# Chronic Tension-Type Headache

## Treatment with Acupuncture, Physical training and Relaxation training

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UNIVERSITY OF GOTHENBURG

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*To My Family*

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## Treatment with Acupuncture, Physical training and Relaxation training

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## ABSTRACT

The overall aim of this thesis was to compare the effect of acupuncture, physical training and relaxation training on chronic tension-type headache (CTTH) and related symptoms through measurements of headache intensity, headache frequency, symptom characteristics associated with daily headache, muscle tenderness and subjective well-being.

There are four studies that underpin this thesis:

In paper 2 and 4, the study cohort comprised 90 consecutive patients with CTTH. Study 1 is cross-sectional determining the symptom characteristics and the daytime headache frequency in 74 of the 90 patients with CTTH compared with controls. Measurements in study 3 included 75 out of the 90 patients with CTTH. In studies 2, 3 and 4, patients with CTTH were randomly allocated to one of the three intervention groups.
The main findings were: Daytime headache intensity was lowest in the morning, worsening throughout the day. Headache-free periods were few but occurred most commonly in the morning and became less common as the day progressed. Neck mobility was lower in all movements ($p<0.001$), and tenderness in all pericranial muscles was higher ($p<0.001$) when compared to the control group. The pain location was most pronounced in the temporal region and the pain character was described mostly as ‘pressing’ or ‘tightening’. Stress,

ergonomic factors and workload were cited as the most common triggering factors.
When determining the effect of acupuncture, physical training and relaxation training on the frequency of headache-free periods and days the number of headache-free periods ($p<0.03$) and headache-free days ($p<0.01$) was higher in the relaxation group compared with the acupuncture group immediately after the last treatment.
Total Tenderness Score (TTS) decreased in all groups (acupuncture, physical training and relaxation training) before to after treatment with no group differences. Three months after treatment, TTS decreased in the physical training group and differed from the acupuncture group ($p<0.001$). Six months after treatment, TTS decreased in the physical training group ($p<0.001$) and the relaxation training group ($p<0.008$) compared to the acupuncture group.
The central nervous system (CNS)-related symptoms and Minor Symptom Evaluation Profile total score in three dimensions were significantly lower in patients with CTTH compared with a reference group. At the three-month follow-up the total score was improved in the physical training group compared with the acupuncture group ($p<0.036$). At the six-month follow-up, the vitality and sleep dimension was significantly improved in the relaxation training group compared with the acupuncture group ($p<0.04$).

**Conclusions**: In patients with CTTH, headache symptoms increase during the day and stress, poor ergonomic factors and workload are the strongest triggering factors. All treatments reduced headache symptoms. Relaxation training and physical training are superior to acupuncture for improvement of CTTH related symptoms for patients with CTTH. A novelty of this study is that physical training has a good effect on CTTH.

**Keywords**: chronic tension-type headache, acupuncture, physical, training, relaxation training, muscle tenderness, CNS-related symptoms, symptom characteristics

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# SAMMANFATTNING PÅ SVENSKA

## Kronisk Huvudvärk av Spänningstyp

### Behandling med akupunktur, fysisk träning och avslappningsträning

Syftet med studien var att jämföra behandling med akupunktur, fysisk träning och avslappningsträning på patienter med kronisk huvudvärk av spänningstyp. I studien utvärderades behandlingseffekten avseende huvudvärkens intensitet, huvudvärksfria perioder och huvudvärksfria dagar. Vi undersökte också symptom associerade med daglig huvudvärk, muskelömhet och välbefinnande.

Patienternas huvudvärk och andra associerade huvudvärkssymptom före behandling och under dagen var signifikant bättre på morgonen för att därefter försämras. Nackrörligheten var signifikant lägre i alla testade rörelseriktningar och muskelömheten i alla perikraniella muskler var signifikant högre jämfört med en kontrollgrupp. Smärtlokalisationen var vanligast i den temporala regionen och smärtkaraktären var av "pressande och tryckande" kvalitet. Stress och ergonomiska faktorer var de vanligaste utlösande faktorerna till huvudvärken.

Behandling med avslappningsträning ökade signifikant huvudvärksfria perioder och huvudvärksfria dagar jämfört med akupunkturgruppen direkt efter avslutad behandling.

Förändring uttryckt som en summa av muskelömheten var signifikant lägre efter tre månader i den fysiska träningsgruppen jämfört med akupunkturgruppen. Sex månader efter avslutad behandling var både avslappningsgruppen och den fysiska träningsgruppen signifikant förbättrade jämfört med akupunkturgruppen beträffande muskelömheten.

Välbefinnandet var signifikant lägre hos patienter med jämfört med en referensgrupp. Vid tre månaders uppföljning efter behandlingen var

välbefinnandet signifikant högre i den fysiska träningsgruppen jämfört med akupunkturgruppen. Vid sex månaders uppföljningen var vitality och sleep dimentionen signifikant förbättrad i avslappningsgruppen jämfört med akupunkturgruppen.

Konklusion; Patienter med kronisk huvudvärk av spänningstyp upplevde ökande huvudvärkssymptom under dagen. Stress och dålig ergonomi var de vanligast utlösande faktorerna. Alla behandlingarna reducerade huvudvärken. Avslappningsträning ger fler huvudvärksfria perioder och fler huvudvärksfria dagar och fysisk träning och avslappning ger bättre välbefinnande och minskar muskelömhet i förhållande till akupunktur och är att rekommendera för patienter med CTTH. Ett nytt rön i denna studie är att fysisk träning har god effekt på kronisk huvudvärk av spänningstyp.

# LIST OF STUDIES

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. **Söderberg E**, Stener-Victorin E, Carlsson J. Daytime headache frequency and symptom characteristics in patients with chronic tension-type headache. Submitted.

II. **Söderberg E**, Stener-Victorin E, Carlsson J. Chronic tension-type headache treated with acupuncture, physical training and relaxation training. Between group differences. Cephalalgia. 2006; 26:1320–1329.

III. **Söderberg E**, Stener-Victorin E, Carlsson J. Muscle tenderness in patients with chronic tension-type headache: Effects of acupuncture, physical training and relaxation training: A randomized controlled study. Submitted.

IV. **Söderberg E**, Carlsson J, Stener-Victorin E, Dahlöf C. Subjective well-being in patients with chronic tension-type headache: effects of acupuncture, physical training, and relaxation training. Clin J Pain. 2011;27 (5):448-456.

# CONTENT

# ABBREVIATIONS

| | |
|---|---|
| ACU | Acupuncture |
| BVCF | Baseline Value Carried Forward |
| CNS | Central Nervous System |
| CTTH | Chronic Tension-Type Headache |
| ETTH | Episodic Tension-Type Headache |
| IHS | International Headache Society |
| ITT | Intention To Treat |
| MSEP | Minor Symptom Evaluation Profile |
| MTT | Medical Training Therapy |
| PHYS | Physical Training |
| RELAX | Relaxation Training |
| RCT | Randomized Controlled Trial |
| SC | Statistically Corrected |
| TTH | Tension-Type Headache |
| TTS | Total Tenderness Score |
| QL | Quality of Life |
| VAS | Visual Analog Scale |

# DEFINITIONS IN SHORT

| | |
|---|---|
| Chronic Tension-Type Headache | TTH headache with a frequency over 15 days a month for at least three months. |
| Cross-Sectional Study | A study of a group of subjects at a specific point in time. In a cross-sectional study conclusions are drawn about a population by comparing different characteristics of the individuals. |
| Episodic Tension-Type Headache | TTH with a frequency under 15 days a month. |
| Frequent Episodic Tension-Type Headache | TTH with a frequency of at least 10 headache episodes occurring on one or more but not more than 15 days per month for at least 3 months. |
| Infrequent Episodic Tension-Type Headache | TTH with a frequency at least 10 episodes per year occurring on less than one day per month on average more than 12 days a year. |
| Randomized Controlled Study (RCT) | A study in which subjects are randomly allocated to receive one of several treatments. RCTs seek to measure and compare the outcomes after the participants receive the interventions. RCTs are quantitative studies. |
| Reliability | The extent to which a measurement is consistent i.e. the measurement of a particular phenomena is the same each time the instrument is used, even if some conditions have varied such as different people, times and places. |

| | |
|---|---|
| Trigger Point | A hyper sensible spot within a palpable taut band having local twitch response elicited by palpation and elected referred pain. |
| Validity | Is a result of that the measurement correspond to the true state of the measured data. That the data measure what they are intended to measure. |

# 1 PREFACE

My interest in chronic tension-type headache (CTTH) began during my physiotherapist's education at the University of Gothenburg. I wrote my bachelor's paper on the benefits of massage in patients with CTTH.

I found patients with CTTH very interesting as physiotherapy offered a non-pharmacological treatment option, which could be beneficial to patients with CTTH.

When I started working as a physiotherapist in primary care, I encountered more and more patients who might benefit from physiotherapy treatments. I found the potential importance of physiotherapy in the treatment of patients with CTTH.

However, I also soon established that the treatments used were not thoroughly evaluated. As such, we were unable to categorically state whether, and to what extent, these treatments benefitted the condition of CTTH.

As a result, I decided to return to university as a PhD student with the goal of filling this gap in our scientific evidence.

Since concluding my PhD studies I have become convinced of the importance of continuing to develop and evaluate physiotherapy treatment options for patients with CTTH.

CTTH is a chronic illness, but it does not have to be a lifelong chronic illness. By improving the knowledge about CTTH, and learning about the tools, which can help to control and improve the headache, patients can vastly improve the management of their condition.

# 2 INTRODUCTION

Tension-type headache (TTH) is the most common type of headache and has a high socio-economic impact (1). It is also one of the most neglected headache types and (2), in its chronic form, chronic tension-type headache (CTTH) is one of the most difficult types of headache to treat (1). TTH is characterized by a mild-to-moderate headache intensity, a pain that is described as 'pressing' and 'tightening' and can occur with differing frequencies and durations. The frequency threshold for having CTTH is defined as having headache on more than 15 days per month (1).

## 2.1 Prevalence

The prevalence of TTH ranges between 30 and 78% in the general population (3). Of the adult population 24-37% have TTH several times a month. Ten percent have it weekly and 2-3% of the adult population experience CTTH (1). TTH is most common between 30 and 39 years of age and often starts at an age of 25-30 (3, 4). CTTH is more frequent in women than in men, with five women experiencing CTTH for every four men (5, 6).

