Can mindfulness alter pain sensitivity?

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Synopsis

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Preface

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1 | Introduction

Probably everybody experienced pain once, for instance due to a cut, a burn or a fall. The pain occurring right after an injury is called acute pain and disappears near-term. However, if the pain does not disappear the pain is look apon as chronic pain. [**Briggs2010**, **Mello2016**]

Approximately 1.5 billion people, which equals 20% of the population suffer from permanent pain [**Zeidan2016**, **Macfarlanea2016**]. The characteristic of chronic pain is a duration more than three months [**Mello2016**]. Due to the persistence of pain the patients get restricted physically as well as psychically. The patients' ability to participate in diverse activities decreases. Those activities are not only physically but also socially. Like maintaining an independent lifestyle and relationships to friends and family can be affected. Besides the impacts on life, pain has impact on the work life. A survey in nine european countries [1], indicates that the persistence of pain had a lasting effect on their employment status for 25% of the patients. These patients changed their job, the job responsibilities or lost their job. Furthermore 21% of the employees were diagnosed with depression. [**Breivik2006**]

25 % of the chronic pain patients suffer from neck pain [**Macfarlanea2016**]. Those patients are restricted by negatively affected fatigue and concentration [**vanRanderaat2016**]. Furthermore they suffer, like the majority of chronic pain patients, from anxiety and depressed mood, cognitive distress and the resulting physical limitations. [**gross2013**]

At the moment there is no cure for chronic pain patients. The current treatment methods only provide possibilities to relieve the pain. [**marcus2009**, **pope2017**] Nevertheless, the majority of the patients feels pain daily and this pain is increasing throughout the day due to the daily activities. [**Breivik2006**] Chronic pain is mainly treated by medication. However, those medicaments have side effects like abuse or organ damage. To avoid those risks, alternative methods are used. One of those methods is mindfulness meditation. Whereby meditation is used as mental training to achieve diminished judgment of emotions, cognitive control and existential insight. [**Zeidan2012**]

Previous studies show that mindfulness meditation provides the ability to enhance a broad spectrum of cognitive health outcomes. Furthermore stress, depression and anxiety can be relieved. This improvements are due to the mental training achieved by mindfulness meditation. Especially because of emotion regulation, cognitive control, acceptance and positive mood. [**Zeidan2012**, **Zeidan2016**]

The present study addressed if mindfulness meditation can alter pain sensation in the

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[1]FiXme Note: UK, France, Germany, Italy, Spain, Poland Sweden, Norway, Denmark

neck by measuring pressure pain threshold and pressure pain tolerance before and after short-term mindfulness meditation. Therefore the hypothesis *"Short-term mindfulness meditation practice increases the pressure pain threshold and pressure pain tolerance in the upper trapezius"* was tested.

2 | Background

2.1 Pain

Pain is defined, by the International Association for the Study of Pain, as an unpleasant sensory and emotional experience associated with actual or potential tissue damage [**Kerstman2013**]. Pain is a sudden or slow onset of any intensity from mild to severe pain [**Mello2016**] and can be categorized based on the pain experience as acute, chronic and intermittent pain [**Goldberg2011**]. Acute pain is anticipated or predictable, while chronic pain is not anticipated or predictable. Chronic pain has a duration greater than three months with a constant or recurring of pain. Contrary to chronic pain, intermittent pain is not constant but has interruptions in between [**Mello2016**].

Pain is a worldwide problem and affects all populations regardless of gender, age, income, ethnicity or geography. However, the distribution across the globe differs due to different risk factors such as female gender, injury and psychosocial environment [**Macfarlanea2016**]. The prevalence and incidence is high despite the complexity of quantifying pain. It is estimated that 20% of the world's populations adults suffer from pain and each year 10 % is diagnosed with chronic pain [**Goldberg2011**].

The frequently causes of pain are trauma, surgery, cancer, osteoarthritis and rheumatoid arthritis, injuries and spinal cord problems. Furthermore, pain can lead to different conditions, such as depression, inability to work, limited social relationships and suicidal thoughts. [**Goldberg2011**, **Breivik2006**]

People with chronic pain often complain of cognitive problems which interfere with their daily functions. Additionally, it is indicated that among people with chronic pain there is a consistent evidence for disturbances in attentional capacity, processing speed, and psychomotor speed. However, the relationship between pain and cognitive problems is unknown. [**Geisser2018**]

2.1.1 Types of pain

Pain can be divided into nociceptor pain and neuropathic pain [**Steeds2013**]. Nociceptor pain can be classified attending to the location of pain as somatic pain or visceral pain. Somatic pain occurs when nociceptors in skin, muscles, skeleton, joints or connective tissues are activated. Visceral pain is defined as pain that results from the activation of nociceptors in the thoracic, pelvic or abdominal viscera. Unlike somatic pain, visceral pain is harder to localize within the body. Another type of pain is neuropathic pain, which is caused by a primary lesion or dysfunction of the peripheral nervous system or central nervous system. The main difference from nociceptor pain is that neuropathic pain has an absence of continuous nociceptive inputs. [**Kerstman2013**]

2.1.1.1 Nociceptor pain

Nociceptors are free nerve endings and have a high threshold for mechanical, chemical or thermal stimulation. There are two types of nociceptors, $\alpha\delta$ and C fibers. $A\delta$ fibers are myelinated nerve cells with a diameter between 2 and $5\mu m$, which produce fast well localized sharp pain. Those fibers are mostly distributed in the body surface, muscles and joints. C fibers are unmyelinated nerve cells with a diameter below $2\mu m$, which produce slow and poorly localized burning and throbbing pain. The C fibers are distributed in most tissues. [**Steeds2013**]

When a noxious stimulation occurs, the nociceptors will be activated and propagate the pain information to the spinal cord via dorsal horn, which is illustrated as the red arrow on figure 2.1 [**Martini2012**]. The second order neuron is activated by the release of neurotransmitters from the nociceptor. The second order neuron receive these information and cross over to the opposite side of the spinal cord and brings the information towards the brain via the lateral spinothalamic tract, which is indicated by the white arrow on figure 2.1. This information will be transmitted by releasing neurotransmitters to the third order neuron in the thalamus. The third order neuron localizes and discriminates the pain in the brain, illustrated as a black arrow on figure 2.1, but in the opposite side from where the pain actually occurred. Perception of pain on the right side of the body is processed on the left side of the brain and vice versa [**Martini2012**].
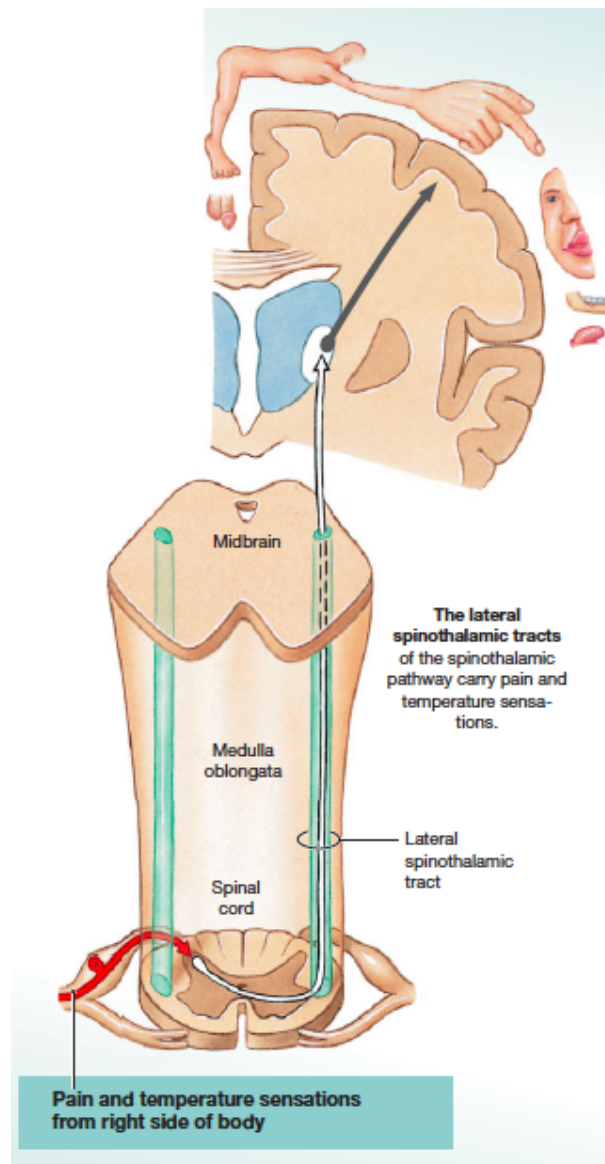
Figure 2.1: Spinothalamic pathway. Modified [**Martini2012**]

