

# Can mindfulness alter pain sensitivity?

2. Semester project - Spring 2018 Group number



Title:

Can mindfulness alter pain sensitivity?

Theme:

Biomedical Signals and Information

Project period:

Spring  $2018\ 02/02/2018 - -/-/2018$ 

Project group:

-

18 gr 8405

Participants:

**Supervisors:** 

Pages: -

Appendix: -

Handed in: -

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$\mathbf{S}_{i}$	ynopsis

# Preface Contents

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### 1 Introduction

Probably everybody experienced pain once, either due to a cut, a burn or a fall. The pain occurring right after an injury is called acute pain and disappears near-term. [Briggs2010;Mello2016]

Approximately 1.5 billion of people [Zeidan2016], which equals 20% of the population suffer permanent from pain, so-called chronic pain [Macfarlanea2016]. The characteristics 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 exercising, walking or lifting, but also social activities. So are also maintaining an independent lifestyle and relationships to friends as well as to family, sexuality and sleeping affected. Besides the impacts on life, pain has impact on the work life. 25% indicated in a survey that the persistence of pain had a lasting effect on their employment status. These patients changed their job, the job responsibilities or lost the job. As a result of this impacts 21% of the chronic pain patients are diagnosed with depression. [Breivik2006]

15 % 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 all chronic pain patients from anxiety and depressed mood, cognitive distress and the resulting physical limitations. [gross2013]

At the moment there is no cure for those chronic pain patients. The current treatment methods only provide possibilities to relieve the pain. [marcus2009;pope2017] Nevertheless the majority of the patients feel 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 enhanced. 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 the question if mindfulness meditation can relieve low back / neck pain. Therefore an experiment was conducted whereby the pressure pain threshold and the pressure pain tolerance of the subjects were measured by an algometer. After five days with 20 min mindfulness meditation each the pressure pain threshold and the pressure pain tolerance was measured again. To ensure that the difference between the

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measurements is not caused by adaption or habituation to the pressure a controlled trial has been performed and a control group has been measured with the same time difference but without mindfulness meditation. This experiment was conducted to either accept or reject the hypothesis "Short-term mindfulness meditation increases the pressure pain threshold and the pressure pain tolerance.".

## 2 | Background

#### 2.1 Pain

In this section acute and chronic pain will be described, but with the focus on chronic pain. Different treatments of chronic pain will be presented. Both the medical and alternative treatment methods for reliving pain will be assessed.

#### 2.1.1 Acute and chronic 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 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 have interruptions in between [Mello2016].

Pain is a worldwide problem and affects all populations regardless of gender, age, income, ethnicity or geography, but the distribution across the globe differs. 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 be the causes of different following 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]

### 2.1.2 Nociceptive and neuropathic pain

Pain can be divided into nociceptor pain and neuropathic pain [Steeds2013]. Nociceptor pain can be classify 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

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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]

#### 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 between 2 and  $5\mu$ m and produce fast well localized sharp pain. The distribution of these fibers are in the body surface, muscles and joints. C fibers are unmyelinated nerve cells below  $2\mu$ m and produce slow and poorly localized burning and throbbing pain. The distribution of C fibers are 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, 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 write arrow. 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 reverse from where the pain actually had occured. Perception of pain on the right side of the body is processed on the left side of the brain and vice versa [Martini2012].

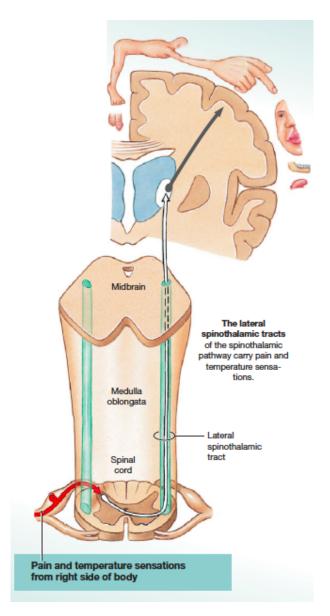


Figure 2.1: Spinothalamic pathway. Modified [Martini2012]

Pain is modulated by the descending pathways, where the Periaqueductal Grey (PAG) and the Nucleus Raphe Magnus (NRM) are involved in reducing pain. PAG, also known as anti-nociceptor, is important in the control of pain and surrounds the cerebral aqueduct in Mesencephalon. When this region is electrical stimulated it produces profound analgesia and injection of morphine. PAG receives inputs from the thalamus, hypothalamus, cortex and the spinothalamic tract. Neurons from the PAG region excite the cells in NRM which have a direction towards the spinal cord and block the pain transmission by the dorsal horn cells. Stimulation of NRM produce a strong analgesia and release serotonin which activates the inhibitory interneuron and blocks the pain transmission. The key neurotransmitter is noradrenaline and 5-hydroxytryptamine by modulation pain. [Steeds2013]

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#### 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, because the distribution is no longer respect by nerves, roots, segments, proximal or distal territories. However, neuropathic pain can be described based on a 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. Furtermore, pain can be divided into different types according to the evoked pain, which is illustrated in table ??