## 2.2 Classification

In the international classification of headache disorders set out by the International Headache Society (IHS), TTH is classified into three subtypes depending on the frequency of the headache (1), of which, CTTH is one. The frequency of CTTH should be headache on more than 15 days a month. The other two subtypes are infrequent episodic TTH (infrequent ETTH), <1 day of headache a month for ten months and frequent episodic TTH (frequent ETTH), with headaches occurring on 1-14 days per month) (1). An overview of the diagnostic criteria for CTTH is shown in (fig 1).

Diagnostic criteria for CTTH

Headache occurring on ≥15 days per month on average for >3 months (≥180 days per year) and fulfilling criteria B–D

B. Headache lasts hours or may be continuous

C. Headache has at least two of the following characteristics:

1. Bilateral location

2. Pressing/tightening (non-pulsating) quality

3. Mild or moderate intensity

4. Not aggravated by routine physical activity such as walking or climbing stairs

D. Both of the following:

1. No more than one of photophobia, phonophobia or mild nausea

2. Neither moderate or severe nausea nor vomiting

E. Not attributed to another disorder (1)

*Figure 1. Diagnostic criteria for chronic tension-type headache*

## 2.3 Clinical differences between ETTH and CTTH

CTTH has a different and more complex pathophysiology than the two other subtypes of TTH (1, 7-9). Moreover CTTH has a more central component, with sensitization of the central nervous system (1, 7, 10-12).

The infrequent ETTH is a mild headache occurring less than once monthly, easy to treat, and does not need medical attention. The peripheral mechanisms are, in this case, more important in the pathophysiology (1, 7, 8, 13). The quality of life (QL) also differs substantially between the ETTH and the CTTH. Patients with CTTH also report that they experience reduced QL (1, 14).

The treatments between ETTH and CTTH differ substantially and ETTH is much easier to treat than CTTH. CTTH requires long-term treatment of both a symptomatic and a prophylactic nature (14, 15). Patients with frequent ETTH often consume a large quantity of pharmaceuticals and do not seek medical advice as early as they should (16). Thus ETTH can often develop into CTTH and this leads to patients needing greater medical attention than might initially have been required. Additionally, patients with CTTH consume more pharmaceuticals than patients with ETTH (14, 16, 17).

## 2.4 Pathophysiology

The pathogeneses for THH and CTTH is unclear and different pathological factors influencing CTTH have been suggested (7-9, 12). Peripheral pain mechanisms are most likely to play a role in infrequent ETTH and in frequent ETTH (1, 15), while central pain mechanisms play a more important role in CTTH (1, 12).

## 2.5 Muscle factors

Muscular factors are also considered to be of importance (1, 11, 12). A common symptom in patients with TTH is increased tenderness of pericranial myofascial tissue in both ETTH and CTTH (7, 18). One predominant theory in CTTH is that sustained nociceptive input from

the pericranial myofascial tissue increases the excitability by sensitization of pain pathways in the central nervous system (7, 12, 13). This seems to be responsible for the transmission of ETTH into CTTH (5, 6). The central sensitization of the nociceptive pathways and impairment in the descending inhibitory system is the most dominant theory in the pathophysiology of CTTH (7, 12, 13, 19-21).

## 2.6 Peripheral factors

Pain is mediated by thin myelinated A-δ and non-myelinated C-fibers. The Aß-fibers normally mediate innocuous sensations. Different mechanical and chemical stimuli may excite and sensitize Aα, Aß, and A-δ as well as C-fibers (22). In TTH various stimuli can contribute to this excitation and sensitization of myofascial nociceptors and cause increased pain sensitivity (22). Tooth clenching, static exercise, chemical mediators, local contractions and low muscle blood flow, as well as inflammatory processes could, for example, lead to muscle pain in TTH, but further research is needed to elucidate the potential impact of these factors (23-26). In addition, CTTH has been shown to be at least partly associated with referred pain caused by active trigger points in the head, neck and shoulder muscles (27-30). A trigger point is a hypersensitive spot within a palpable taut band, having local twitch response elicited by snapping palpation, with elicited referred pain during palpation (29, 30). The nociceptive input from multiple active trigger points may contribute to CTTH (13, 27, 31). However, the referred pain mechanism in CTTH is not yet fully understood (27).

## 2.7 Central factors

The increased myofascial pain sensitivity in TTH may be caused by central factors such as sensitization of second order neurons at the spinal dorsal horn/trigeminal nucleus level, sensitization of supraspinal neurons as well as decreased antinoceptive activity from the supraspinal structures (12, 13, 19). Studies have demonstrated a dysfunction of endogenous supraspinal pain modulation systems in patient with CTTH (20, 21). This may contribute to the development and/or maintenance of central sensitization (20, 21).

## 2.8 Well-Being

Quality of life (QL) is a multidimensional concept that cannot be distinctly defined, because it is a persons own sense of well-being that stems from satisfaction or dissatisfaction with the areas of life that are important to him or her. Quality of life refers to the physical, social, physiologic and existential aspects of well-being that might be affected by diseases, disability and its treatments (32, 33).

Measuring these health-related components can assess the broad concept of QL. It is recommended that both generic and condition-specific instruments should be used (34, 35). Well-being and QL can be measured by a generic tool such as the 36-Item Short Form (SF-36) (36). Such generic tools are useful when comparing different disorders in the population but are not always sensitive enough to detect changes in specific diseases (35). Some disease–specific tools are therefore necessary to more accurately measure well-being and QL. To adequately assess the different health-related components of QL in this study, a condition-specific QL questionnaire the Minor Symptom Evaluation Profile (MSEP) was used (37).

MSEP has been used for measuring well-being in patients with headaches (37) and indicates that well-being, differs between ETTH and CTTH (1).
Patients with CTTH have a demonstrated lower well-being and QL (1, 14, 38) and a Danish population study found a greater tendency to anxiety and depression in patients experiencing frequent TTH (39).
The impact on QL in patients with CTTH is probably due to different factors, though the frequency of the headache plays an important role in the reduction of well-being and QL (40, 41).
The consequence of CTTH on QL is (12, 13) is described by Bendsen et al thus: “A person having headaches every day from the time of waking, persisting until bedtime, month in and month out, is disabled” (14).

Muscle contraction can also be a somatic expression of anxiety and psychological stress, which is commonly described in TTH (42). In a study of 245 patients with CTTH, Holroyd et al demonstrated that it were three to 15 times more likely than matched controls to be diagnosed with anxiety and mood disorders. They further noted that

half of the patients exhibited significant symptoms of anxiety or depression (38) and that patients' emotional well-being was frequently impaired (43, 44).
Mongini et al found that 63% of women with CTTH had symptoms of anxiety and depression (38, 42). In addition, in a medical outcomes study SF-36 questionnaire, ratings for QL were seen to be significantly lower for chronic daily headache patients than for the healthy controls (43, 44).

In addition, Jensen found that patients with CTTH have lower QL than patients with episodic TTH (45), which was further evidenced by the Rollnik et al study on differences in coping with illness, which found that QL was lower and symptoms of depression were greater in women than in men with CTTH (46).

## 2.9 Triggering factors

Triggering factors for headache (47) are not well documented. The most common documented trigger factors for TTH are stress, irregular meals, high intake of coffee, dehydration, sleep disorders, reduced or inappropriate physical exercise, psycho-behavioral problems and hormones (48, 49).
Stress is reported to be the most frequent triggering factor (50, 51) inducing more headaches in patients with CTTH when compared to a healthy control group (51).
It is important for patients with CTTH to identify triggering factors so that they can learn to cope with them rather than having to avoid them (52). It is also suggested that stress is involved in the translation of ETTH into CTTH (53).
When patients with CTTH were exposed to a stressful task of one-hour's duration, headaches occurred in 91% of the patients with CTTH and in 4% of the control group (51). As a result, it was concluded that stress triggers headache through hyperalgesic effects on already sensitized pain pathways in patients with CTTH (50, 51).

An acute headache attack can be triggered by physical stress or a bad working position, often in combination with psychological stress. The muscle strain caused by a bad working position produces an increased nociceptive input (11, 13) It is suggested that emotional

mechanisms/stress can increase muscle tension through the limbic system and reduce function in the descending pain inhibiting system (54).

## 2.10 Pharmacological treatment

Pharmacological treatment of TTH includes muscle relaxants and antidepressants, as well as analgesics (14, 15). For single acute headache attacks analgesics and NSAIDs such as ibuprofen, ketoprofen, acetylsalicylic acid, naproxen, diclofenac and paracetamol/ acitominophen are the most effective therapies (14, 15). It is important to avoid regular use in order to prevent the risk of developing medication overuse syndrome, which in itself can cause headaches (14, 55, 56). For the prophylactic treatment of CTTH, amitriptyline is drug of first choice and mirtazapine and venlafaxine are drugs of second choice (14, 15).

Many patients with headache tend to increase their consumption of analgesics, and this can increase headache frequency (14-16). When the episodic form of TTH becomes chronic, the overuse of drugs frequently plays a role in aggravating the ETTH disorder (16, 57, 58). Paradoxically, the use of medication decreases if the headache becomes chronic (59). It is important to reduce analgesic consumption as a first step in the treatment of TTH (55).

## 2.11 The role of Physiotherapy in CTTH

Human movement is a central concept in physiotherapy (60). Physiotherapy is defined as a science of movement and it views functional movement as central to the concept of health (60). According to the World Confederation for Physical Therapy, physiotherapy aims to develop, maintain, and restore maximum movement and functional ability throughout life (61). Physiotherapy involves the identification and maximization of QL and movement potential, which encompasses physical, psychological, emotional, and social well-being (60-62).

Physiotherapists work in partnership with patients used their unique knowledge and skills about the body and its movements (61). The knowledge of a physiotherapist in the treatment of CTTH is important. Physiotherapists have long experience and tradition in treating patients with CTTH. The first steps in the treatment of CTTH aim to reduce the intake of pharmaceuticals and to try different physiotherapy treatments (1, 14, 15).

## 2.12 Physiotherapy treatments

Common physiotherapy treatments are relaxation training, acupuncture, physical training, massage, spinal manipulation, hot and cold packs, transcutaneous electrical stimulation, and improvement of posture, however, there is not yet enough scientific evidence to demonstrate an effect on CTTH (62, 63).
An important part in the physiotherapy treatment of CTTH is to provide the patients with knowledge and understanding about their condition and give them tools to improve their headache. It is important to identify factors that trigger headaches so that patients can develop techniques to cope with them (64).