2.1.1.2 Neuropathic pain

Neuropathic pain is caused by a disorder in the somatosensory system and is often a chronic condition related to injuries or diseases [**Mindruta2013**]. The disease occurs at different levels in the nervous system and affects the signaling of pain. It is difficult to localize the distribution of neuropathic pain compared with nociception pain. However, neuropathic pain can be described based on the mechanism and be divided into peripheral, central or mixed syndromes correspond to the anatomy and the underlying disease. This mechanism can, however, produce painful symptoms in the same disease, but it would take different aspects. The sensation can be described as a sudden pain which is burning, tingling, shooting stabbing or numb and can be intermittent or continuous.

[**Mindruta2013**]

2.2 Assessment of Pain

Pain is described as a complex and subjective experience that poses a number of measurement challenges due to its subjective nature. Nevertheless, pain measurements are necessary for pain studies as well as the evaluation of methods to control pain. [**Jensen2001**] There is no valid and reliable method of objectively quantifying pain at the moment. Despite the challenges that pain measurement present, several tools and approaches can be employed in order to collect useful pain estimates. [**Younger2010**] The aim of pain assessment is to diagnose the cause, understand the impact, identify appropriate pain relief strategies and evaluate their effectiveness [**Briggs2010**].

There are different dimensions of pain experience that can be assessed: pain intensity, pain affect, pain quality and pain location. Pain intensity defines how much the pain hurts. Pain affect refers the degree of emotional arousal or changes in action due to the sensory experience of pain. Whereas pain quality concerns certain physical perceptions, which are associated with the description of pain, such as pins and needles, prickling or burning.

The intensity of pain can be assessed using unidimensional scales, which explore only one dimension of pain [**Jensen2001**]. Chronic pain is too complex to assess with only unidimensional scales, as the pain affect the patients' functions, quality of life, emotional state, vocational status, social life and well-being, why multidimensional scales are necessary [**Ebert2010**].

2.2.1 Unidimensional scales

One used unidimensional tool is the Verbal Rating Scale (VRS) which consists of a list of adjectives describing different levels of pain intensity, as illustrated on figure 2.2. This type of scales are easy to administer, score and apprehend. However, it has several statistical disadvantages and criticism raised due to the fact that assumes equal intervals between the adjectives. [**Jensen2001**] For this particular reasons along with others it is used when the patient's conditions require it [**Jensen1986**].

[ ] No pain   [ ] Mild pain   [ ] Moderate pain   [ ] Servere pain

Figure 2.2: Verbal Rating Scale (VRS). Modified [**Jensen2001**]

Another possibility of unidimensional scales is a Visual Analogue Scale (VAS). VAS consists of a 10 cm line, as shown in figure 2.3, the ends of this line are labeled as the extremes of pain. The scale is scored by measuring the distance from 'no pain' end to the patient's mark. This fact makes the VAS more sensitive to changes in pain intensity. However, one

of the drawbacks is that scoring time is higher than for other methods. [**Jensen2001**]

Figure 2.3: Visual analogue scale (VAS). Modified [**Jensen2001**]

Another method is the Numerical Rating Scale (NRS), which is illustrated on figure 2.4 and is the most used by clinicians, due to the usefulness of administration and scoring [**Fillingim2016**]. NRS consits of an numerical scale from 0 to 10, being described 0 as 'no pain' and 10 equal to 'higest level of pain'. The advantage of NRS is that it not requires patients mobility because the response is given verbally. NRS is a valid method and demonstrates positive and significant correlations with other measures of pain intensity [**Jensen2001**].

Figure 2.4: Numerical Rating Scale (NRS). Modified [**Jensen2001**]

Pictures or face scales can be used to illustrate facial expressions of different intensities of pain. The primary purpose of these scales was to offer individuals, which have problems with written language or cognitive difficulties, an option to express pain intensity. There is evidence that the pictures or face scales are a valid method [**Jensen2001**].

2.2.2   Multidimensional scales

[1] Multidimensional scales are convenient in relentless pain conditions. There are a lot of multidimensional scales, which purpose are to measure several dimensions of pain with different combinations of these dimensions. These scales offer a more detailed reflection of the patient's pain experience [**Briggs2010**].

The most common used is MPQ, which consists of 78 words and describe the pain in sensory, affective and evaluative terms. These terms are arranged in groups according to the quality of pain and intensity of this pain. A 6-point VRS is used to determine the intensity of the pain. The MPQ is proved as a valid method support by several studies. One disadvantage of the MPQ is the length and complexity, why a brief form of this questionnaire has been introduced, the short-form McGill Pain Questionnaire (SF-MPQ), which consists of 15 different descriptors in sensory and affected terms. Each descriptor is rated on a 4-point VRS scale. [**Katz2001**]

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[1]FiXme Note: rearrange this section!!!

Another scale, Brief Pain Inventory (BPI), was developed to assess cancer pain and has been proven as a useful instrument to asses different kinds of pain in several clinical settings. The BPI measures pain severity, pain quality and the disturbance in the patients' daily life. Two subscales score pain intensity and pain interference [**Katz2001**].

Pain drawing is often used for estimating the location of pain and involves a front and back drawing of the human body. A second common used method is the checklist, which is a simple list of possible sites of pain. [**Jensen2001**]

2.2.3   Quantitative sensory testing

The Quantitative Sensory Testing (QST) is a method to assess the patients' response to quantifiable sensory stimuli in order to characterize the location of pain relating to somatosensory function or dysfuction. QST is used for assessing neuropathic pain and includes different modulations of stimulation, such as thermal (heat, cold), mechanical (tactile, pressure, vibration), electrical, ischemic and chemical. These stimuli and parameters can be selected in order to systematically evaluate the somatosensory transmission and pain processing by engaging different nerve fibers, endings and pathways of the central nervous system. [**Fillingim2016**] Approaches for QST, which are used in clinical practice, are the Frey monofilmaments and tuning forks which are used to measure mechanical sensation. Heated or cooled metal rods can be used to assess thermal sensitivity. The sensitivity of pressure pain can be assessed by a pressure algometer. [**Fillingim2016**]

2.2.3.1   Assessment of Pain Thresholds

As a result to a set of experimental noxious stimuli, it is possible to obtain different parameters such as pain thresholds, tolerance or suprathreshold pain intensities. Threshold is defined as the stimulus that produces an arbitrary but defined level of performance. There is a distinction between receptor or absolute threshold and psychophysical or sensory threshold. Absolute threshold is the energy required to elicit response in the primary afferent while the psychophysical or sensory threshold, is the minimal energy necessary to reach perception. Due to the fact that receptor threshold is lower than sensory threshold, the sensory threshold is a convenient parameter which offers the transition point between non-painful and painful stimulus. [**Yarnitsky2006**] Pain tolerance is defined as the maximum level of pain a person can tolerate.