#### 2.1.3 Common types of chronic pain

A survey by [Breivik2006] assessing chronic pain in 15 European countries inclusive Israel, 16 countries in total, found the most common types of chronic pain within 4839 participants suffering from chronic pain. The study found 50 % of the participants to suffer from back pain, 40 % suffering from joing pain, especially knee pain and 20 % suffering from head pain, neck pain, hand or leg pain. Participants aged between 41-60 suffered mostly from chronic pain. The cause of the pain where mostly due to arthritis, osteoarthritis, traumatic injury and herniated or deteriorating discs within the vertebrae. [Breivik2006]

### 2.1.4 Treatment of chronic pain

There are several ways of treatment for chronic pain patients, depending on the modalities and intensity of the pain. Besides conservative methods, alternative methods are applied to reduce chronic pain. The benefit of the alternative methods is a treatment without the risk of negative side-effects. [marcus2009, pope2017]

None of the different treatment methods is 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, as mentioned, to relieve the suffering. [marcus2009, pope2017] A lot of different methods for relieving pain exists, some of these will be described in the following subsections.

#### 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

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

Non-opioid analgesics are used to reduce intermittent mild to moderate pain. To this category belong nonsteroidal anti-inflammatory drugs, which decrease inflammation and give analgesic properties. Non-opioid analgesics are especially used in short-term-therapy. Non-opioid analgesics inhibit the prostaglandin synthesis. Prostaglandin has a protective effect. 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

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 abuse 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]

#### Surgery

Surgery is a less frequent treatment technique. Commonly it is used to relieve patients from pain due to anatomic abnormalities. [marcus2009, pope2017] But also patients suffering from chronic low back pain can be treated by surgery. It is always necessary to weigh risk and benefits of surgery. Where appropriate it should be harked back to other and less invasive treatment options. [pope2017]

#### 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 phys-

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ical fitness, achieve weight loss and decrease the risk of chronic diseases encouraged by inactivity. [marcus2009, pope2017]

#### Psychological therapy

Psychological therapy 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]

#### 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 to avoid medicine related insomnia. Obesity is a risk factor in the likelihood to develop chronic pain, besides, it encourages other health problems for example cardiovascular disease or diabetes. It is known that chronic pain occurs more often in people which are overweighted. This is encouraged by the side effects of obesity like psychological disability or musculoskeletal pain. To improve this condition, weight loss should be achieved by the combination of diet and exercises. This will influence the recovery abilities from pain positively. [marcus2009, pope2017]

#### Chiropractor

Chiropractic treatment is adjustment and manipulation of the spinal cord in the patient to alignment the vertebrae of the spine to reduce pressure on the nerves running down the spine [Gerald2013]. This therapy will, just after a few treatments, relief pain and increase flexibility of the spine of the patient [Peterson2012]

#### Acupuncture

Acupuncture is a treatment 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 round the shoulder joint, headaches, neck and shoulder pain, arthritis/osteoarthritis and low vack pain. The effect of the treatment is often long lasting, up to 80 % after 3 month duration [Junnilla1983].

#### Hypnosis

Hypnosis is a process where the 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 the 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 to relieve pain, but only on a short term basis. [Dhanani2011]

#### 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 [Whitehead2017] found that yoga could improve the functionality of the back and a slight effect of treating pain compared to non-yoga participants.

#### Mindfulness meditation

Mindfulness meditation is practicing of being aware in the present moment, a form of mental training. Mindfulness can be practiced through meditation, which is one of the common ways of practicing mindfulness. Mindfulness meditation practice is said have several health benefits like increase in cognitive function, decrease stress, depression and anxiety. Through some of these mechanisms pain can be altered, eventually leading in a relieve in pain. [Zeidan2016]

#### **2.1.5** Summary

Summarized, all of the methods are used in relieving pain and more exists. No one of the treatment is a cure of pain and they are often interwoven to work together for the best effect for the patient. Most of the methods described require an external person to apply the therapy and medication has side effects. Mindfulness meditation is an easy technique to implement in the patients daily living and is a technique worth to investigate further in depth to see if this kind of treatment can relief the pain for the patient.