Physiotherapy treatments in CTTH aim to decrease the excitability and sensitization of the central nervous system, thereby decreasing general pain sensitivity, as theorized above (14, 65).
While non-pharmacological treatments are widely used and should always be considered for patients with TTH (14), the evidence for their efficacy is limited (14, 66, 67) and further studies are needed to evaluate the effects of physiotherapy treatments (63, 67-69).

Acupuncture, physical training and relaxation training treatments relieve pain mainly in two different ways. The first aims to reduce the peripheral sensitization as described above. The second aims to activate the descending inhibitory pathways (12, 14, 19, 65).

A predominant theory is that central sensitization is caused by prolonged nociceptive inputs from the muscle tissue, which is central in the pathophysiology of CTTH. It may therefore be of importance to reduce muscle tension in order to reduce the pericranial nociceptive inputs (13).

A further function of physiotherapy treatments is to activate the descending pain inhibitor pathways. A previous study indicate that physiotherapy treatment with transcutaneous electrical nerve stimulation and acupuncture aims to modulate pain-inhibitory systems at both spinal and central level involving the secretion and release of endogenous opiods (70).

## 2.13 Relaxation Training in CTTH

The aim of relaxation training is to help patients to recognize when their muscles are tensed and relaxed and to teach them to control muscle tension in their daily life.

Progressive relaxation training (71) and autogenic relaxation training (72) are commonly used techniques in the treatment of CTTH. Relaxation training may also involve cognitive and behavioral techniques and breathing exercises.
Relaxation training has been compared with no treatments, waiting list, or with other treatments (73-75) with conflicting evidence.
A meta-analysis with 53 trials demonstrated the usefulness of relaxation and electromyography (EMG) biofeedback in the treatment of TTH (76).
In patients with CTTH, the combination of stress management therapy and tricyclic antidepressant was demonstrated to be more effective than behavioral treatment or drug treatment alone (58). A physiotherapy program combined with relaxation training, massage and home-based exercise has also been shown to be beneficial in

CTTH but not in ETTH (77). In a study by Carlsson et al. on CTTH, a long-term effect of relaxation training was shown (78).

No other controlled studies on CTTH and relaxation training and CTTH have been found, but a recent review (14, 15) concluded that relaxation training might have effect in TTH and CTTH. However, there is conflicting evidence that relaxation training is better than being on a waiting list or receiving no treatment.

## 2.14 Acupuncture in CTTH

The aim of acupuncture treatment is to stimulate sensory afferents via needle insertion which in turn modulates the transmission of pain in the spinal cord and in the central nervous system (79). The effect of acupuncture has been dedicated to the release of opioid peptides and certain neuropeptides with the aim to activate pain relieving pathways (79). Large Randomized Controlled Study (RCT) indicates that acupuncture relieve nociceptive pain conditions e.g. osteoarthritis and low back pain (80).

There are a number of studies evaluating the efficacy of acupuncture in the treatment of TTH and CTTH (81). Two studies report better effects of acupuncture on THH and CTTH than standard treatment or being on a waiting list (81, 82). One of them was a multicenter, randomized, double-blind trial with 270 patients with ETTH and CTTH and acupuncture (needles inserted in muscle tissue) had a clinically relevant effect compared to the waiting list (82), while sham acupuncture (needles inserted only superficially at points distal from the commonly used acupuncture points) also had an effect (82).

A drawback with previous RCTs evaluating the effect of acupuncture is the inclusion of patients with a mixture of different types of headache e.g. migraine, ETTH, CTTH. Therefore no conclusion can be drawn concerning the effect of acupuncture on CTTH, although there was sufficient evidence to suggest that acupuncture could be a valuable option for the more frequent form of TTH (14, 83). Importantly, no previous study has investigated the efficacy of acupuncture compared to other physiotherapy treatments in patients with CTTH.

## 2.15 Exercise in CTTH

Exercise (in this thesis called physical training) is part of physical activity that is planned, structured, repetitive and has the aim to improve or maintain one or several component of physical fitness (84).

In this study patients performed muscular endurance training that is based on different physical components (85). The definition of muscular endurance is the ability of a muscle group to execute repeated contractions over a period of time sufficient to cause muscle fatigue, or to maintain a specific percentage of maximum voluntary contraction for a prolonged period of time (85).
Exercise, per se, has a pain modulating effect during (87-89), and after a exercise bout (86). The most common theory about the pain modulating effect of exercise is the release of endogenous opioids. The pain modulating effect works on different levels both through the dorsal spinal horn and by activating the descending inhibitory pathways (12, 19, 87). In addition, exercise has a positive impact on well-being, symptoms of depression, and stress (88, 89). These effects may be explained by modulation of the central serotonergic system, as exercise has been shown to result in higher levels of serotonin (88, 90).

Further, a positive effect of exercise has been demonstrated when applied in combination with relaxation and home-based exercise programs and cranio-cervical training for various kinds of headaches (77, 91, 92). Still, because of the low number of studies evaluating the effect of exercise on CTTH symptoms, no conclusions can be drawn.

# 3 AIM

The overall aim of this study was to characterize and in detail describe the symptom characteristics of patients with CTTH and the frequency of daytime headaches, comparing the effectiveness of acupuncture, physical training and relaxation training. This was achieved by evaluating and comparing the effects on headache intensity, headache free days and headache free periods, muscle tenderness and subjective well-being.

The specific aims of each paper were:

**Paper 1**. To characterize and in detail describe the symptom characteristics of patients with CTTH and the daytime headache frequency.

**Paper 2.** To compare acupuncture, physical training and relaxation training as treatments in patients with CTTH, evaluating their effect on headache intensity, headache-free days and headache-free periods.

**Paper 3**. To compare the influence of acupuncture, relaxation training, and physical training on subjective central nervous system-related symptoms that might affect subjective well-being in patients with CTTH.

**Paper 4**. To investigate the efficacy of acupuncture, physical exercise and relaxation training on muscle tenderness in patients with CTTH and to investigate the correlation between muscle tenderness and headache intensity.

# 4 PATIENTS AND METHODS

## 4.1 Patients

In all, 90 patients were evaluated in four separate studies (fig 2), and assessed against different control groups.

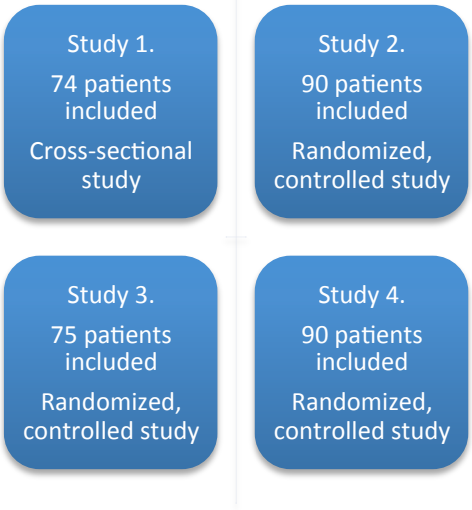



*Figure 2. Study overview*

Of the 90 patients with CTTH, 17 were men and 73 women, all were aged between 18 and 65. All had been examined and referred for physiotherapy treatment by their physicians at one of three primary care units in the city of Gothenburg and its suburbs between March 1997 and September 1999. The patients were also examined a second time by one of the authors (E.S., a registered physiotherapist) at their respective primary care units to confirm the diagnosis before randomization of the patients into the treatment groups.

The inclusion and exclusion criteria were established according to guidelines for trials of drug treatments in TTH (16). Inclusion criteria were: aged between 18 and 65 years and with a diagnosis of CTTH as defined by the HIS classification 1988 occurring on at least 15 days

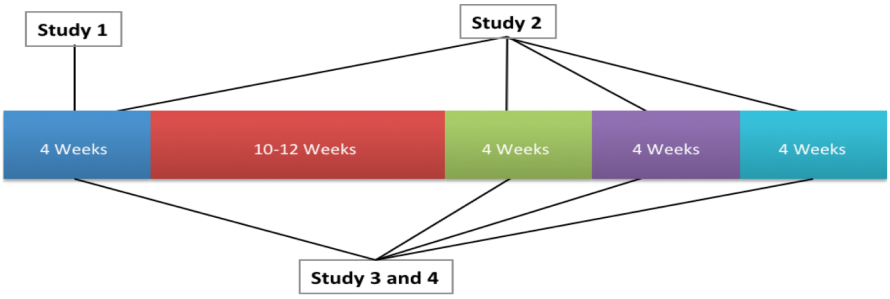
each month for at least six months (93). The classification was published in a revised version 2004 (1).

Exclusion criteria were as follows: headache that began after the age of 50 years, migraine occurring more than once a month during the last year, inability to speak or read Swedish, serious somatic or psychiatric disease, drug abuse or the use of analgesics or triptans for 10 days per month or more (16).

The patients received written information about the study. After agreeing to participate, patients signed the informed consent. The 90 patients were randomized, using sealed envelopes, into one of three different treatment groups: an acupuncture group (n = 30), a physical training group (n = 30) or a relaxation training group (n = 30).

The study comprised a pre-treatment period of four weeks, a treatment period of 10-12 weeks and a post-treatment period of four weeks immediately after treatment, and repeated for four weeks at three months after treatment and again at six months after treatment (fig 3).

## 4.2 Timeline (Fig3)




-4 weeks before treatment
-10-12 weeks treatment period
-4 weeks follow up immediately after treatment
-4 weeks follow up 3-months after treatment
-4 weeks follow up 6-months after treatment

*Figure 3. Timeline illustrating the main design of the study*

The Ethics Committee of Gothenburg University approved the study.

In Study 1, the first 74 patients were included and only the baseline values were studied.

In Study 2, all 90 patients were included and followed the whole timeline above.

In Study 3, the first 75 'included patients' participated and followed the whole timeline above.

In Study 4, all 90 patients were included and followed the whole timeline above (fig 3).

## 4.3 Controls

A control group consisting of 30 healthy women aged 19 to 56 years (mean age 36 years) selected from a non-clinical population was used to compare neck mobility and muscle tenderness and has previously been described in detail in study 1 (78).

A reference group was randomly selected from a large epidemiological sample of 2.162 healthy individuals. For each patient with CTTH a reference person of the same age and sex was randomly selected. The reference group of 88 people was selected from the southern third of Sweden to compare the CNS-related symptoms in study 4 (94).

