Norges Helsehøyskole
Campus Kristiania

Bachelor thesis

Will Increased Knowledge of Pain Physiology Affect Reported Pain in Subjects Exposed to a Cold Pressor Task - a Quantitative Pilot Study

by

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Preface

As students in the field of manual therapy, one of our tasks is to help patients struggling pain. To be able to reduce pain, we need to better understand it. Knowledge within the field is getting better and better, though the phenomenon is far from clarified. In respect to our patients and profession, we should therefore aim against a better understanding of how pain works.

Based on the *Body-Self Neuromatrix* by Melzack and Katz, it is hypothesised that the subjects' pain experience can be affected if the subject possesses knowledge of pain physiology. The goal of this pilot study was therefore to investigate method and design suitable for investigating this.

Thanks to the students at Campus Kristiania who participated as subject and made this study possible. Thanks to Robert James Froud who helped us with the statistical analysis, and a great thanks to our supervisor Pål Andre Amundsen who has guided and helped us through the process of this bachelor thesis.

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Abstract

Background:

This pilot study used the theory of *The Body-Self Neuromatrix* as a foundation. The theory suggests that pain is a product of complex brain activity. It suggests that the brain evaluates information from emotion-related areas, cognitive-related areas, and sensory signalling systems in its process of pain production. Therefore, it was hypothesised that the subjects' pain experience can be affected if the subject possesses knowledge of pain physiology. The goal of this pilot study was therefore to investigate method and design suitable for investigating this hypothesised effect.

Topic question:

How does possessing knowledge of pain physiology affect the pain experience, when evaluating results from a Numeric Rating Scale, comparing a pain-educated group with a control group, while applying both groups the same nociceptive stimulus?

Method and design:

This pilot study used a quantitative method, with the design of a small scale Randomised Controlled Trail (RCT). A pain education course was held for an intervention group, who together with a control group were exposed for a Cold Pressor Task (CPT). Experienced pain intensity was addressed by using NRS, to measure and quantify experienced pain intensity.

Results:

From the analysis of data collected in this pilot study, no difference between groups of statistically significance was found; only a weak trend can be observed.

Conclusion:

Method and design had some limitations, but by adjusting the factors discussed in this study, further studies should be able to better investigate the topic question.

1.0 Introduction

1.1 Introduction of background theory

The World Health Organisation (WHO) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (1). As the definition states, pain is an experience associated with actual or potential tissue damage, and thus not a direct reflection of tissue damage.

A lot has happened since Descartes´ specificity theory. Descartes´ theory suggested that specific pain receptors were activated when injury occurred, and then sent pain impulses to a pain centre in the brain (2:2). Today, the theory of *The Body-Self Neuromatrix*, that may be the leading theory in the field of brain function and pain, suggest that pain is a multifactorial experience produced by the constant evaluating brain (2:4). Pain is a necessary physiological protective mechanism, when it works as it is designed to do (2:8). Pain is unpleasant in its existence, but is important to help us survive and to stay healthy, and it does so by making us aware of threat and by forcing us to rest when healing is necessary (3:42). Pain is often caused by tissue damage, like when you stumble while running and sprain your ankle, or burn your fingers on a hot stove (3:11). Though, in some cases individuals are experiencing great pain without sign of pathology, while other with severe injuries doesn't feel pain at all (3:13). Pain is beneficial when it reveals threat or tissue damage, but in cases when there is no threat or tissue damage, it is clear that the existence of pain is both unbeneficial and unnecessary.

It is of importance to understand that nociception and pain are two separate terms, as described by Brodal: "It is important to realize that pain perception and nociceptor activity are not synonymous terms. Thus, nociceptor activity and the feeling of pain may occur independently of each other" (4:205).

Nociception is many times a trigger for pain and its function is to reveal tissue damage (4:205). The nociceptive pathway from peripheral somatic tissue to the brain consists different neuroanatomical structures; it starts with a peripheral first-order nerve out in the peripheral somatic or visceral tissue (5:190). The axon of the nerve cell goes in to the dorsal root ganglion, which is just after it splits from the segmental spinal nerve (5:190). The signals deriving from the peripheral somatic or visceral tissue goes through the nerve fibre, which has small cell-organs on the end that reacts to stimulus (5:190). Some of these organs react to a specific kind of stimulus, for instance temperature or chemical stimulus (5:190). Though, many of these organs are polymodal, which means that they can be activated from different types of noxious stimulus (5:190). When the nerve impulse has travelled along the axon, it synapses with a second order nerve in the grey matter of the spinal cord (5:190). The second order nerve then changes side in the spinal cord, and runs up to the thalamus in the brain (5:190).

