppressing severe chronic pain is markedly related to the frequency of the conditioning stimulation. In the present group of 12 patients only one experienced real pain relief during 2/s stimulation compared to a suppression of pain in seven patients when the conditioning was performed with high frequencies. These effects seem to be in contradiction to the

effects on the pain threshold observed in healthy volunteers (Andersson & Holmgren 1975, Andersson et al. 1975 a, b) who showed a marked increase of the pain threshold in the teeth by 2/s conditioning stimulation of the cheeks but only transient threshold effects during stimulation with 100/s. It is, however, not possible to make a direct comparison. The most important factor to consider is the intensity of the conditioning stimulation. The patients with severe pain were not able to tolerate strong stimulation since the beating sensation and the muscle twitches elicited by low frequency stimulation produced considerable discomfort or even pain and it was not possible to reach the high intensity of the conditioning stimulation required to induce the increase of the pain threshold (Andersson et. al. 1975 b, Holmgren 1975). Both Chinese and Western clinical reports emphasize the importance of a sufficient intensity of the conditioning stimulation (Holmdahl 1973, Peking Acupuncture Anaesthesia Co-ordinating Group 1973), and in some Chinese reports it is claimed that the efficiency in suppression of pain is dependent on the patient's ability to tolerate the conditioning as such (Department of Anesthesiolo-

gy, Peking 1973). Thus, it can be assumed that the intensity of conditioning stimulation required to give a pain suppression from 2/s stimulation was not reached. This conclusion necessitates further investigations in patients suffering from pain conditions which in themselves do not prevent sufficient intensity being used. It is also important to note that chronic pain can be considered as neurophysiologically and psychologically different from experimental pain, and it is difficult to predict the effect on clinical pathological pain from pain threshold measurements only (Houde 1966, Andersson & Holmgren 1975).

From a clinical point of view, conditioning stimulation with 2/s had very little to offer as a complement to other pain relieving methods since only one patient out of 12 obtained a good pain relief after the stimulation. The high frequency conditioning stimulation, however, gave pain relief in seven of the patients. This observation is in agreement with other reports on transcutaneous high frequency stimulation (Wall & Sweet 1967, Shealy & Maurer 1974, Augustinsson et al. 1974). The long-term effect of transcutaneous stimulation is not yet known but experiences from dorsal column stimulation via implanted electrodes indicate a decreasing effect after months or years of use (Nashold & Friedman 1972). Since pain relief is obtained only in some of the patients and since the post-stimulation effect is short and possibly decreases during long-term use, it is important to elucidate underlying neurophysiological mechanisms in order to improve the method.

With regard to the present effects on pain conditions psychological factors have to be considered. All the patients had previously been treated with various methods aimed at reducing their pain, including surgery, chemical analgesics, and injections of local anesthetics, in combination with strong suggestive in-

fluences, without any lasting effect on the pain. Furthermore, patients 1-8 were initially conditioned with 2/s stimulation without any significant effect on the pain. It should be noted that the patients participated in the investigation with a great expectation of being relieved from pain although positive suggestions regarding pain suppression were avoided. During the period of successive stimulations at 2/s some degree of disappointment developed regarding the stimulation procedure. Several of these patients experienced a substantial pain relief when they later were conditioned by high frequency. This effect can hardly be due to suggestive factors since they would already have been disclosed at the initial series of stimulations. We therefore conclude that the pain suppression is not due to a mere psychological distraction or suggestion but implies a basic neurophysiological mechanism.

Empirical evidence indicates that activity in non-pain afferents blocks the sensation of pain. Melzack & Wall (1965) proposed a "gate control theory" according to which activity in low threshold large diameter afferents closes a "gate" in the pain pathway. Several of the specific features in this model have been severely criticized (Franz & Iggo 1968, Zimmermann 1968, Vyklický et al. 1969, Schmidt 1972, Whitehorn & Burgess 1973). An alternative theory, explaining the segmental and to a certain extent non-segmental effects on the pain threshold and on the pain, obtained by high and low frequency conditioning stimulation, has been proposed. This theory takes into account the segmental organization of the central connections from the afferents which elicit the flexion reflex as well as the supraspinal control of these connections. An extensive discussion of these mechanisms is given elsewhere (Andersson & Holmgren 1975).

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