# 5 ASSESSMENTS

One of the authors (E.S.) made all assessments but did not perform any treatment.

## 5.1 Headache Intensity and Headache-Free Periods

Headache intensity was measured using a visual analog scale (VAS), which consists of a 100-mm straight line with 'no pain' as the left end-point and 'worst possible pain' as the right end-point (95). Patients marked their actual pain intensity on the line. The patients were asked to keep headache dairies for four weeks before treatment and for four weeks immediately after treatment. At three months and six months after the last treatment session, the patients were again asked to keep a headache diary for four weeks. Each diary contained one VAS per page, using four pages per day, so that patients could make four ratings of pain intensity each day and would be influenced as little as possible by their previous ratings. Headache intensity was measured four times a day (range 0-100). Headache-free days per week (range 0–7) and headache-free periods per four-week period (range 0–28) were calculated for each group (study 1, 2).

## 5.2 Neck Mobility

Neck mobility was measured using Inclinometer (Myrin) measurement equipment (96). During the measurements the patients were instructed to sit straight back into a chair. During flexion and extension movements, a Velcro band was firmly fixed around the head above the eyebrows. The Inclinometer was then placed on the band just above the ear, the zero-point being lined up with the tragus. During side flexion the Inclinometer was simply moved to the front of the head with the zero-point lined up with the nose. For rotation the Inclinometer was placed on top of the head with the zero-point lined up with the bridge of the nose. For each movement, the subject was instructed to move their head as far as possible. We ascertained pure cervical movement of the head and ensured that movement of the shoulders and/or back were minimized (study 1).

## 5.3 Pain Location

Pain location was described in a pain drawing. Patients marked their pain location on a paper, with a pre-drawn head, with a pen. A pain drawing makes it easier for patients to show their pain location. Pain location areas were then divided into four groups: the neck region, the temporal region, the forehead, and behind the ear (study 1).

## 5.4 Pain Characteristics

Pain characteristics were described by sensory words. Patients were asked to mark all characteristics describing the quality of their pain. They could choose between seven different characteristics. All characteristics described pain quality, the sensory component, and how the pain felt. The characteristics were described as: Pressing/ Tightening, Nagging, Throbbing, Radiating, Cutting, Burning and Stabbing (study 1).

## 5.5 Triggering Factors

Triggering factors for their headaches were reported by marking all triggering factors they believed could trigger their headache. The triggering factors were: Stress, Ergonomic factors/Work, Sleep, Hormones, Bite, Posture, Other illnesses, Noise, Vision, Hearing, Weather changes, Medication and Mood (study 1).

## 5.6 Muscle Tenderness

The degree of muscle tenderness was evaluated by manual palpation of six to eight pericranial muscles bilaterally in the head and neck. In study 1, it was six muscles and in study 2, it was eight muscles. The muscles assessed are closely associated with muscle tenderness and correspond to the location of headaches and are commonly used in headache research (fig 4).

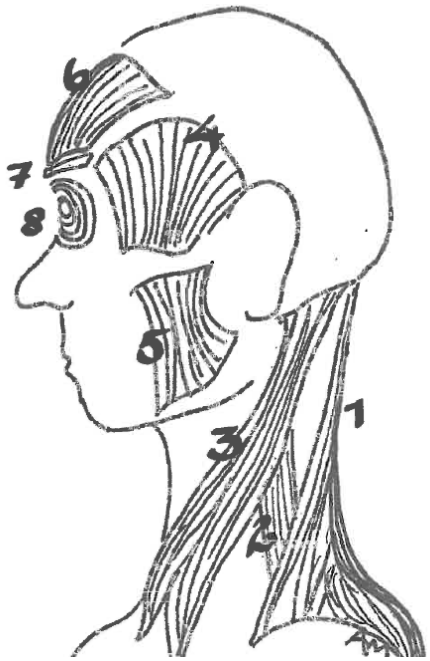



*Figure 4. Pericranial muscles palpated*

1. M. Trapezius, origin at the external occipital protuberance.

2. M. Levator scapulae, insertion at the angelus superior scapulae.

3. M. Sternocleidomastoideus, insertion at the mastoid process.

4. M. Temporalis, the upper anterior part of the origin of the muscle.

5. M. Masseter, origin of the superficial part of the muscles at the anterior two-thirds of the lower border of the zygomatic arch.

6. M. Frontalis, in the middle of the head, two and a half centimeters above the first and second third of the medial part of the eyebrow.

7. M. Corrugator, origin at the medial end of the superciliary notch.

8. M. Orbicularis, origin at the medial corner of the eye.

Manual palpation was performed according to Langemark and Olesen , and muscle tenderness was assessed according to a four-point scale (0-3) (97). The reliability of manual palpation has been reported to be acceptable (98). In study 1, palpation scores for both the left and right sides were summarized into a Total Tenderness Score (TTS) (98) (study 2). The maximum score for each patient was 12x3=36 (study 1) and 16x3=48 (study 2).
To secure as similar pressure as possible, manual palpation was compared to a palpometer (99) in 45 patients. Reliability of the palpometer is good (98).

## 5.7 Well-Being

CNS-related symptoms were assessed by the Minor Symptom Evaluation Profile questionnaire (MSEP) (37). The MSEP is designed to detect changes in subjective symptoms considered to be CNS-related (100). The MSEP comprises 24 self-administered standardized items using a VAS (98). Low-scoring values reflect positive feelings; high-scoring values reflect negative feelings. Dahlof et al (100) categorized items into three dimensions based on factor analysis of the responses of 374 patients:

- Contentment (seven items): happiness, tranquility, self-control, decisiveness, self-confidence, mental fatigue and general well-being.

- Vitality (five items): enthusiasm, initiative, endurance, concentration and responsiveness.

- Sleep (three items): nocturnal sleep, quality of sleep and insomnia.

The internal consistency, which provides the homogeneity of the dimensions in this version of the MSEP, was calculated for each dimension using Cronbach a-coefficient. The results were: contentment a=0.81, vitality a=0.81, and sleep a=0.77 (37).

The remaining nine independent MSEP items had low factor loadings and were thus treated as independent items and evaluated separately:

sexual interest, muscular tension, numbness, self-consciousness, sociability, appetite, sweating, physical competence, and dreams. The MSEP has been shown to discriminate between symptoms induced by different classes of drugs, and differences in the subjective well-being of normotensive, borderline hypertensive and hypertensive (94, 100).

In addition, construct validity has been established by calculating the correlation coefficients between dimensions of the MSEP and those in other questionnaires, such as, for example, the Nottingham Health Profile (34). Compared with the equivalent dimensions of other questionnaires for measurement of health-related QL, the dimensions of the MSEP were found to be relevant. We used the MSEP in the Swedish language. MSEP assessments were made at the clinic: before treatment, immediately after treatment, and at three and six months after treatment (study 4).

## 5.8 Statistics

In general, all data were presented applying descriptive statistics using frequency and relative frequency for categorical variables and the mean, standard deviation (SD), median and range (skewed distributed data) for continuous variables. All tests performed were two-sided and $p<0.05$ was regarded as statistically significant. Imputation for missing data was done using the last-observation-carried-forward method.

### Study 1.

Headache intensity and headache free periods were summarized over 28 days and at various points of time during the day, i.e., 08.00, 12.00, 16.00 and 20.00. For other continuous variables, patients participating in the study were compared to a control group using a t-test for variables that could be assumed to be normally distributed in a non-parametric test, the Wilcoxon rank sum test. Differences among time points were tested using the ANOVA repeated measures design. Correlations between neck mobility and the headache intensity were calculated using the Spearman rank order correlation coefficient.

### Study 2.

Non-parametric tests were chosen for the analysis of the VAS, which was regarded as ordinal scaled data. The Wilcoxon rank sum test and

the Kruskal-Wallis test were used in continuous variables and chi-square test and Fisher's test were used for categorical data (101).

### Study 3.

Differences between treatments for categorical variables were tested using the Chi-square test with respect to the proportion of improved results immediately after treatment, at the three- and six-month follow-up, compared to baseline. Within-group changes were tested using the Wilcoxon matched pairs test. The correlation between changes in pain intensity measured by VAS and changes in TTS was analyzed using the Spearman rank order correlation coefficient in each group and in all patients.

### Study 4.

The total score of MSEP data were analyzed as dichotomized variables with regard to improvement and deterioration of assessments over time. Derivation of improvement was set to numerical decreases (-) and deterioration was set to numerical increases (+), when assessments at the three time points: immediately after the last treatment and three and six months after treatment, was compared to the assessment at baseline. Assessment of the various dimensions of the MSEP were dichotomized and derived as improvement if decreases were 10 or 25 units respectively, and deterioration as increments of 10 or 25 units respectively, compared to the baseline assessments.

The endpoint for statistical analyses was further the proportion of subjects with an improvement in the MSEP scores. Statistical analyses were done using the Chi-square test and Fisher's test.

## 5.9 Statistical considerations

It is always important to minimize the missing values. There is no exact rule how to handle missing responses and drop outs, and different approaches are relevant in different situations. In study 2 missing values were treated according to the last value carried forward approach. It was a substantial amount of missing values, 11-13 of 30 subjects in each group at the six month follow up visit. Intention-to-treat, ITT analysis was applied for and last-observation-carried-forward was used to impute the missing values. The missing values were also equally distributed among the three randomized groups,

which indicate the randomness of its pattern. In study 4 and 5 the missing values were treated according to the baseline value carried forward approach. This was considered to be the most appropriate methodology in these cases (102).

## 5.10 Statistical power

Overall, in this RCT study, power was calculated with respect to the primary outcome variable, which was the proportion of subjects with an improvement of headache free periods. The clinical relevant difference to be detected was set to an absolute difference between proportions of 25%, with power 80%.

## 5.11 Methodological considerations

Headache diary is often used as a diagnostic tool and is the most important tool when evaluating headache intensity, frequency and headache duration and is highly recommended to be used in the guidelines for non-pharmacological RCT studies (16, 103). We used a diary based on four VAS ratings each day during a pre-treatment period of 4 weeks and a post treatment period of 4 weeks. This was done in order to evaluate not only the headache intensity, frequency and headache duration but also to evaluate the occurrence of headache during the day. The use of VAS in headache diaries has been shown to be valid for registration of headache and other pain. It is also recommended to use 4-ratings per day and preferably with VAS.