#### 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. However, 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 defined how much the pain hurts,

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where pain affect is more complex. Pain affect refers the degree of emotional arousal or changes in action due to the sensory experience of pain. The quality of pain is about the physiological sensations associated with pain.

The intensity of pain can be assess using unidimensional scales, which explore only one dimension of pain [Jensen2001]. Chronic pain is complex to assess with only unidimensional scales, as the pain affect their 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 Scales (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 adjective. [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 Scales (VRS). Modified [Jensen2001]

Other 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]

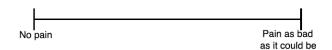


Figure 2.3: Visual analogue scale (VAS). Modified [Jensen2001]

Another method is the Numerical Rating Scale (NRS), which is illustrated on figure 2.4 and is the most used in 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 demonstrate positive and significant correlations with other measures of pain intensity [Jensen2001].

0 1 2 3 4 5 6 7 8 9 10

No pain

Pain as bad as it could be

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. Even though the primary purpose of this scales were to offer individuals with written language or cognitive difficulties an option to express pain intensity, there is evidence that the methods are valid [Jensen2001].

#### 2.2.2 Multidimensional scales

Multidimensional scales are convenient in relentless pain conditions. Multidimensional scales 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].

There is a lot of multidimensional scales, but there is six commend used in clinical trials for assessing pain quality. Three of the methods are editions of McGill Pain Questionnaire (MPQ).

The most commend used of MPQ 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 determ 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) [Katz2001]. <sup>1</sup>

Furthermore, consists two of the six commend in the field of neuropathic pain and the last one is the Pain Quality Assessment Scale(PQAS). Another scale, breif pain inventory (BPI), was developed to assess cancer pain and have been proven as a useful instrument to assess different kinds of pain in several clinical settings. The BPI measures pain severity, pain quality and the disturbance caused in the patients daily life. Two subscale scores pain intensity and pain interference [Katz2001].

For estimating the location of pain is pain drawing often used, which involve a front and back drawing of the human body. A second commend used methods is the checklist, which is a simple list of possible site of pain. [Jensen2001]

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 $<sup>^1\</sup>mathsf{FiXme}$  Note: 15 different descriptors in sensory and affected terms. Each descriptor is rated on a 4-point VRS scale.

#### Quantitative sensory testing

A method to assess the patients response to quantifiable sensory stimuli in order to characterize if the pain is somatosensory function or dysfunction is the quantitative sensory testing (QST). QST is used for assessing neropathic pain and include different modulation of stimulation, such as thermal(heat, cold), mechanical (tactile, pressure, vibration), electrical, ischemic and chemical. These stimulus and parameters can be selected in order to systematically evaluate the somatosensory transmission and pain processing by engage different nerve fibers, endings and partways of the central nervous system. [Fillingim2016]

Approaches for QST, which is used in clinical practice is the Frey monofilmaments and tuning forks which is used to measure mechanical sensation. Heated or cooled metal rods can be used to assess thermal sensitivity. The sensitivity of pressure pain can be assess by a pressure algometry. [Fillingim2016]

### 2.3 Assessment of Experimental Pain

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]

#### Types of physiophysical methods

Psychophysical research has been mostly concentrated on thresholds measurement owing to, the desire to isolate low-level sensory mechanisms using operationally defined tasks that are intended to minimize the roles of perception and cognition [Pelli2010]. The three most commend methods used for testing the perception in stimulus detection is the methods of adjustment, methods of limits and methods of constant stimuli.

Methods 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]

Methods of limits: The magnitude of the stimulus are presented in eater a ascending or a 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]<sup>2</sup>

<sup>&</sup>lt;sup>2</sup>FiXme Note: Look at the uncomment part. I am not sure if it relevant. I think it nice to know but

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. This method generates data, when this data fitted with the appropriate psychometric function, 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]