As a result to a set of experimental noxious stimuli, it is possible to obtain different parameters such as pain threshold or tolerance. Threshold is defined as the stimulus that produces an arbitrary but defined level of performance. There is a distinction between receptor or absolute threshold and psychophysical or sensory threshold. Absolute threshold is the energy required to elicit response in the primary afferent while the psychophysical or sensory threshold, is the minimal energy necessary to reach perception. Due to the fact that receptor threshold is lower than sensory threshold, the sensory threshold is a convenient parameter which offers the transition point between non-painful and painful

stimulus. [**Yarnitsky2006**] The pain tolerance is the highest intensity of painful stimulation that a tested subject is able to tolerate. Psychophysical research has been mostly focusing on thresholds measurement [**Pelli2010**]. The three most common methods used for testing the perception in stimulus detection are the method of adjustment, method of limits and method of constant stimuli.

- **Method of adjustment**: The magnitude of a stimulus dimension is adjusted until a prespecified criterion is reached. This method is useful for obtaining a rough threshold estimate to guide the choice of stimulus magnitudes for a forced-choice procedure, when there are different conditions to be measured. [**Kingdom2016**]

- **Method of limits**: The magnitude of the stimulus is presented either in ascending or descending order. The subject indicates whether or not the stimulus differs from the baseline. Accordingly, the threshold in each case is the stimulus magnitude at which the response switches from non perception to perception and/or vice versa. [**Kingdom2016**]

- **Method of constant stimuli**: The magnitude of the stimuli is randomly selected from a predefined set. This range is selected to straddle the threshold value. If the data generated by this method fits with the appropriate psychometric function, it provides the most accurate estimates of the threshold. The choice of this stimulus set sometimes demand pilot work to obtain an estimate of the threshold. [**Kingdom2016**]

2.3 Treatment of chronic pain

There are several treatments for chronic pain patients, depending on the modalities and intensity of the pain. Besides conservative methods, alternative methods are applied to reduce chronic pain. [**marcus2009**, **pope2017**]

None of the different treatment methods are enough or sufficient when applied alone. But an individual combination considering the needs of each patient alleviates the suffering of the chronic pain. At the moment it is not possible to cure chronic pain, but to relieve the suffering. [**marcus2009**, **pope2017**]

The commonly used treatment method is medication. The disadvantage of medication is the risk of side effects. In contrast to medication, alternative methods do not provide any negative side effect. However some of those methods require a specialist for instruction and/or application, which results in high cost. [**marcus2009**, **pope2017**]

2.3.1 Medication

Medication is a common way to treat severe chronic pain patients. Those medicaments can be divided in three groups, the coanalgesic medicaments, the non-opioid and the

opioid analgesics. [**marcus2009**]

- **Coanalgesics** are normally used to treat other diseases, for example depressions, but still provide analgesic qualities. They are often used to treat fibromyalgia, chronic headache and neuropathic pain. Often coanalgesics are combined with analgesicts to extended pain-relief. [**marcus2009**]

- **Non-opioid analgesics** are used to reduce intermittent mild to moderate pain. To this category belong nonsteroidal anti-inflammatory drugs, which decrease inflammation and provide analgesic properties. Non-opioid analgesics are especially used in short-term-therapy. Non-opioid analgesics inhibit the prostaglandin synthesis. Prostaglandin has a protective effect to the organs. A permanent use of non-opioid analgesics encourages prostaglandin effects, which conduct in severe organ toxicity. Known side effects are for example gatrointestinal toxicity, pephrotoxicity and a increased risk of cardiovascular diseases. [**marcus2009**, **stein2007**]

- **Opioid analgesics** provide stronger analgesic qualities than non-opioid analgesics and show no prostaglandin effect. These analgesics work by bending in the central nervous system to the opioid or NMDA receptors. Because of this better long-term tolerability, opioid analgesics are used in patients which suffer from chronic non-malignant pain. But the use of opioid analgesics accompanies with the risk of abuse and misuse. Studies have shown that the median time until abusive behavior is 24 months. Treatment targets and specific requirements are set to minimize this risk. [**marcus2009**, **stein2007**] The decision, if non-opioid or opioid analgesics are used, is based on weighing safety, tolerability and effectiveness. The superior effectiveness and the lower organ toxicity of opioid analgesic outweigh the risk of abuse or misuse. [**marcus2009**]

2.3.2 Physical therapy

Physical therapy is applied with the aim to enhance the patients' flexibility, general fitness and musculature. This is achieved by motion exercises and passive joint mobilization to enhance the muscle function and the joint stability and mobility. A special program is adapted to the patients' needs. Components of this program might be moist heat, cryo therapy, ultrasound and transcutaneous electrical stimulation. Furthermore, assistance can be provided by manual therapy or exercise, which is included to improve the physical fitness, achieve weight loss and decrease the risk of chronic diseases encouraged by inactivity. [**marcus2009**, **pope2017**]

2.3.3 Lifestyle changes

Habits or life circumstances can intensify chronic pain. Changes of the lifestyle may help to decrease chronic pain. It is known that the pain sensitivity is negatively enhanced by

nicotine. Therefore quit smoking can be a step towards relieving chronic pain. Furthermore, chronic pain patients often suffer from insomnia. Sleep hygiene should be applied to reduce the occurrences as well as the severity of the sleep disturbances. If insomnia is due to medication, it should be revised, if it is possible to change the medication. Obesity is a risk factor in the likelihood to develop chronic pain, this is encouraged by the side effects of obesity like psychological disability or musculoskeletal pain. Besides, it encourages other health problems for example cardiovascular disease or diabetes. To improve this condition, weight loss should be achieved by the combination of diet and exercise. This will influence the recovery abilities from pain positively. [**marcus2009**, **pope2017**]

2.3.4   Psychological therapy

Psychological therapies have been promoted due to their potential effectiveness for the management of chronic pain and its conequences [**Eccleston2002**]. Psychological treatments are characterized as cognitive or behavioural strategies [**Eccleston2013**] which purpose is to helps patients to reduce depressions or anxiety and enhance a positive attitude. Also it assists patients to identify necessary lifestyle changes and implement them. [**marcus2009**, **pope2017**]. The most popular treatment program is Cognitive Behavior Therapy (CBT). The patients learn that their chronic pain condition has no cure but can be managed using different skills such as relaxation training, environmental changes or behavoiral experiments [**Burger2016**]. It has been shown that CBT can reduce pain right after a treatment, however the effect is slight[**Eccleston2013**]. Psychological trauma, victimization or serious emotional and relational conflict are not addressed on CBT, which is one of the limitiations.

2.3.5   Surgery

Surgery is a less frequent treatment technique. Commonly it is used to relieve patients from pain due to anatomic abnormalities. [**marcus2009**, **pope2017**] In some cases surgery is not a recommended treatment, where risk and benefits of surgery should be considered. In addition to this is surgery also one of the most frequently cases of getting chronic pain, as mention in section 2.1. Therefore, is should be weighted if it should be harked back to other and less invasive treatment options. [**pope2017**]

2.3.6   Alternative treatments

Beside the primary treatments others can be considered in a addition to these, also know as alternative treatments. Most of the alternative treatments are often associated with spritually and is not very well documented, why some people tend to be skeptical for these treatment types. However, many alternative treatments have shown to have an positive effect on chronic pain patients.

2.3.6.1 Acupuncture

Acupuncture is a treatment method where small sterile needles are inserted into the skin of the patient. The needles are inserted at specific acupuncture points related to the type of pain that the patient is experiencing. [**Dhanani2011**]. Acupuncture has shown promising results in reducing pain in patients with soft tissue around the shoulder joint, headaches, neck and shoulder pain, arthritis/osteoarthritis and low back pain. The effect of acupuncture can last for more than 3 months in 80 % of the patients [**Junnilla1983**].