Pain is a multifactorial experience, produced by the brain when it interprets threat or danger, when it feels the need to protect (2,3:8). *The Body-Self Neuromatrix* theory suggests that pain is the result of a certain neurosignature (2:4). A neurosignature is a given synaptic neuron activation in the neuromatrix (2:4). The neuromatrix is defined as the network of neurons and their loops, in and in-between thalamus, cortex and the limbic system (2:4). A neurosignature for pain can therefore derive from both cognitive, sensory and emotionally inputs.

It is due to *The Body-Self Neuromatrix* theory, together with the book *Explain Pain* by Moseley and Butler, that the theory of this thesis was established, and therefore also the need for this pilot-study (2,3). *Explain Pain* is a book aiming on helping those who struggle with persistent pain by teaching them about their pain, pain physiology, how pain works, and how to live with pain (3). *The Body-Self Neuromatrix* theory sees pain as a product of complex brain activity generated by multiple inputs where both physiological and psychological factors are of importance (2:4). A possible benefit from increasing knowledge about pain is the impact it may have on the neurosignature for pain. An increase in knowledge about pain can hypothetically influence cognition and therefor hypothetically also perception. It is already suggested that cognition and perception are playing important roles in the neuromatrix when a neurosignature for pain is generated (2:4).

With *The Body-Self Neuromatrix* theory as a foundation, perceived pain is a multifactorial experience, a product of brain activity (2:4). The brain is constantly evaluating accessible information, which is information coming from emotion-related areas, cognitive-related areas, and sensory signalling systems (2:4). Therefore, how will in advance learning and knowledge about pain physiology, its functions and limitations, and its complexity, affect emerging pain experiences? Can this knowledge help the average individual to perceive pain in a more functional or rational way, than if the individual did not possess this knowledge? The background theory for this pilot study was that knowing more about pain would help the individuals' brain to produce a more rational pain experience when exposed to a noxious stimulus. Therefore the purpose was to test method and design, to enable for a later investigation of the hypothesis. Furthermore, it was the importance of information coming from cognitive-related brain areas that was of interest to evaluate. The value of information from emotion-related brain areas was not taken into consideration. Activation of nociceptive free nerve endings was the choice of method to inflict pain, which is the part of the sensory signalling system most relevant for pain production. These nociceptive nerves act as a danger alarm system, revealing threat or tissue damage (3:30).

1.2 Outline of The Body-Self Neuromatrix

The theory of *The Body-Self Neuromatrix* by Melzack and Katz is a conceptual model that they have based on these four conclusions, drawn from Melzack´s earlier findings while looking at the phantom limb phenomena:

> *The network of neurons and their loops, in and in-between thalamus, cortex, and the limbic system is defined as the body-self neuromatrix. The structure as well as the synaptic links of the neuromatrix is thought to be genetically determined, although formed and influenced by sensory inputs. The complex activity with the loops in and in-between neurons of the neuromatrix allows for sundry components to interact at once. When nerve impulses are repeated frequently, they produce a specific pattern that is called a neurosignature. A neurosignature is the result of the total neural activity within the neuromatrix. From the neuromatrix flows a constant stream of neurosignatures as output to the sentient neural hub, the brain area suggested to be responsible for the conversion of neurosignatures to awareness. The feeling of the "self" is thought to be a result of the main pattern, the neurosignature for the body-self. Furthermore, due to a constant change in neural patterns in the neuromatrix, so called sub signatures occurs and rides on this main pattern, creating the feeling of the body-self with its "constantly changing qualities". In other words, it is because of these sub signatures that multiple ranges of feelings are felt, such as pain at different levels. The outputs from the neuromatrix are also responsible for the respective*

homeostatic and behavioural responses at each given situation. The sub signatures are consequences of different inputs to the neuromatrix. Inputs arriving the neuromatrix are either from sensory signalling systems, cognitive-related brain areas or from emotion-related brain areas. Sensory signalling systems include all information coming from the body (e.g. viscera, skin, bones, and muscles). Inputs from cognitive-related brain areas are related to cognitive states like anxiety, attention and memories. Emotion-related brain areas participate with inputs mainly from the limbic system (3:4).

1.3 Suggested topic question for a RCT

How does possessing knowledge of pain physiology affect the pain experience, when evaluating results from a Numeric Rating Scale, comparing a pain-educated group with a control group, while applying both groups the same nociceptive stimulus?

1.4 Suggested hypothesis for a RCT

H0 – there is no difference in experienced pain between the two groups.
H1 – there is a difference in experienced pain between the two groups.