#### 2.4 Mindfulness Meditation

Mindfulness is usually defined as being in the mental state of non-elaborative, non-judgmental awareness [Zeidan2012, Zeidan2016, Tang2017]. Mindfulness is viewed upon as a lifestyle and this kind of lifestyle can be practiced through meditation, which is called mindfulness meditation. Practicing mindfulness meditation includes control over sensory, emotional and cognitive happenings. Hereby the ability to control these sensations without being distracted by them as so the ability to abstract from past and future representations of memory. Thus can be said that mindfulness meditation is training of the mind. [Tang2017] Thoughs and emotions are involve in the preception of pain. Mindfulness meditation will not make the pain go away, but the patient will be able to deal with it easier ,reducing the fear associated with pain. Thereby the subjects engage more in the treatment instead of reeling and focusing on the medication. [Jacob2016]

#### 2.4.1 Meditation classification

The most well practiced types of meditation are focused attention (FA) and open monitoring (OM).[Zeidan2016]

#### Focused attention

FA is the training of concentration, the subjects keep their focus at an object or specific thing, only focusing on that thing. Often the flow of breath is the focus, when practicing FA meditation. When 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 his or her attention back to the focus. [Zeidan2016]

#### Open monitoring

OM is the cultivation of open presence, were 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. It is believed that this form of meditation is easier to learn when the person masters the meditation of FA, whereby the OM form is easier to master. [Zeidan2016]

#### 2.4.2 Mechanisms of mindfulness meditation

Enhanced emotion regulation, cognitive control, acceptance and positive mood have been linked with health benefits as well as pain modulation. These mechanisms have been shown to be modulated during mindfulness meditation practice. A study by Perlman et

needed

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al. [Perlman2010] shows that practicing meditation could not lower the intensity of pain, but instead lower pain unpleasantness in the participants. [Zeidan2012, Perlman2010]

The typical response, when using a placebo analgesia is, increased activation of the dorselateral prefrontal cortex during pain anticipation. Effect that predicts reductions in pain perception and activity of pain related brain regions. Mindfulness meditation does not involve dorselateral prefrontal cortex activation. [Zeidan2012]

The findings on mindfulness meditation and pain modulation are split, but experiments in controlled settings are still needed to confirm if the effect of mindfulness meditation works on pain modulation. [Zeidan2012, Perlman2010]

Different brain regions are involved the practice of mindfulness meditation. The most important are the prefrontal cortex (PFC), involving the anterior cingulate cortex (ACC) and the medial PFC as illustrated in figure 2.5. The striatum, the insula and the default mode network (DMN), which include the medial PFC and the posterior cingulate cortex (PCC). 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.

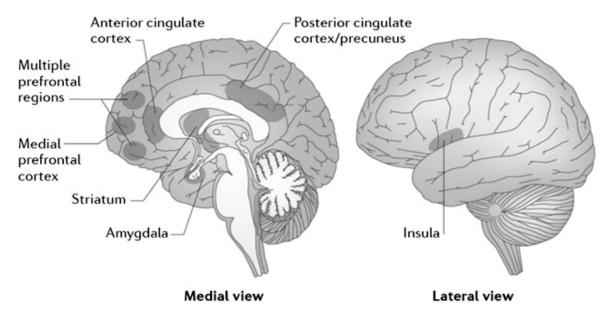


Figure 2.5: Image of the brain highlighting specific regions relevant when practicing meditation [Tang2017]

#### Attention control

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. 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**

Emotion regulation include 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 in regulating the emotional thoughts through the limbic system also responsible for goal setting. This need for regulating the emotional control is important because during the meditation practice the participant need to be able to handle boredom or negative mood during the meditation. Stronger subgenual and adjacent ventral ACC activity 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.

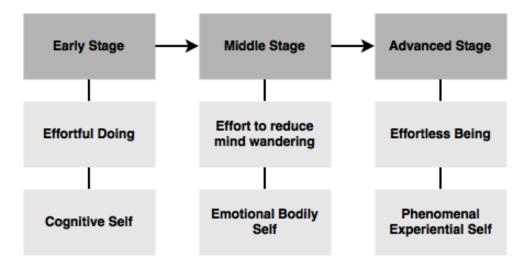
#### **Self-awareness**

Self-awareness includes the awareness of one self, 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. Reduce activity in midline cortical structure including the DMN, more reduction in the posterior part PCC, than the anterior part medial PFC, but increase in perigenual ACC activity.

#### 2.4.3 Meditation practice

Different expertises of meditation, early, middle, advanced 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 takes 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 ??, determine the amount of effort to get into the meditative state[Tang2017].