2.3.6.2 Chiropractor

Chiropractic treatment is adjustment and manipulation of the spine in the patient to alignment the vertebrae of the spine to reduce pressure on the nerves running down the spine [**Gerald2013**]. In some cases this therapy will after a few treatments, increase flexibility of the spine of the patient and relieve the pain [**Peterson2012**].

2.3.6.3 Hypnosis

Hypnosis is a process where one comes into the state of trance and feels deep relaxation and is open to conversation verbally. Hypnosis is a guided process and can be carried out alone or by others. [**Gerald2013**] Factors as anxiety, depression and other states of mood and in general the social life of the patient has been shown to play a role in chronic pain. These mechanisms might be altered by hypnosis. In the literature hypnosis has shown positive results in pain relief, but only on a short term basis. [**Dhanani2011**] One of the drawbacks of hypnosis is the lack of standardization in hypnotic induction and interventions [**Alkis2010**]. Also the hypnosis susceptibility varies from person to person, why not everyone will have the same effect from it [**Spiegel2013**].

2.3.6.4 Yoga

Yoga is a form of mind to body practice discipline, or tradition originating from India. In the practice of yoga different physical postures, breathing techniques and more are the routine. Yoga is both, a form of personal evolution, but most popular because of the exercise which benefits the health. A review by Whitehead et al. [**Whitehead2017**] found that yoga could improve the functionality of the back and a slight effect of treating pain compared to non-yoga participants.

2.3.6.5 Meditation

Meditation can be described as the intentional self-regulation of attention from moment to moment [**Kabat1982**]. The term meditation encompasses a variety of mental-training practice which depend on the mental activity promoted, the amount of training recommended, the use and qualifications of an instructor, and the degree of emphasis on religion or spirituality. There are some meditative techniques integrated into an alternative approach such as dietary or yoga. [**Goyal2014**] Meditation practice can be divided into two main classes, concentration meditation and mindfulness or awareness meditation. While

the concentration methods restrict the attention to a point, an object, the breath or a mantra (mental sound) [**Kabat1982**], mindfulness meditation is the practice of being aware in the present moment [**Zeidan2016**]. The practice presupposes concentration to maintain steady attention instead of restricting attention to one object [**Kabat1982**]. Mindfulness meditation practice is said to have several health benefits like increase in cognitive function and decrease in stress, depression and anxiety. Through some of these mechanisms pain can be altered, eventually leading in pain relief. [**Zeidan2016**]

2.4 Mindfulness

Mindfulness has its roots in Buddhism and yogic tradition and is described as a non-elaborative and non-judgmental awareness of the present moment [**Kabat1982**, **Zeidan2012**, **Zeidan2016**, **Tang2017**]. Within a mindfulness stage one is focusing from one moment to the other and is aware of emotional, cognitive and sensory events. Those events are perceived as temporary, fading and changeable. Moreover one is neither rating nor reacting cognitive or emotional to those events. The mental state of mindfulness can be achieved by with mental training. [**Zeidan2012**, **Zeidan2016**] Thus can be said that mindfulness meditation is training of the mind [**Tang2017**].

Since thoughts and emotions are involved in the perception of pain, mindfulness provides the ability to relieve pain. Mindfulness cannot cure pain, but the patients will be able to deal with the pain easier and reduce the fear associated with pain. Thereby the patients engage more in their treatment instead of relying and focusing on the effects of medication. [**Jacob2016**] Often used methods to reach mindfulness are meditation and yoga practice [**Kabat1982**]. In this study meditation was used, because physical limitations are not affecting the meditation practice and no prior knowledge is needed [**Tang2017**].

2.4.1 Meditation classification

The most well practiced types of meditation are focused attention (FA) and open monitoring (OM).[**Zeidan2016**] FA is the training of concentration. The subjects keep their focus at an object or specific thing. Hereby the flow of breath is often used. If any disturbance comes by, like a thought, sound or other environmental distractions, which will often lead to a drift in attention, the person should always bring the attention back to the focus. [**Zeidan2016**] OM is the cultivation of open presence. The mind is open to anything, not focusing on any specific thing, just being in the present. If any thought or disturbance comes by, the thought or sensation should be noticed briefly, but then left without thinking more over it. FA is used to slide into OM, therefore it is necessary to master FA before one can reach OM. [**Perlman2016**, **Zeidan2016**, **Kabat1982**] Hence the chosen meditation practice in this study is FA.

2.4.2   Mechanisms of mindfulness

Previous research indicates that mindfulness meditation is promising for relieving pain, even though the research is limited, and the mechanisms behind mindfulness meditation are not fully understood yet [**Perlman2010**]. Studies show that enhanced emotion regulation, cognitive control, acceptance and positive mood have been linked with health benefits as well as pain modulation. These mechanisms are modulated during mindfulness meditation practice.

With mindfulness meditation one is able to take the attention away from the emotional component of pain. Therefore meditation practice can reduce the brain process areas related to anticipation of pain, which does not imply that meditation reduce the brain process related with pain. [**Brown2010**] Pain as well as meditation alter sensory, cognitive and affective dimensions of subjective experience. Therefore brain areas activated during meditation and nociception should be interconnected in a way. [**Zeidan2011**]

A study by Perlman et al. [**Perlman2010**] shows that practicing meditation could not lower the intensity of pain, but instead lower pain unpleasantness in the participants. [**Zeidan2012**, **Perlman2010**] Similarly, a study by Brown and Jones et al. [**Brown2010**] showed that the greater the experience is with meditation the lower the perception of pain unpleasantness. This results in lower activation of the right inferior parietal cortex (IPC) and midcingulate cortex (MCC). This findings are supported by a study by Lutz et al. [**Lutz2012**] which shows that unpleasantness rating of pain decrease with meditation experience.

A study by Gard et al. [**Gard2011**] reported that the brain pattern related with pain modulation during mindfulness differs to other pain coping strategies. An increased activation in the rostral anterior cingulate cortex (rACC) and the ventromedial PFC (vmPFC) in the anticipation of pain stage was found for mindfulness practitioners. The activation of this areas has been identify with positive emotions. Furthermore, the study by Gard et al. [**Gard2011**] found for mindfulness practitioners an increased activation in the rACC/vmPFC while anticipating pain. As well as decreased activation in the bilateral lPFC and increased activation in the posterior insula/S2 when receiving a stimuli. Moreover, a study by Grant et al.[**Grant2011**] showed that mindfulness practitioners have different neuronal responses to painful stimuli with a greater activation in the insula and thalamus and a decrease activity in PFC.

Different brain regions are involved in the practice of mindfulness meditation.
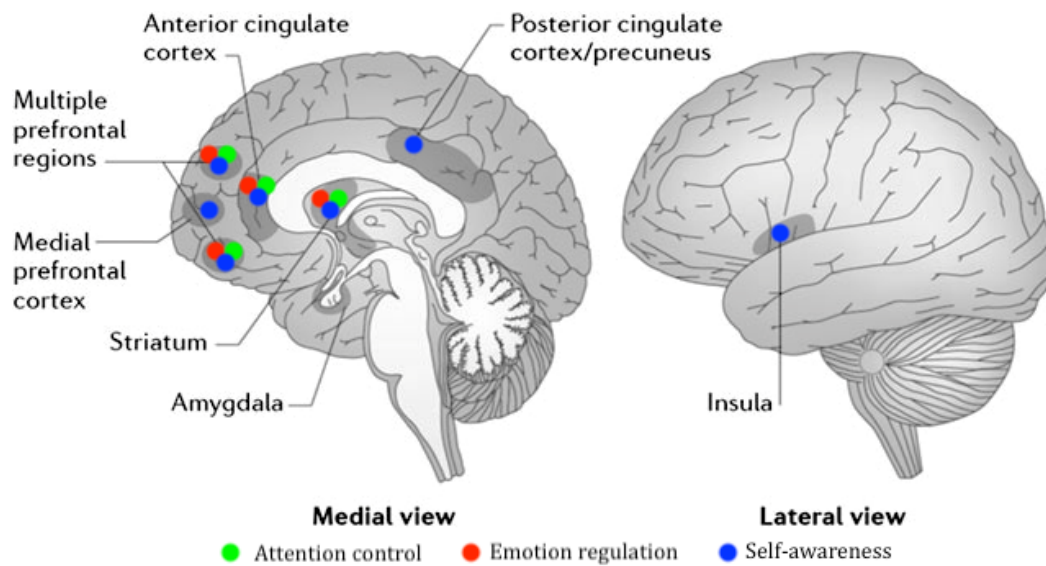
Figure 2.5: Specific regions in the brain involve when practicing mindfulness meditation [**Tang2017**].