## 5.12 Treatments

Seven registered physiotherapists treated the patients at their usual primary care units (three different clinics). All therapists had documented education at a comparable level for all treatments (study 4).

## 5.13 Acupuncture

Acupuncture was mainly given by five registered physiotherapists at the three different clinics. They used the same technique and all had long experience in treating patients with acupuncture. Disposable

needles (Huanchou, Medema, Stockholm, Sweden) with a dimension of 15x0.25 mm and 30 or 40x0.30 mm were used. The needle length was dependent on the location of the acupuncture point. The needles were inserted to a depth of 2–5 mm or 10–30 mm, depending on location. The needles were twilled by hand three times during each 30-minute treatment, until the patient felt the characteristic needling sensation the so-called 'de qi' sensation of soreness, numbness or distension (appendix 1).

The recommended (79), and clinically most used, acupuncture points for CTTH were chosen according to the area of pain, segmental points using a total 10–12 needles, of which not more than eight were distal with peripheral needles in the hands and legs (79).

Mandatory points to be needled were GB 20, GB 14, LI 4 and ST 44: optional points were PC6, PC7, SP6, GB34, ST8, EX2 and EX 1 (107) (appendix 1). Treatment comprised 10–12 sessions over a period of 10–12 weeks. Twenty-nine patients underwent 12 treatments and one patient underwent 10 treatments (appendix 1).

## 5.14 Physical Training

In the physical training group, training was performed by five, although mainly four, registered physiotherapists working at three different clinics. The therapists had long experience and a documented education in treating patients with physical training. Treatment lasted two and a half to three months and included 10 training sessions at the clinic and an additional home training program. The training consisted of the same exercises for all patients, but the weights were individually adapted (appendix 2).

Patients performed either: two 45-min training sessions a week at the clinic for five weeks and then a home-training program three times a week for a further five weeks (a total of 25 training sessions), or: one training session at the clinic followed by a home training program once or twice a week for 10 weeks (a total of 25 training sessions).
The physical training at the clinic was performed according to the principles of Medical Training Therapy (104), which include achieving 80% of maximum fatigue. Both the performance requirements and the amount of exercise were the same for all patients.

Each training session consisted of five exercises repeated 35 times and three sets of each (105 times). The patients rested for one-to-two minutes between each exercise. The exercises focused on the neck and shoulder muscles. Each session began with five-to-10 minutes of ergometric bicycling. The training took place in a group of a maximum of five patients. At least eight out of 10 training sessions were carried out under the supervision of a physiotherapist.

The home exercise program also focused on the neck and shoulder muscles. It consisted of five exercises repeated 10 times and three sets of each (30 times). Patients rested for one-to-two minutes between each exercise. Each session began with two warm-up exercises and ended with one stretching exercise (appendix 2).

## 5.15 Relaxation Training

In the relaxation group, relaxation training was performed mainly by three registered physiotherapists working in three different clinics. The physiotherapists each had long experience and documented skills in treating patients with relaxation training. The relaxation training program described by Larsson and Daleflod and is based on progressive and autogenic relaxation techniques (71, 72).

Progressive relaxation training by Jacobson is a neuromuscular technique in which different muscle groups are systematically tensed and relaxed (71). Autogenic relaxation training by Schultz is a form of self-hypnotic training where the patient is taught a method of controlling the body's physiological reactions by repeating selective verbal phrases (72). Besides progressive and autogenic relaxation training (71, 72) the relaxation group practised relaxation and breathing techniques, stress coping techniques, how to relax during activity and how to relax in everyday living (appendix 3).

Eight to 10 sessions of relaxation training were performed individually under the supervision of a physiotherapist once a week. Twenty-nine patients performed 10 sessions and one patient performed eight sessions. The patients also received an audiotape for home use. The audiotape included the last training session and the patients were instructed to train once daily. After the last session the patients

received a tape that included all eight to 10 training sessions and instructions to continue training once a day.

The patients performed the training in a comfortable, recumbent position on their back, sitting in chairs, or standing or walking depending on the type of relaxation training. All training took place in a darkened environment (appendix 3).

# 6 RESULTS

## 6.1 Patients

### 6.1.1 Dropouts

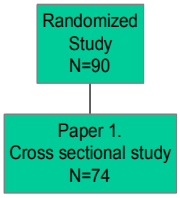
All patients completed the baseline measurements in studies 1-4, and treatments in studies 2-4. One patient in the acupuncture group was in a car accident and was excluded from the three-month and six-month follow-ups in studies 2-4. In the relaxation training group, one patient chose to seek other treatment and was excluded from the three-month and six–month follow-up in studies 2-4.

In study 2, at the three-month follow-up, three patients in the acupuncture group, four in the physical training group and four in the relaxation-training group did not return their diaries. One of the patients in the acupuncture group who did not return their diary at the three month follow up was the same patient who was involved in the car accident described above. At the six-month follow-up, one patient in the acupuncture group refused to continue with their diary and eleven patients did not return their diaries. In the physical training group 11 patients did not return their diaries. In the relaxation-training group 10 patients did not return their diaries.

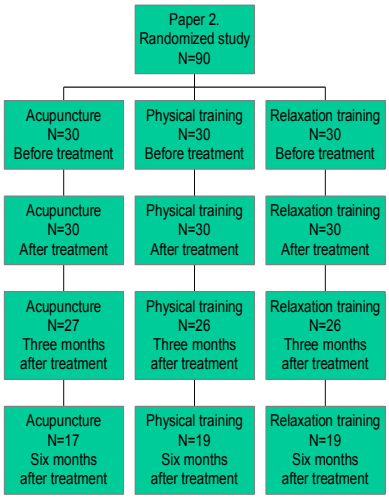
In study 3, one patient in the relaxation training group was missing from the six-month follow-up. In the physical training group one patient was excluded from the six-month follow-up.

In study 4, in the acupuncture group, one patient was missing at the follow-up directly after treatment and one patient was missing at the three-month follow-up. In the physical training group all patients completed the follow-ups (fig 5).

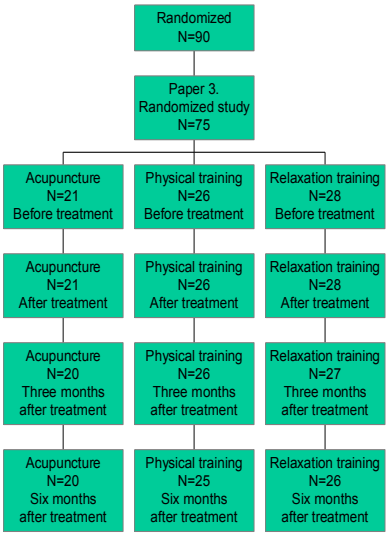
Study 1.




Study 2.




Study 3.




Study 4.

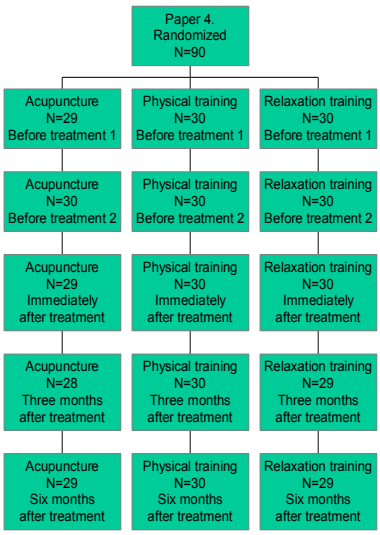



*Figure 5. Flow charts studies 1-4*

### 6.1.2 Patient Characteristics

Patient characteristics, together with social and headache history in each study are listed in the table below. There were no significant difference between the studies according to characteristics, social and headache history. All patients were aged 18–59 years.

Of the 90 patients with CTTH who participated in studies 2 and 4, 17 were men and 73 women, aged 18–59 years.

Seventy-five patients participated in study 3, 14 (19%) were men and 61 (81%) women. Seventy-four patients participated in study 1, 14 (19%) were men and 60 (81%) women. Differences in gender, living arrangements, education, work and headache duration were non-significant between the three treatment groups (acupuncture, physical training and relaxation training) before treatment, studies 2-4. However the mean age in the relaxation group was significantly higher compared with the acupuncture group ($p < 0.05$) and the physical training group ($p < 0.01$). The education level was lower in the relaxation-training group compared with the acupuncture and the physical training group (table 1).

*Table 1. Patients characteristics, social and headache history in each study*

| Characteristics | Studies 2 and 4 | Study 3 | Study 1 |
|---|---|---|---|
| | N=90 | N=75 | N=74 |
| Male (%) | 17 (19) | 14(19) | 14(19) |
| Female (%) | 73 (81) | 61 (81) | 61(81) |
| Age/year at baseline | | | |
| Mean | 37 | 37 | 37 |
| Range | 18-59 | 18-59 | 18-59 |
| Living situation (%) | | | |
| Living with others | 82 (91) | 68 (91) | 67(91) |
| Living alone | 8 (9) | 7 (9) | 7(9) |
| Children | 68 (66) | 57(76) | 57(76) |
| Education (%) | | | |
| Compulsory level | 70 (78) | 58 (23) | 57(77) |
| Higher level | 20 (22) | 17 (23) | 17(23) |
| Headache duration/years | | | |
| Median | 7.5 | 7 | 7 |
| Mean | 11 | 11 | 11 |
| Range | 2.0-37.0 | 2.0-37.0 | 2.0-37.0 |

## Headache Intensity on a Daily Basis (study 1)

There was a significant variation in headache intensity among the four time-points during the day ($p<0.001$). When measured daily for 28 days headache intensity was lowest in the morning and worsened during the day. The mean headache intensity during the entire day was 19, with a standard deviation of 14, and a median of 15, with a range of 2 to 62. The headache intensity was higher at 12.00 am, 4.00 pm, and 8.00 pm compared with 8.00 am ($p<0.001$), and at 4.00 pm ($p<0.01$) and 8.00 pm ($p<0.05$) compared with 12.00 am.

## Headache Intensity, Between-Group comparisons (study 2)

There were no differences in headache intensity between the three treatment groups in the baseline ratings taken at four weeks prior the treatment period, after treatment and at the three and six month follow-ups.

## Headache Intensity, Within-Group comparisons (study 2)

In the acupuncture group, headache intensity decreased three and six months after the last treatment compared with baseline. In the physical training group, headache intensity decreased immediately after the last treatment and at the six-month follow-up compared with baseline. In the relaxation training group, headache intensity decreased immediately after, and three and six months after the last treatment.