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**Figure 2.6:** The three stages of meditation practice, describing how much effort one must use to get into the meditative state

[Tang2017]

In the early stages 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 is shown to occur when using more effort. With less effort, the ACC and striatum will participate more. [Tang2017]

The neural mechanisms behind mindfulness meditation in reliving pain has been researched. Experiments where stimulating with nociceptive pain there has been shown an increase in activity areas of the PFC when meditating. Participants express that they are able to feel the pain but 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 don't 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]

Examining long term meditators, the findings are a thicker gray matter in mid cingulate cortex and bilateral secondary somatosensory cortex, which are involved in pain related regions overlapping the functional effect. A correlation with the number of years practicing meditation and the mid cingulate was also found. This gives evidence to long lasting effects of meditation. [Zeidan2012]

However, short-term mindfulness training can have positive effect in pain relieve. The study by [Zeidan2012] showed an effect of mindfulness meditation practice during four days for 20 min per session, even though most studies conduct the experiments for a period of more than six weeks. [Zeidan2012]

### 2.5 State of the Art

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# 3 | Methods

#### 3.1 Protocol

This protocol will describe the present study, which consist of two experiments testing pain tolerance and pain threshold after practicing mindfulness meditation or after not practicing mindfulness meditation.

#### 3.1.1 Purpose

The treatment of chronic pain has constraints, as the treatments are only relieving the pain instead of curing the pain. Another issue is that some of these treatments, example medication, have side effect, as described in ??.

There is alternative to medication such as yoga, hypnosis and mindfulness, which have shown to have an influence on relieving pain.

An alternative to the present treatment is mindfulness meditation, as described in ??.

In order to investigated the influence of mindfulness meditation on pain threshold and pain tolerance following hypothesis is proposed:

• Short-term mindfulness meditation increases the pressure pain threshold and the pressure pain tolerance.

#### 3.1.2 Subjects

Forty healthy subjects were recruited for the experiment, 20 males (M) and 20 females (F) with a mean age  $\pm XX$ . A homogeneous group of participants were enrolled in order to limit the amount of variables in the study. For insuring this, specific inclusion and exclusion criteria have been formed for this experiment.

#### Inclusion criteria:

- Healthy subjects age between 20-30 years
- Must have time to meditate for 4-5 days, 30 minutes per day.
- Normal BMI (F: 19-24 M: 20-25)

#### Exclusion criteria:

- Ongoing meditation practice
- Acute or chronic pain

- Pregnancy
- Neurological, musculoskeletal or mental illness
- Signs or symptoms of any serious systemic diseases
- Psychiatric, analgesic or other medications that might influence their response to pain
- Abusive drug or alcohol use
- Lack of ability to cooperate

Furthermore, is it not necessary that subjects believe in the effect of mindfulness meditation.<sup>1</sup>

#### 3.1.3 Setup

The Pressure Pain Threshold (PPT), defined as the pressure at which the sensation changed from pressure to pain, has been recognized as an effective and reliable way to quantify pain measures. In this study PPT was measured using (our ALGOMETER). PPT were measured in the upper trapezius. Testing points were marked to ensure reliable and rapid location during the experimental procedure. The algometer was applied four times, two on the left side and two on the right side of the upper trapezius, and the average of the registrations was filed. The subjects had a 5 minutes resting time between measurements. PPT values were measured two times, the first day of the study and after 4-5 days since the first measure.

### 3.1.4 Approach

For this particular experiment a parallel study was conducted. The subjects recruited for the experiment were randomly assigned in two different groups, the control group or the treatment group, with a equal amount of female and males in the groups. The control group consisted of twenty subjects no meditation. The treatment group consisted of twenty subjects meditation. The structure of the study design is illustrated on figure ??.

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<sup>&</sup>lt;sup>1</sup>FiXme Note: I don't know about this sentence, i think it does not fit in here. Maybe it is more something we should write for the participants or could we put it in as one of our criteria?.

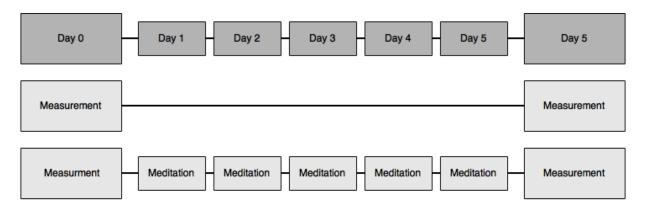


Figure 3.1: Parallel study design.

#### 3.1.5 Procedure

Control group Treatment group

#### Mindfulness meditation

Guided meditation for 30 minutes in groups, sitting positions.

# 4 | Data analysis

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# 5 | Results

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# 6 | Discussion

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# 7 | Conclusion

# 8 | Appendices

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