Hence, the most involved in pain modulation via mindfulness meditation is the PFC and the ACC as illustrated in figure 2.5. Furthermore, striatum, insula and Default Mode Network (DMN), which includes the medial PFC and the Posterior Cingulate Cortex (PCC) are shown in figure 2.5. These regions play a big role in the effect of mindfulness meditation and are highly regulating the mechanisms of meditation which can generally be catergorized into three catagories: attention control, emotion regulation and self-awareness.

- **Attention control** is the ability to maintain focus, for instance on the breath during FA meditation. This mechanism includes mainly ACC, PFC and the striatum, which are illustrated in figure 2.5 as the red dots. Increased activity in the dorsal lateral PFC is required to hold an increased attention, as well as deactivation of the areas of the brain that makes the mind drift, which include the medial PFC. [**Tang2017**]

- **Emotion regulation** includes the emotions that arise, when they occur and how they are experienced and expressed. This mechanism involves multiple prefrontal regions, limbic regions and striatum, which are regions primary regulating the emotional thoughts through the limbic system also responsible for goal setting. These regions are illustrated as green dots on figure 2.5. This need for regulating the emotional control is important because the participant needs to be able to handle boredom or negative mood during the meditation. Stronger subgenual and adjacent ventral ACC activity is present with meditation. This brain area is involved with emotion regulation and attention control. The dorsal lateral PFC and amygdala plays some role in regulation of emotion. [**Tang2017**]

- **Self-awareness** includes the awareness of oneself, the awareness of being conscious as well as meta-awareness, which is the awareness of the internal bodily state. Regions of the brain involves midline cortical structure DMN, ACC, the insula, medial PFC and PCC, as illustrated in figure 2.5 as blue dots. Reduced activity in midline cortical structure including the DMN, more reduction in the posterior part PCC, than the anterior part medial PFC, but increased in perigenual ACC activity. [**Tang2017**]

2.4.3   Stages of meditation

Different expertises of meditation appear to modulate the dynamic balance between anterior and posterior midline networks involved in different aspects of self, cognitive self, bodily self and phenomenal experiential self. This reflects self plasticity following meditation. The effort to get into the meditative state varies according to your experience level with meditation. Often this experience level can be divided into three stages, early, middle and advanced practice of meditation. These stages, illustrated in figure 2.6, determine the amount of effort to get into the meditative state [**Tang2017**].
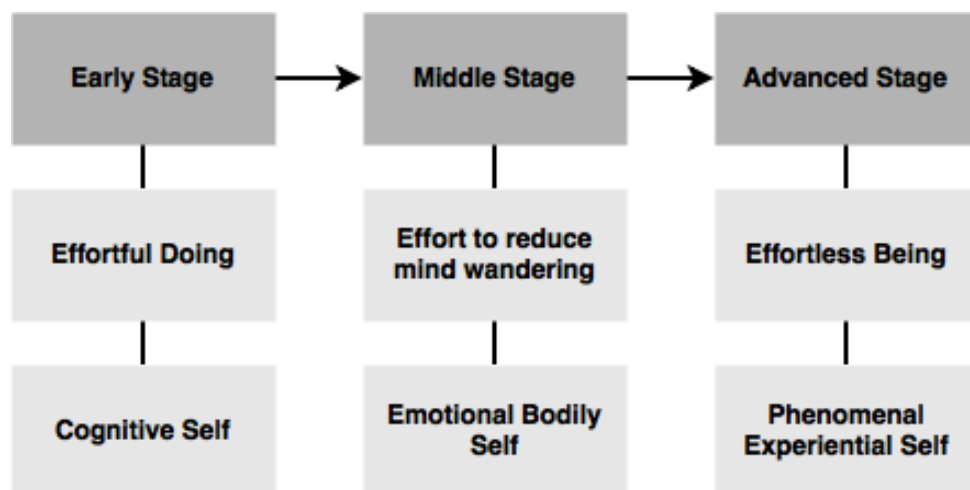
Figure 2.6: The three stages of meditation practice describe the effort, which is necessary, to get into the meditative state. [**Tang2017**]

In the early stage more mental effort is required. Here the dorsal lateral PFC and partial cortex are often involved and activated more. A stronger deactivation in the DMN occurs when more effort is used. With less effort, the ACC and striatum will participate more. [**Tang2017**]

The neural mechanisms behind mindfulness meditation in relieving pain has been researched. Experiments with stimulation of nociceptive pain have shown an increase in active areas of the PFC while meditating. Participants express that they feel the pain but are able to deal with it better during meditation focusing on the breath. The mechanisms

working in analgesia are not the same as the mechanisms during meditation, why the two methods do not interfere with each other. [**Jacob2016**]

The different areas of the brain show either a reduction or increase in activity when performing meditation. Through meditation the person trains the mind, and specific regions will grow. [**Zeidan2012**]

2.5   State of the Art

Chronic pain has been investigated for years in order to understand the mechanisms behind and the topic is still relevant to explore as many people suffer from chronic pain. Furthermore, it is an issue that pain is difficult to treat due to the individually experience of pain and the subjective assessment of pain. [**Briggs2010**, **Norton1999**]

Currently there is no cure for chronic pain, only relief treatments. The primary treatment is pharmaceutical, which has possible side effects, such as abuse or toxicity. Alternative treatments like physical therapy, chiropractic and acupuncture have shown an impact in relieving pain. But these treatments will most likely be used in combination with pharmaceutical treatments. Many alternative treatments have disadvantages such as high costs, why the decision for these treatments should be considered well, to ensure that it suits the patients' needs and to maximise the effect for the cost. [**marcus2009**, **pope2017**]

Mindfulness meditation has proved to relieve conditions such as stress, depression and anxiety through the ability to enhance emotion regulation, cognitive control, acceptance and positive mood [**Zeidan2012**, **Zeidan2016**]. Studies have investigated the usefulness of mindfulness meditation for people with chronic pain showing promising results in pain relief. [**Kabat1982**, **Rosenzweig2010**]

The most commonly used mindfulness-based intervention is Mindfulness Based Stress Reduction (MBSR) [**Cramer2012**]. MBSR consist of 8 or 10 weeks of mindfulness meditation where the patient have to attend once a week a course for 2 hours and 45 minutes session at home 6 days per week [**Kabat1982**, **Chiesa2010**]. Patients suffering from chronic pain improved pain symptoms as well as life quality after the finalization of MBSR [**Zeidan2012**]. Patients suffering from chronic pain improved pain symptoms as well as life quality after the finalization of MBSR. [**Zeidan2012**] Hence, MBSR provides significant improvement for patients suffering from neck pain [**Rosenzweig2010**].

Even though long-term mindfulness meditation is the most investigated, short-term mindfulness training has also shown relief of pain. The studies have investigated different duration of meditation practice and time period within short-term mindfulness meditation. Consequently the boundaries of short-term mindfulness meditation are not well defined. A study by Ussher et.al. [**Ussher2012**] showed in a clinical setting that 10 minutes mindfulness-based body scan reduces distress and the perception of pains' impact on daily living. However, the study found no effect outside the clinical environment

[**Ussher2012**]. Another study by Zeidan et.al. [**Zeidan2012**] proved that only three days of mindfulness meditation with a 20 minutes session each day have an effect on relieving chronic pain.