## Headache-Free Days and Headache-Free periods (studies 1 and 2)

The mean of the headache-free days during the baseline four-week period was 2 (3.5), the median was 1, with a range of 0-12. The headache-free periods were more frequent in the morning and decreased during the day ($p<0.02$). The mean headache-free periods were 17 (20), and the median 11, with a range of 0-78.

## Headache-Free Days and Headache-Free Periods, Between-Group comparisons (study 2)

There were no differences in headache-free days or headache-free periods between the three treatment groups in baseline ratings in the four weeks prior to the treatment period. The relaxation group reported a higher number of headache-free days ($p<0.01$) and headache-free periods ($p<0.05$) compared with the acupuncture group immediately

after the last treatment. There were no other significant group differences between the study groups at any time point (study 2).

## Headache-Free Days and Headache-Periods, Within-Group comparisons (study 2)

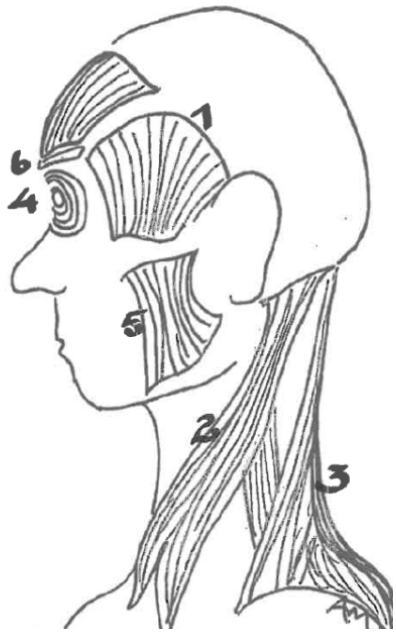
There were no changes in headache-free days or headache-free periods in the acupuncture group. In the physical training group, headache-free days and headache-free periods increased significantly immediately after the last treatment and at the six-month follow-up compared with baseline data. In the relaxation training group, headache-free periods increased immediately after, and at both follow-ups (study 2).

In the relaxation training group, headache-free periods increased immediately after, and at three and six months after the last treatment.

**Summary:** CTTH symptoms increase during the day. Relaxation training induced the most pronounced effects on headache-free days and periods directly after the treatment period, compared with acupuncture and physical training. There were no long-lasting differences between the interventions. All treatments reduced headache intensity, and increased headache-free days and periods in patients with CTTH.

## Muscle Tenderness compared to Controls (study 1)

Muscle tenderness was higher compared to controls in all pericranial muscles investigated ($p<0.001$). There was no difference between left and right sides in muscle tenderness. The tender muscles were m.Temporalis (Mean 2.75 ± SD 0.44), m. Sternocleidomastoideus (2.74 ± 0.45) and m. Trapezius (2.72± 0.45) (fig 6).




1. m.Temporalis (mean 2.75)
2. m.Sternocleido-mastoideus (mean 2.74)
3. m.Trapezius (mean 2.72)
4. m.Orbicularis (mean 2.45)
5. m.Masseter (mean 1.34)
6. m.Corrugator (mean 0.51)

*Figure 6. Illustration of muscle tenderness in chronic tension-type headache*

## Muscle Tenderness, Between-Group comparisons (study 3)

There were no between-group differences immediately after the final treatment. A higher proportion of individuals in the physical training group improved in TTS compared with the acupuncture group at the three- ($p<0.001$) and six-month ($p<0.001$) follow-ups. A higher proportion of individuals in the relaxation training group improved in TTS compared with the acupuncture group ($p<0.008$) at the six-month follow-up.

## Muscle Tenderness, Within-Group comparisons (study 3)

Within the relaxation training group, 12 (43%) patients decreased their TTS immediately after treatment, 14 (50%) had decreased TTS three months after treatment, and 17 (61%) decreased their TTS six months after final treatment. Within the acupuncture group, 8 (38%) improved their TTS compared to baseline immediately after treatment, 7 (33%) improved three months after treatment, and 6 (29%) improved six

months after treatment. Within the physical training group, 16 (62%) improved immediately after training, 22 (85%) improved three months after treatment, and 20 (77%) improved six months after treatment.

### Correlation Between Pain Intensity and Muscle Tenderness (study 3)

There were positive correlations between changes in pain intensity (VAS) and TTS in each group and in the entire group for changes at all time points ($p<0.001$).

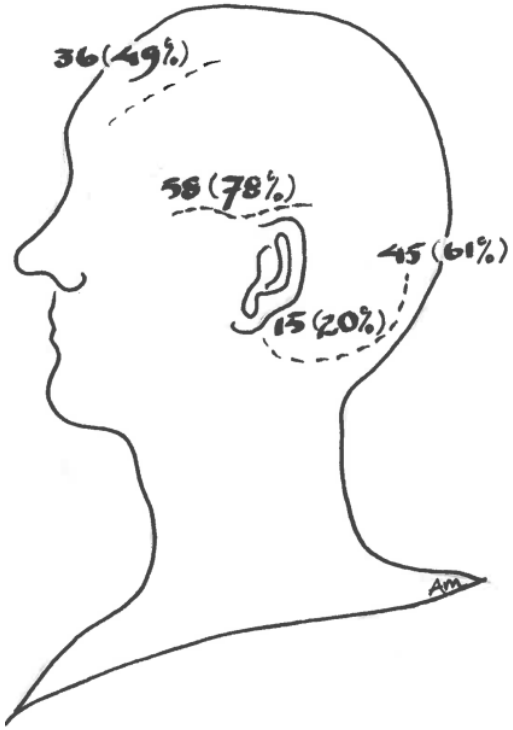
**Summary:** Patients with CTTH had more muscle tenderness compared to controls. All groups decreased muscle tenderness at all time points after treatment, although physical training and relaxation training were both superior to acupuncture at three and six months after the final treatment.

### Neck Mobility (study 1)

Neck mobility was lower in patients with CTTH compared to the control group in all movements ($p<0.001$). There was no correlation between neck mobility and headache intensity.

### Pain Location (study 1)

The headache pain was located in the temporal regions in 58 patients (78%), in the neck regions in 45 patients (61%), in the forehead in 36 patients (49%), and behind the ear in 15 patients (20%). All patients had bilateral muscle tenderness (fig 7).




*Figur 7. Headache pain location in numbers of patients and percent*

## Pain Character (study 1)

CTTH patients described their pain as: pressing/tightening, 56 patients (76%), nagging, 39 patients (53%), and throbbing, 29 patients (39%).

## Triggering Factors (study 1)

The most common triggering factors were: stress in, 74 patients (68%), ergonomic factors/work in, 10 patients (14%), and sleep disturbance in, six patients (8%), hormones in, six patients (6%).

**Summary:** In patients with CTTH, symptoms increase during the day and stress and poor ergonomics/work load are the strongest triggering factors. These findings underline the importance of defining specific symptoms and triggering factors in patients with CTTH in clinical practice.

## CNS-related Symptoms and Quality of Life (study 4)

Baseline values of the total score of the 24 MSEP items and the three dimensions were lower compared with an age- and gender-matched reference group. Quality of sleep and muscular tension differed markedly compared with the reference group. No significant differences were found between the three treatment groups during the baseline period.

## Between-Group comparisons (study 4)

No difference in MSEP was found immediately after treatment among the three treatment groups when total scores were compared. At the three-month follow-up, the proportion of individuals with an improved total score was greater in the physical training group compared with the acupuncture group ($p<0.036$). No significant differences were found at the six-month follow-up.

When 15 of the items were categorized into the contentment (7), vitality (5), and sleep (3) dimensions, improvement rated as >10 units and >25 units on the VAS. Vitality was higher in the relaxation training group compared with the acupuncture group at the six-month follow-up. Sleep was also higher in the relaxation training group compared with the acupuncture group at the six-month follow-up.

## Within-Group comparisons (study 4)

In the acupuncture group, total MSEP scores of 17 (56.7%) patients were improved immediately after, and at three and six months after

treatment compared with baseline. In the physical training group, total MSEP scores were improved in 19 patients (63.3%) immediately after training and in 26 (86.7%) and 24 (80.0%) patients at the three-month and six-month follow-ups, respectively, compared with baseline. In the relaxation training group, total scores were improved in 23 (76.7%) patients immediately after treatment and in 20 (66.7%) and 22 (73.0%) patients at the three-month and six-month follow-ups, respectively, when compared with baseline.

**Summary:** All treatments improved CNS-related symptoms at all time points after treatment. Physical training and relaxation training was superior to acupuncture for the improvement of subjective CNS-related symptoms that might affect patients' subjective well-being and QL.

# 7 DISCUSSION

## 7.1 General Discussion of the Results

The present study is unique in that we investigated the CTTH pattern for the entire day over a four week period. These patients had very few headache-free periods during the day. There was a tendency toward more headaches in the afternoons as compared to mornings. To have a daylong, low intensity headache of more than 15 days / month is associated with a negative impact on well-being and QL (1, 14). The patients well-being in this study was lower compared to controls.

We can clearly see that patients with CTTH can benefit from physiotherapy. All three investigated treatments: acupuncture, physical training and relaxation training, improved CTTH and related symptoms. Relaxation training was superior to acupuncture in increasing headache-free periods and headache-free days, while both physical training and relaxation training improved subjective well-being and muscle tenderness more effectively compared to acupuncture. The physical training group was superior to relaxation training in a total score

A new finding is that physical training has a positive effect in the treatment of patients with CTTH. To the best of our knowledge there are no previous studies evaluating the efficacy of physical training, as a single treatment modality, in patients with CTTH. This is an important finding with clinical relevance. Traditionally there is a limited use of physical training in the treatment of these patients due to the believed risk of worsening the headache and other associated symptoms.

In this study we can conclude that the patients do not get worse in their headache or in other associated symptoms. In fact they improve in all investigated parameters. This is of great importance for clinical practice.
The positive effect of relaxation training has previously been shown in a study although it has never been directly compared with acupuncture and exercise (78). Additionally, a combined treatment program incorporating four weeks of physical training with massage, relaxation

techniques, stretching training and a home training program have been shown to improve headache-free days in CTTH (77).