Some studies have studied the effect of mindfulness meditation for musculoskeletal chronic pain unifying lower and upper back pain, shoulder and cervical pain [**Chiesa2010**]. Nevertheless, there is not much literature available focusing on chronic neck pain, which about 25 % of the patients suffer from [**Macfarlanea2016**]. The most investigated method is MBSR, mostly over a time period of two months or more. A shorter time period of mindfulness meditation has not been investigated focusing on neck pain.

3 | Problem formulation

Approximately 375 million people suffer from chronic neck pain. The primary treatment for those patients is medication. But medication has side effects, as described in 2.3. Besides medication, alternative treatment methods are used, often in combination with medication. For example physical therapy, chiropractor or psychological therapy have showed a positive influence on pain relief. Most of the alternative treatment methods are related with high costs, because they require a specialist for the application. Whereas mindfulness meditation can be practiced alone. Hence a lot of studies focused on the ability of mindfulness meditation to relieve pain. As mentioned in 2.5, there are not many studies which show the effect of mindfulness meditation on chronic neck pain. Since a lot of people suffer from chronic neck pain this study investigates the influence of mindfulness meditation on neck pain.

Pain levels of chronic pain patients are not easy to assess and quantify. Chronic pain patients experience an habituation effect to the pain, also there are variations of the pain sensitivity between days and throughout the day which makes difficult to get reliable and comparable pain levels on these patients. Furthermore, chronic pain is a subjective and multidimensional experience. Hence, another way to get comparable values of pain was chosen. Therefore pressure pain was applied with an algometer to healthy subjects. Pressure pain threshold and pressure pain tolerance values were used to test the following hypothesis: *Short-term mindfulness meditation practice increases the pressure pain threshold and the pressure pain tolerance in the upper trapezius.* Even though the study was conducted in healthy subjects, the sensation of the pain and the effects of meditation to the pain sensitivity can be transferred to chronic pain patients.

4 | Methods

4.1 Subjects

42 healthy subjects were recruited for the experiment, 21 males (M) and 21 females (F) with a mean age of 23.93 ± 2.74 years. To get a homogeneous group of participants, specific inclusion and exclusion criteria were formed for this experiment.

Inclusion criteria:
- Age between 20 and 30 years
- No obesity
- Must have time to meditate for 5 days, 20 minutes per day.

Exclusion criteria:

- Ongoing meditation practice
- Pregnancy
- Neurological, musculoskeletal or mental illness
- Abusive drug or alcohol use [1]
- Medication with antidepressant or analgesic properties
- Lack of ability to cooperate

4.2 Study design

The subjects, recruited for the experiment, were assigned in two different groups. Whereby an equal amount of females and males were assigned. The treatment group was measured before and after the intervention, which was the practice of mindfulness meditation. To ensure that a measured effect was not due to habituation to the measurement, a control group was measured with the same time difference. Moreover, to minimize bias, the examiner was blinded. The structure of the study design is illustrated on figure 4.1.

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[1] FiXme Note: Think about this 'abusive'
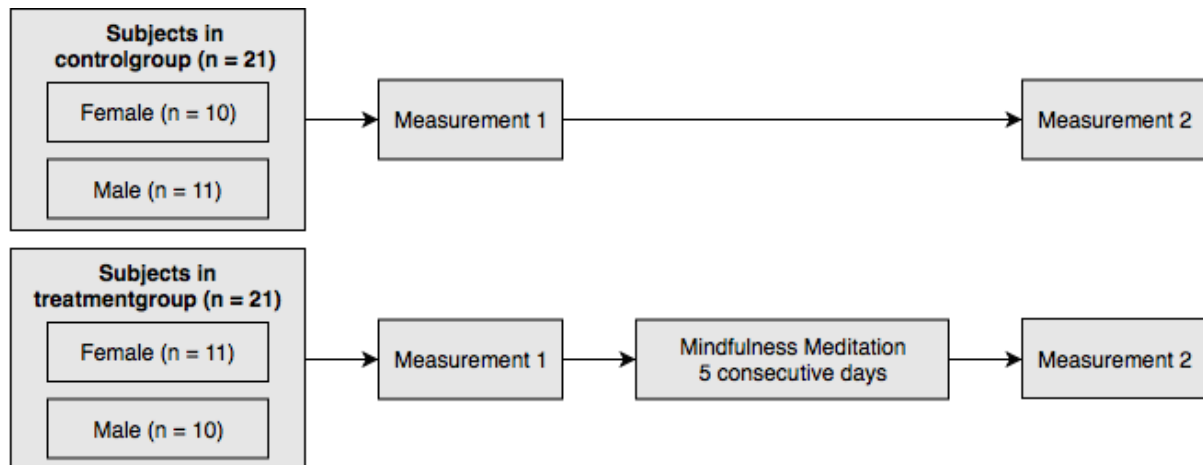
Figure 4.1: Parallel study design.

4.3 Procedure

First of all, general information about the subjects' were collected, such as gender and BMI, which is illustrated in section 8.1. Furthermore, information about the experiment was given to the subjects. Measurement points were marked at the upper trapezius on right side, as illustrated on figure 4.2 while the subjects lay prone to ensure reliable and rapid location during the experimental procedure. The location of the upper trapezius was determined between the acromion and 7th cervical vertebra. The distance was notated so the same locations could be used for each measurement session.

Figure 4.2: Measurement on the upper trapezius. The measurement points are mark with black dots.

The pressure pain threshold was measured with an algometer (Wagner Force Ten ™ Digital force Gage). Firstly, the algometer was applied until the subject begins to feel pain and the pain threshold was notated. Secondly, the pressure pain tolerance was measured with the same algometer at the same points and the pressure was applied until the subject reached the maximum level of pain.

The same measurement routine was conducted three times. Each measurement was no-

tated and an average was used for the pain threshold and pain tolerance respectively. To avoid oversensation, there was 5 minutes pause in between the measurements.

To test the effect of mindfulness meditation on the pressure pain threshold and the pressure pain tolerance, the treatment group practiced 20 minutes mindfulness meditation for 5 consecutive days. To ensure same meditation conditions for all of the subjects, a guided meditation in form of an audio file was used. Furthermore, subjects were told to have the most comfortable position during the meditation. Additionally a short introduction to mindfulness meditation was provided on the first day.

The subjects of the control group continued their normal routine. After the last meditation session of the treatment group the second measurements were conducted. The same time interval between the measurements were used for the subjects of the control group. The second measurement session was conducted likewise the first measurements.

4.4 Data Analysis

5 | Results

5.1 Difference in Threshold and Tolerance

The mean of the threshold and tolerance before and after and the difference between these values for the treatment group and control group are illustrated in table 5.1 and table 5.2 respectively. The standard deviation for these values are illustrated in table 8.3 and table 8.4 in section 8.2. The tolerance for some of the subjects are not representative, as the examiner was not able to applied a valid force with the algometer.

	Threshold			Tolerance		
	Pre [KgF]	Post [KgF]	Diff [%]	Pre [KgF]	Post [KgF]	Diff [%]
#T1	1.84	1.53	-17.03	4.21	3.93	-6.66
#T2	2.95	2.85	-3.50	7.63	5.70	-25.26
#T3	2.13	3.07	43.75	7.75	8.13	4.99
#T4	0.94	2.34	148.94	3.85	4.95	28.55
#T5	1.35	1.71	26.11	3.11	3.94	26.55
#T6	0.31	0.94	206.52	5.95	5.99	0.67
#T7	2.07	2.74	32.15	5.44	8.82	62.13
#T8	1.82	3.59	97.44	7.21	10.11	40.11
#T9	2.17	2.84	31.08	6.98	9.62	37.82
#T10	4.71	4.85	3.12	12.37*	13.24*	7.06
#T11	2.22	4.31	93.99	4.45	7.76	74.25
#T12	1.99	2.51	26.51	4.45	4.79	7.49
#T13	1.14	2.37	108.19	4.48	6.57	46.58
#T14	1.69	1.01	-40.55	6.04	3.93	-34.88
#T15	2.03	2.58	27.30	8.57*	14.28*	66.56
#T16	2.79	2.39	-14.32	13.35*	13.59*	1.80
#T17	3.24	2.76	-14.81	11.75	11.77*	0.11
#T18	2.16	1.98	-8.33	8.38*	11.93*	42.32
#T19	1.77	2.10	18.42	9.66	10.91	12.87

#T20	2.28	3.35	46.78	7.20	14.01*	94.54
#T21	3.91	3.82	-2.22	7.18	10.58	47.35

Table 5.1: Threshold and tolerance before and after and the percentage difference between these values for the treatment group. The asterisk indicated that the tolerance was not representative.

	Threshold			Tolerance		
	Pre [KgF]	Post [KgF]	Diff [%]	Pre [KgF]	Post [KgF]	Diff [%]
#C1	3.04	5.00	64.47	7.80	12.07	54.79
#C2	1.85	2.27	22.30	7.35	9.45	28.68
#C3	1.92	1.81	-5.90	4.90	4.32	-11.84
#C4	1.93	2.09	7.93	6.25	7.31	16.97
#C5	2.01	4.73	134.77	11.46*	13.77*	20.19
#C6	2.60	3.45	32.56	7.85*	14.05	79.01
#C7	3.60	4.34	20.56	6.57	8.96	36.31
#C8	1.98	2.57	29.97	10.25	10.91	6.37
#C9	2.59	3.19	7.9	8.89	9.51	6.90
#C10	4.61	6.80	47.61	12.85*	10.65*	-17.17
#C11	1.27	1.29	1.58	3.56	5.21	46.25
#C12	2.31	4.32	87.28	9.45	10.05	6.28
#C13	4.47	2.56	-42.69	8.51	9.67	13.67
#C14	1.85	3.07	66.43	5.17	7.00	35.31
#C15	1.14	1.98	73.68	5.83	5.17	-11.43
#C16	2.05	2.06	0.32	8.21	7.98	-2.84
#C17	1.52	1.81	18.86	10.77	6.91	-35.79
#C18	1.98	2.05	3.70	4.26	4.36	2.35
#C19	5.58	2.36	-39.78	18.17*	14.39*	-20.81
#C20	2.41	2.97	23.27	7.80	8.96	14.87
#C21	3.83	4.06	5.91	11.65	11.32	-2.78

Table 5.2: Threshold and tolerance before and after and the percentage difference between these values for the control group. The asterisk indicated that the tolerance was not representative.

The total difference in threshold and tolerance with associated standard deviations are illustrated in table 5.3. [1]

	Threshold Difference [%]	Tolerance Difference [%]
Treatment	38.35 ± 61.11	25.47 ± 33.22
Control	26.42 ± 41.68	12.77 ± 27.27

Table 5.3: The total percentage difference between threshold and tolerance and the associated standard deviation for both treatment and control group.

5.2 Statistics

Statistics tests were tested on the threshold and tolerance before and after and difference between threshold and tolerance for both the treatment and control group. As some of the tolerances were not representative the test have been divided into a test with all the subjects, and one test which excluded the subjects with a valid tolerance.

5.2.1 All subjects

A Shapiro-Wilk test ($\alpha > 0.05$) has been used to test for normality for the threshold and tolerance before and after for both treatment and control group. The result from the test is illustrated in table 5.8.

	Threshold		Tolerance	
	Pre	Post	Pre	Post
Treatment (21)	0.173*	0.852*	0.149*	0.121*
Control (21)	0.016	0.080*	0.155*	0.514*

Table 5.4: Shapiro-Wilk test for normality for threshold and tolerance before and after for treatment and control respectively. The asterisk indicate normality.

A normal distribution was not seen between the treatment and control group for all the subjects, why a non parametric test, Kruskall Wallis ($\alpha < 0.05$), was used to test if there is a difference between the groups. Result from this test is illustrated in table 5.5.

	Threshold		Tolerance	
	Pre	Post	Pre	Post

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[1]FiXme Note: Would it be better to have this earlier with the other text?

Subject (42)	0.327	0.352	0.155	0.669

Table 5.5: Kruskal Wallis Test for threshold and tolerance difference for treatment and control respectively. The asterisk indicate normality.

There was no significant difference between the threshold and tolerance before and after. To test the normality of the difference between threshold and tolerance a Shapiro-Wilk test ($\alpha > 0.05$) has been used. The result from the test is illustrated in table 5.6.

	Threshold	Tolerance
	Difference	Difference
Treatment (21)	0.013	0.888*
Control (21)	0.233*	0.856*

Table 5.6: Shapiro-Wilk Test for normality for threshold and tolerance difference for treatment and control respectively. The asterisk indicate normality.

A normal distribution was not seen between all the threshold and tolerance difference, why a the, Mann Whitney U ($\alpha < 0.05$), was used to test the if difference between the groups. Result from this test is illustrated in table 5.7.

	Threshold	Tolerance
	Difference	Difference
Subject (42)	0.850	0.195

Table 5.7: Mann whitney for threshold and tolerance difference for treatment and control respectively.

The test indicate that there was no significant difference between the difference in threshold and tolerance.

5.2.2   Without excluded subjects

A Shapiro-Wilk test ($\alpha > 0.05$) has been used to test for normality for the threshold and tolerance before and after for both treatment and control group. The result from the test is illustrated in table 5.8.

	Threshold		Tolerance	
	Pre	Post	Pre	Post
Treatment (15)	0.377*	0.930*	0.582*	0.142*

Control (17)	0.077*	0.107*	0.976*	0.426*

Table 5.8: Shapiro-Wilk Test for normality for threshold and tolerance before and after for treatment and control respectively. The asterisk indicate normality.

For the treatment group and control group with not all subjects included there were a normal distribution between the threshold and tolerance before and after. A two-way mixed ANOVA test ($\alpha < 0.05$) was used to test if there is a difference between the groups, as the sample size was unequal. The measurements, threshold and tolerance before and after, are the within subjects and the groups, treatment and control, was the between subjects. The test showed an equality of covariance (p=0.955) and a equality of Error Variances (p>0.05) for threshold before and after and tolerance before and after. Result from the two-way mixed ANOVA test is illustrated in table 5.9

Within-Subjects Effect			**Between-Subjects Effect**		
	F	Sig		F	Sig
Measurement	13.051	0.001*	Group	1.492	0.231
Measurement*Group	0.154	0.507			

Table 5.9: Two-way mixed ANOVA for the threshold and tolerance before and after for treatment and control respectively

The test indicated that there was a significant main effect on measurement, $F(1,30) = 13.051$, p=0.001. However, was there no significant main interaction between measurement and the groups, $F(1,30)=0.154$, p=0.507 and no significant main effect on the group $F(1,30)=1.492$, p = 0.231.

To test the normality of the difference between threshold and tolerance a Shapiro-Wilk test ($\alpha > 0.05$) has been used. The result from the tests is illustrated in table 5.10.

	Threshold	**Tolerance**
	Difference	Difference
Treatment (15)	0.197*	0.975*
Control (17)	0.148*	0.929*

Table 5.10: Shapiro-Wilk Test for normality for threshold and tolerance difference for treatment and control respectively. The asterisk indicate normality.

A normal distribution was seen for the difference in threshold and tolerance for the treatment group and control group, why a T-test ($\alpha < 0.05$) was used to test if there was

a difference between the groups. There was seen a equality of Error Variances for the tolerance (p=0.159) and no equality of Error Variance for threshold (p=0.013). Result from this test is illustrated in table 5.11.