All three treatments improved muscle tenderness. Physical training was superior to acupuncture at the three- and six-month follow-ups while relaxation training was also superior to acupuncture at the six-month follow up. In both groups, patients were taught to use recommended techniques and strategies and could perform physical training and relaxation training at home. A plausible explanation of the greater improvement in the physical training and the relaxation training groups could be that the patients involved continued with these exercise/relaxation techniques and learned to control their headache by themselves. The acupuncture group on the other hand, had no more treatment and did not have the option of home treatment after the study treatment period ended.

All three treatments investigated were based on a predetermined program with minor individual variations. This fixed program base was necessary in the evaluation of each treatment program in order to be able to reproduce the program. In physiotherapy treatment adaptation to individual needs is important and a physiotherapist's unique knowledge is the key to the effective adaptation of all three investigated physical treatment programs. Given this, it is logical to conclude that the further patient-specific development and a combination of these programs in the clinic may generate even better results.
Patients might also benefit from a more intensive regime of physical training and a more individually tailored physical training program than offered as part of this study.

## Muscle Trigger Points

In this study we examined muscle tenderness and did not examine trigger points.

CTTH might be at least partly associated with referred pain caused by active trigger points in the head, neck and shoulder muscles (27). The nociceptive input from multiple active trigger points may contribute to CTTH (7) by central sensitization pain (109).

The referred pain mechanism in CTTH is not yet fully understood. According to Travell (30) there are two possible explanations as to

why patients may not be aware of trigger points. Firstly, latent trigger points are painful only when palpated. Secondly, an active trigger point produces pain during motion and at rest (27).

A recent study found that women with CTTH have multiple active trigger points in the neck and head muscles with more trigger points in the neck muscles than in the head, suggesting that headache is referred pain from tender neck muscles (27, 30).

## Palpation of Pericranial Muscles

Manual palpation is clinically relevant for evaluating muscle tenderness. In the present study, manual palpation was performed according to Langemark and Olesen (97). Muscle tenderness was assessed according to a four-point scale (0-3) (97, 98). Reliability of manual palpation is acceptable (97) and variability may be influenced by palpation pressure intensity and tenderness scoring (98).

In a previous study the palpometer was found to be a valuable tool for measuring pressure intensity during palpation (99). It also demonstrated that palpation pressure was stable within observers from week to week but that there were differences in pressure intensities between observers (99, 105). Careful standardization of the palpation procedure is necessary in order to achieve acceptable reliability (98). Obviously, if sufficient pressure is applied, tenderness can be found in anyone. Reproducibility of manual palpation is, however, high if applied by the same trained investigator (98). To secure equal manual palpation pressure in the present study, in 45 patients manual palpation was compared with palpometer and we found high agreement between manual palpation and the palpometer.

## How CTTH becomes chronic

CTTH is the most common type of headache and is very difficult to treat (1) CTTH occurs more frequently than migraine and has a high socio-economic impact on society due to its prevalence in the general population (1). CTTH originates from ETTH. CTTH often starts as an infrequent ETTH and evolves into a frequent ETTH until it finally becomes CTTH. There are many different factors involved in the progression of TTH to a chronic condition. For example, an increased intake of pharmaceuticals can lead to sustained muscle tenderness and stress, itself a trigger for headaches (1, 12, 53).

CTTH has a different and more complex pathophysiology than the two other subtypes of TTH (1, 7-9).

Treatment approaches differ substantially between ETTH and CTTH, CTTH requires long-term treatment with both a symptomatic and a prophylactic nature (14, 15), while ETTH is easier to treat.

It is therefore of great importance to reach the patients while the TTH still is in its frequent form before it turns into a CTTH. It has also been shown that relaxation training might have a positive effect on TTH (73, 74). A meta-analysis comprising 53 trials demonstrated also the usefulness of relaxation and electromyography (EMG) biofeedback in the treatment of TTH (102). Acupuncture has also shown a positive effect on TTH. The most recent Cochrane review included five independent studies concluded that there was a better effect from acupuncture compared to sham acupuncture in patients with TTH (83).

## How to treat CTTH with Physiotherapy

While non-pharmacological treatments should always be considered for CTTH, the evidence for their efficiency is limited (14, 66, 67) and further studies are needed to evaluate the effects of physiotherapy treatments (63, 66, 67, 69).

As discussed earlier, the pathophysiology of CTTH is complex, with peripheral factors, central factors and psychological factors (12, 14, 19). Physiotherapy treatments in CTTH relieve pain mainly in two different ways. The first is to reduce the peripheral sensitization as described above. The second is to activate the descending inhibitory pathways (12, 14, 19, 65).

The treatment of CTTH is therefore long term. Because of the individuality of the patient and the complexity of the pathophysiology, the best option might be to evaluate treatment programs with an individual combination of different treatment modalities.

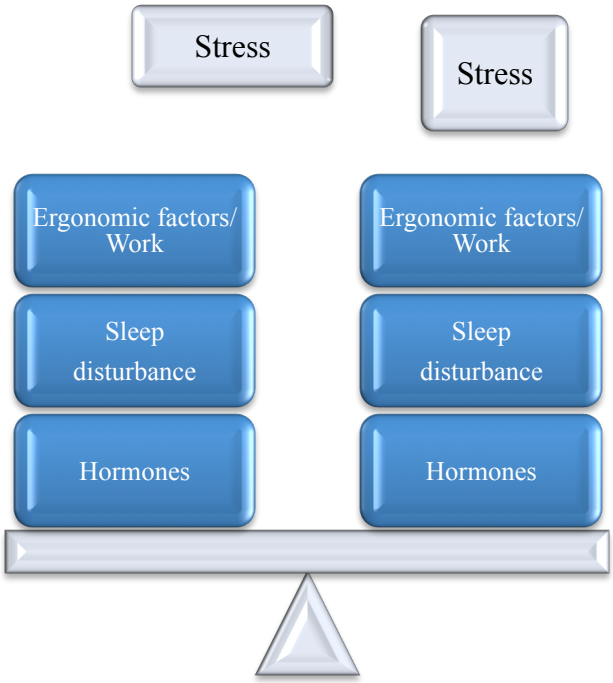
In the physiotherapy treatment of CTTH, the goal is to provide patients with knowledge and understanding about their CTTH and give them the tools to handle and improve their headache.

This knowledge can be provided by collecting information by anamnesis, headache diary, pain drawing, pain character and well-

being instruments. A thorough physical examination of the patient is important in order to observe the patient's facial expression, their posture in sitting standing and walking (especially the positions of head and shoulders) and to examine neck and shoulder mobility as well as any tense or shortened muscles, and whether any palpations tenderness can be seen in the pericranial muscles.

Finally, it is important to explain the results from these investigations to the patient so they better can understand their headache and can develop the tools that will help them to manage and prevent future headaches. They can do this by developing techniques such as relaxation training, physical training programs or by learning how to control the triggers of headaches. Each of these techniques can help to reduce muscle tension which, in turn, can help reduce pericranial nociceptive inputs.
A further function of physiotherapy treatments in reducing headache pain is activation of the descending pain inhibitor pathways that are disturbed by central sensitization (14, 65).
The most common theory about the pain modulating effect of physical training is the release of endogenous opioids. The pain modulating effect works on different levels both through the dorsal spinal horn and both by the descending inhibitory pathways (12, 19, 87).

Active treatment strategies are often recommended for the treatment of CTTH. There is no previous study investigating the effect of physical training as a single treatment for relief of CTTH symptoms. There are studies demonstrating a positive effect of exercise in the combinations with relaxation and home-based exercise programs and cranio-cervical training for various kinds of headaches (77, 91, 92).




*Figur 8. Triggering factors triggering chronic tension-type headache*

## Trigger Factors

It is important to identify the factors that trigger headaches so that patients can develop techniques to balance and cope with them (figure 8) (64). The identification and mitigation of triggers for patients with CTTH is an important part of the treatment of CTTH. The results of the present study shows that stress is the most common trigger factor. These results are in agreement with previous reports, and 68% of the participants thought that stress was the largest single trigger of their CTTH. In TTH in which stress, irregular meals, high intake of coffee, dehydration, sleep disorders, reduced or inappropriate physical exercise, psycho-behavioural problems and hormones was the most common triggering factors (48, 49).

Stress is reported to be the most frequent triggering factor (50, 51) inducing more headaches in patients with CTTH when compared to a healthy control group (50). Investigators concluded that stress triggers headache through hyperalgesic effects on already sensitized pain pathways in patients with CTTH (50, 51). It is also suggested that stress is involved in the translation of ETTH into CTTH (53).

## Other Diagnoses with Similar Symptoms

In IHS classification of headache disorders chronic migraine as well as CTTH classifies as headache on at least 15 days a month. It could then be possible for the patients to have both diagnosis. This is very rare and in this study the patient was only allowed to have migraine once a month. This we could confirm by the headache diaries.

Tender points are common in other diagnoses, e.g., primary fibromyalgia. However, these patients differ from those with CTTH in that they also have tender points in the lower body, hips, legs, and knees (106).
Patients with cervicogenic headache (1) display symptoms that are similar to patients with CTTH, but can provoke their headaches by neck movements (1). The patients in this study could not provoke their headache by neck movements.

## Study Strengths

Strengths of the study include the design, which ensured randomization. Patient compliance was high, with all patients completing their treatment programs and there was a strong level of follow-up immediately after treatment.

The study has and an unusually low dropout rate. The patients were thoroughly examined and diagnosed according to the guidelines recommended for trials in TTH (16).
Measurements were frequent, with a large number of measurements per patient. Headache intensity was measured using VAS and a headache diary. The patients marked their actual pain four times a day. As the diary should follow the patient during the day it was made in a pocket size including four pages per day, so that the patients could make four ratings of pain intensity per day and be as little influenced as possible by their previous rating. When the diaries came back they were checked for being used.
All measurements were measured and put into a computer program. Then checked by a second person for being correctly measured and typed in to the program.
The manual palpation measurement was only performed once per patient so the patient did not get less sensitive for pressure.
Treatments were standardized in terms of information given to patients, performed treatments, time and attention. This should minimize the differences between the treatment groups and the non-specific effects between the groups.

## Study Limitations

Weaknesses of this study include the relatively small sample size and the selection of patients from a relatively small geographic area. This might potentially make it harder to draw generalized conclusions about the results. The non-blinded author making all assessments is another weakness. The author had, however, no special favourable interest in a specific treatment. Additionally, the non-specific effect of attention from the therapists and toward participants in the study might give falsely positive results for the treatments.

Finally, the study was conducted more than 10 years ago, however, the results should still be considered valid since the diagnostic criteria and most common treatments remain unchanged.