	Threshold Difference	Tolerance Difference
Subject (32)	0.149	0.330

Table 5.11: T-test for threshold and tolerance difference for treatment and control respectively. The asterisk indicate a significant difference.

The test indicated that there was no significant difference in the threshold and tolerance.

6 | Discussion

7 | Conclusion

8 | Appendices

8.1 Subject informations

Subject	Gender	Age	BMI
#T1	F	25	27.44
#T2	F	23	23.14
#T3	M	22	21.13
#T4	F	21	22.68
#T5	F	22	21.58
#T6	F	20	23.12
#T7	M	25	25.06
#T8	F	21	24.96
#T9	F	22	21.38
#T10	F	34	24.28
#T11	F	21	21.13
#T12	M	24	26.23
#T13	F	25	19.27
#T14	M	22	20.76
#T15	M	23	28.07
#T16	M	24	31.10
#T17	M	23	24.49
#T18	M	22	21.16
#T19	M	27	25.17
#T20	M	23	23.21
#T21	M	26	26.64
Mean	F(10) M(11)	23.57 ± 2.99	23.90 ± 2.90

Table 8.1: Subject characteristics. Gender is indicated with either F (female) or M (male). The means and standard deviations are calculated for age and BMI.

Subject	Gender	Age	BMI
#C1	F	23	21.89
#C2	F	25	23.84
#C3	F	27	21.13
#C4	F	27	20.96
#C5	M	24	28.06
#C6	M	23	24.74
#C7	F	22	23.77
#C8	M	24	21.91
#C9	M	22	27.17
#C10	M	23	22.59
#C11	F	23	21.30
#C12	M	27	22.74
#C13	F	21	32.80
#C14	M	23	20.28
#C15	F	24	20.28
#C16	F	22	20.28
#C17	F	22	21.37
#C18	F	23	18.17
#C19	M	29	31.21
#C20	M	26	26.58
#C21	M	30	21.80
Mean	F(11) M(10)	24.29 ± 2.47	23.43 ± 3.67

Table 8.2: Subject characteristics. Gender is indicated with either F (female) or M (male). The means and standard deviations are calculated for age and BMI.

8.2 Threshold and Tolerance

	Threshold		Tolerance	
	Pre [KgF]	Post [KgF]	Pre [KgF]	Post [KgF]

#T1	1.84 ± 0.18	1.53 ± 0.30	4.21 ± 0.25	3.93 ± 0.74
#T2	2.95 ± 1.02	2.85 ± 0.06	7.63 ± 1.06	5.70 ± 0.87
#T3	2.13 ± 0.51	3.07 ± 0.29	7.75 ± 0.52	8.13 ± 0.52
#T4	0.94 ± 0.15	2.34 ± 0.10	3.85 ± 1.57	4.95 ± 0.24
#T5	1.35 ± 0.11	1.71 ± 0.35	3.11 ± 0.21	3.94 ± 0.47
#T6	0.31 ± 0.03	0.94 ± 0.18	5.95 ± 1.80	5.99 ± 1.02
#T7	2.07 ± 0.53	2.74 ± 0.41	5.44 ± 0.79	8.82 ± 0.82
#T8	1.82 ± 0.61	3.59 ± 0.38	7.21 ± 1.69	10.11 ± 0.61
#T9	2.17 ± 0.73	2.84 ± 0.50	6.98 ± 0.35	9.62 ± 0.60
#T10	4.71 ± 0.24	4.85 ± 1.48	12.37* ± 1.27	13.24* ± 0.50
#T11	2.22 ± 0.33	4.31 ± 0.97	4.45 ± 0.15	7.76 ± 0.51
#T12	1.99 ± 0.36	2.51 ± 0.37	4.45 ± 0.91	4.79 ± 1.07
#T13	1.14 ± 0.38	2.37 ± 0.52	4.48 ± 0.20	6.57 ± 1.13
#T14	1.69 ± 0.46	1.01 ± 0.04	6.04 ± 0.98	3.93 ± 0.70
#T15	2.03 ± 0.65	2.58 ± 0.73	8.57* ± 1.21	14.28* ± 0.78
#T16	2.79 ± 1.36	2.39 ± 0.13	13.35* ± 2.20	13.59* ± 1.06
#T17	3.24 ± 0.39	2.76 ± 0.79	11.75 ± 1.29	11.77 ± 0.89
#T18	2.16 ± 0.26	1.98 ± 0.82	8.38* ± 2.86	11.93* ± 1.38
#T19	1.77 ± 0.04	2.10 ± 0.49	9.66 ± 2.40	10.91 ± 1.04
#T20	2.28 ± 0.30	3.35 ± 1.36	7.20 ± 1.01	14.01* ± 2.47
#T21	3.91 ± 0.80	3.82 ± 0.45	7.18 ± 0.72	10.58 ± 0.89

Table 8.3: Threshold and tolerance before and after and associated standard deviation for the treatment group. The asterisk indicated that the tolerance was not representative.

	Threshold		Tolerance	
	Pre [KgF]	Post [KgF]	Pre [KgF]	Post [KgF]
#C1	3.04 ± 0.34	5.00 ± 0.80	7.80 ± 0.32	12.07 ± 0.53
#C2	1.85 ± 0.29	2.27 ± 0.50	7.35 ± 1.07	9.45 ± 0.35
#C3	1.92 ± 0.18	1.81 ± 0.33	4.90 ± 1.11	4.32 ± 0.18

#C4	1.93 ± 0.06	2.09 ± 0.49	6.25 ± 1.19	7.31 ± 1.35
#C5	2.01 ± 0.24	4.73 ± 1.42	$11.46^* \pm 3.26$	$13.77^* \pm 0.91$
#C6	2.60 ± 0.23	3.45 ± 1.19	$7.85^* \pm 1.33$	14.05 ± 0.81
#C7	3.60 ± 0.83	4.34 ± 0.86	6.57 ± 0.36	8.96 ± 1.37
#C8	1.98 ± 0.54	2.57 ± 0.32	10.25 ± 0.48	10.91 ± 1.29
#C9	2.59 ± 0.42	3.19 ± 0.55	8.89 ± 1.74	9.51 ± 1.11
#C10	4.61 ± 0.58	6.80 ± 1.36	$12.85^* \pm 2.52$	$10.65^* \pm 0.56$
#C11	1.27 ± 0.22	1.29 ± 0.12	3.56 ± 0.41	5.21 ± 1.09
#C12	2.31 ± 0.39	4.32 ± 1.50	9.45 ± 3.06	10.05 ± 0.72
#C13	4.47 ± 0.11	2.56 ± 0.08	8.51 ± 6.03	9.67 ± 1.66
#C14	1.85 ± 0.22	3.07 ± 0.95	5.17 ± 0.14	7.00 ± 0.81
#C15	1.14 ± 0.09	1.98 ± 0.24	5.83 ± 0.72	5.17 ± 0.98
#C16	2.05 ± 0.51	2.06 ± 0.04	8.21 ± 1.02	7.98 ± 0.76
#C17	1.52 ± 0.64	1.81 ± 0.28	10.77 ± 2.17	6.91 ± 0.09
#C18	1.98 ± 0.50	2.05 ± 0.44	4.26 ± 0.33	4.36 ± 0.32
#C19	5.58 ± 0.38	2.36 ± 0.50	$18.17^* \pm 3.12$	$14.39^* \pm 0.84$
#C20	2.41 ± 0.57	2.97 ± 0.46	7.80 ± 1.91	8.96 ± 0.58
#C21	3.83 ± 1.33	4.06 ± 0.17	11.65 ± 1.59	11.32 ± 0.89

Table 8.4: Threshold and tolerance before and after and associated standard deviation for the control group. The asterisk indicated that the tolerance was not representative.