## Ethics

All patients consulted a physician for their headache problems. None of the three treatments evaluated had proven evidence for relieving CTTH symptoms. Although both relaxation training and acupuncture had been evaluated in a previous study and had demonstrated positive effects in one study (76), there were few studies and no conclusions could therefore be drawn. Physical training had never been evaluated in patients with CTTH symptoms. In the Helsingforsdeklarations the main principle is that a new treatment should always be compared to the best possible treatment (61).

In the information given to the patients, the intention was a neutral approach and patients were informed about the randomization to one of the three treatment modalities. After the study period the patients were offered other treatments if desired. None of the three treatments, in any way, endangered patients' health. The little risk of pain from the acupuncture needle placement and stimulation gave only insignificant pain, the potential benefits outweighed the inconvenience of this minor discomfort.

Patients freely elected to participate in the study and were allowed to end their involvement at any stage of the study. Before entering the study patients received oral and written information about the study and, after agreement, signed an informed consent. The entire study protocol was approved by the Ethics Committee of University of Gothenburg.

## Clinical applications

Finally this study origin from the clinical research question which of three common physiotherapy treatments that is most effective in the treatment of CTTH and related symptoms. The clinical application of the study is that physiotherapist can use all three treatments as they all have a positive effect on the CTTH and associated symptoms. Though, relaxation training and physical training seems to be preferable when used alone. With the current acupuncture protocol, it can't be recommended as a single treatment for CTTH.

CTTH is a complex syndrome, and requires a long term treatment.
It is important for patients to learn about their headache and its associated symptoms, and to identify and manage the triggering factors. Managing strategies together with lifestyle changes including relaxation training and physical exercise are necessary in the long term treatment of CTTH.

# 8 CONCLUSION

In patients with CTTH, headache symptoms had a tendency to increase during the day and stress, poor ergonomic factors and workload are the strongest triggering factors. Further, acupuncture, physical training and relaxation training all reduced the symptoms of CTTH. Relaxation training and physical training are more effective treatments compared to acupuncture for patients with CTTH.

What is new in these findings is that physical training had a significant positive effect in the treatment of CTTH and was more effective than acupuncture in its positive effect on well-being and muscle tenderness.

The conclusions in each study were:

**Study 1.** CTTH symptoms increase during the day and stress and poor ergonomics or workload is the strongest triggering factors. These findings underline the importance of defining specific symptoms and triggering factors in CTTH.

**Study 2**. Relaxation training induced the most pronounced effects in increasing headache-free days and headache-free periods when compared to acupuncture. All treatments reduced the symptoms of CTTH.

**Study 3.** Acupuncture, physical training and relaxation training reduced muscle tenderness over time, and physical training and relaxation training were more effective treatments compared to acupuncture.

**Study 4.** Physical training and relaxation training seem to be more effective physiotherapy treatments for the improvement of central nervous system-related symptoms and subjective well-being for patients with CTTH.

# 9 FUTURE PERSPECTIVES

Several questions have emerged during this study, which could serve as a starting point for future investigations.

In particular, it has become clear that there is a lack of knowledge around several points, which warrant further evaluation:

-The effect of more intense physical training, including different types of exercises (endurance, strength, aerobic), higher intensity, and greater frequency and duration needs to be elucidated.

-The effect of acupuncture resulted in less pronounced effects than physical training and relaxation training. Since previous studies have demonstrated that acupuncture is superior to standard treatment, the effect of a longer treatment period and of electrical stimulation of the needles needs to be evaluated. The number of needles should be fixed but the placement of needles should be adjusted according to pain location.

-As for physical training and acupuncture, the relaxation training program can be further developed and a combination of different techniques needs to be evaluated. Further, the instructions for home relaxation training, including intensity, frequency and duration of the training, could be further developed.

-Because all treatments improved CTTH symptoms, a combination of the three treatment modalities should be evaluated.

Other considerations:

-Continued research and an evaluation of additional physiotherapy treatments on patients with CTTH, such as: ergonomic instructions, biofeedback, massage, manual orthopedic therapy, transcutaneous electrical stimulation and improvement of posture.

-Define different subgroups of CTTH according to the diagnostic criteria, in order to investigate and establish treatment guidelines for each of the different subgroups.

-Develop screening tools for clinicians enabling them to identify ETTH patients in an earlier stage, before their condition progresses to become CTTH.

-Define the factors activating the nociceptive input in order to delay or stop the progression of ETTH into CTTH.

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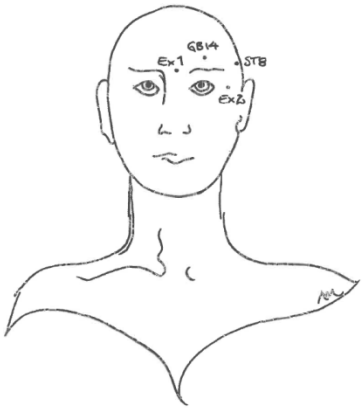
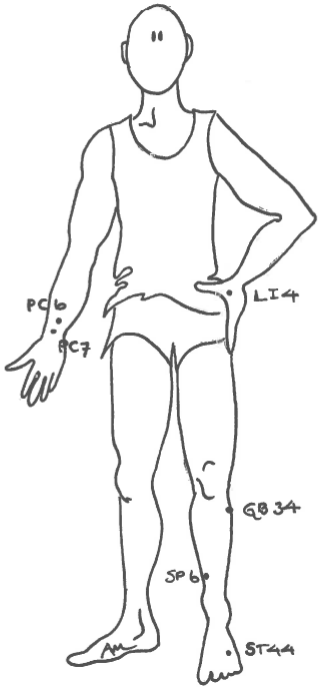
# APPENDIX

## Appendix 1. Acupuncture treatment points








Acupuncture points

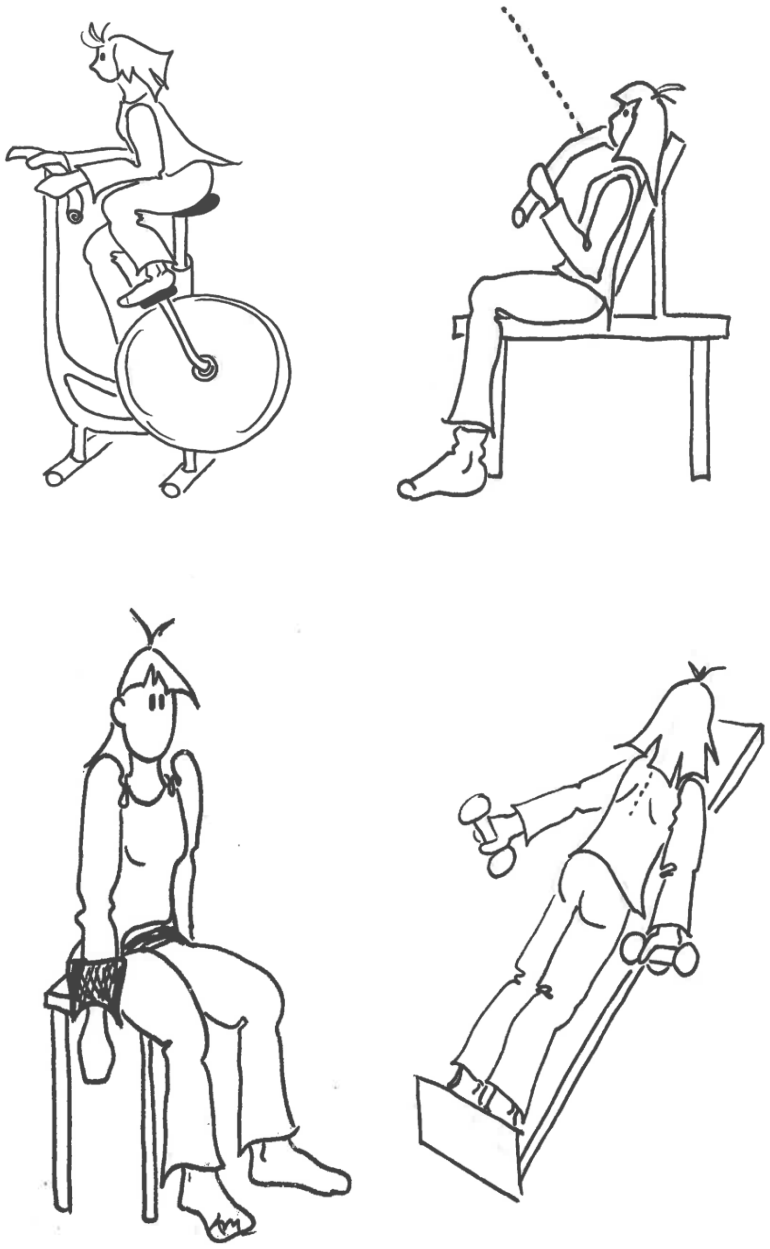
Mandatory points were; GB 20,

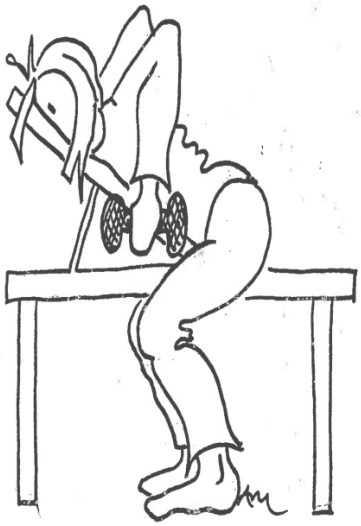
GB 14, LI 4 and ST 44

Optional point were; PC6, PC7, SP6,

GB34, ST8, EX2 and EX 1

# Appendix 2. Physical training program





# Appendix 3. Relaxation training program

**Part 1 and 2**

Progressive relaxation training. Relaxation for arms, face, neck, shoulders breast, stomach, thighs and calves. Learn to feel the difference between tense and relaxed muscles.

**Part 3 and 4**

Autogen relaxation training. Relaxation of different muscle groups with suggestion, and without the tension part. Practice relaxation and breathing.

**Part 5 and 6**

Practical relaxation training. Relaxation for daily life and relaxation in sitting position. “Quick relaxation”, learn to relax during a short period of time 20-30 seconds.

**Part 7 and 8**

Applied relaxation training. Learn how to practice relaxation training in real situations in daily life. Repetition.

**Part 9 and 10**

Practice of more progressive relaxation exercises. Practice of more autogenic relaxation exercises.

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