1.5 Clarification of concepts

Concept:	***Description of concept:***
Bias:	"Systematic deviation of a calculated (estimated) value from the true value" (6:322)
Blind setup:	**"**Method of controlling a threat to internal validity in which the participant does not know whether he or she is receiving the experimental or control treatment" (6:337). "If one has a single blinded setup, the researcher don´t know which group (control group or intervention group) the subjects belong to" (7:78)
Body Mass Index (BMI):	"Body Mass Index (BMI) is a number calculated from a person's weight and height. BMI is a fairly reliable indicator of body fatness for most people. BMI does not measure body fat directly, but research has shown that BMI correlates to direct measures of body fat, such as underwater weighing and dual energy x-ray absorptiometry" (8)
Cold Pressor Task (CPT):	"The Cold Pressor Task (CPT) involves placing a hand or forearm in cold water, a stimulus that produces a slowly mounting pain of mild to moderate intensity and is

	terminated by voluntary withdrawal of the limb" (9)
Confidence interval:	**"**Confidence intervals represent an effective technique used by researchers to help interpret a variety of statistics such as means, medians, and correlations. They are also used in hypothesis testing" (6:106)
Clustering effect:	"Clustering is the unsupervised classification of patterns (observations, data items, or feature vectors) into groups (clusters)" (10)
Confounding factor:	"A factor that obscures the true relationship between an exposure and outcome of interest" (6:323)
Dependent variable:	"The effect of the independent variable; also called the yield" (6:12)
Design:	"Design is the key to controlling the outcome from experimental and quasi-experimental research. The independent variables are manipulated in an attempt to judge their effects on the dependent variable. A well-designed study is one in which the only explanation for change in the dependent variable is how the participants were treated (independent variable)" (6:74)
Dual x-ray absorptiometry (DXA-scan):	Dual x-ray absorptiometry that determinate body composition by measuring bone mineral content, fat mass, and fat free mass (11)
Empiricism/empirical:	"Derived from or guided by experience or experiment" (12)
Hawthorne effect:	"Participant´s performance changes when attention is paid to them, which is likely to reduce the ability to generalize the result" (6:335)
Independent variable:	"The part of the experiment that the researcher is manipulating; also called the experimental or treatment variable" (6:12)
Method:	Method has been understood as the two main directions of research types; qualitative and quantitative method. The different subjects within formulating the method is participants, instruments or apparatuses, procedures, design and analysis (6:67)
Multivariable linear regression test:	**"**Multiple regression is an extension of simple linear regression. It is used when we want to predict the value of a variable based on the value of two or more other variables" (13)
Numeric Rating Scale (NRS):	"Pain intensity is commonly rated on an 11-point Numerical Pain Rating Scale which can

	be expressed as a calculated percentage pain reduction (CPPR), or by patient-reported percentage pain reduction (PRPPR)" (14)
Nociceptor:	"The usual definition of a nociceptor is purely physiological: a receptor that is activated by stimuli that produce tissue damage, or would do so if stimulus continues" (4:205)
Neuroplasticity:	**"**The brain's ability to reorganize itself by forming new neural connections throughout life. Neuroplasticity allows the neurons (nerve cells) in the brain to compensate for injury and disease and to adjust their activities in response to new situations or to changes in their environment" (15)
Population:	**"**The larger group from which a sample is taken" (6:101)
Pilot study/pilot work:	**"**Verifying that you can correctly administer the tests and treatments for your study using appropriate participants" (6:73)
Qualitative method:	"The work concerned with the research that looks at the qualities of a phenomenon. One is mostly concerned with opinions, notability and text. On the contrary to quantitative research, the researchers says that it is no simple relationship between how we see the world, and the world in itself" (16:27)
Quantitative method:	"That work concerned with measuring a phenomenon – one search for a quantification (to measure or to count)" (16:25)
Randomised Controlled Trail (RCT):	"Randomized controlled clinical trials represent the gold standard of research into health-care interventions but conducting a randomized trial requires careful planning, structures and procedures" (17)
Reliability:	"Has to do with how stable are the things we measure. If a research gives a specific result only one time, the result would probably be worthless if one hope to say something about the humanity in general" (16:41)
Randomised selection:	"It is looked upon as the golden standard in how to do a selection. In randomised selections, all the subjects in a population have the same chance of being selected" (16:47)
Sample:	"A group of participants, treatments, or situations selected from a larger population" (6:101)
Significance:	"The reliability of or confidence in the

	likelihood of a statistic occurring again if the study were repeated"(6:132). "Usually we look at a significance of 0.05 – a significance level of 5% - or a significance of 0.01 – a significance level of 1%, some times called "very significant". With a significance level of 5%, is the effect on a dependent variable not caused by the independent variable, but of another random mistake 5 out of a 100 times" (16:121)
Validity:	"Degree to which a test or instrument measures what it purports to measure; can be categorized as logical content, criterion, or construct validity "(6:193)

2.0 Method and design

2.1 Clarification of method and design

A good choice of method is a factor of utter importance in modern science (16:25). It is hard to find a good method and a suitable design to do good research on pain, because of all the factors involved in production of pain. A good first question should be: is it desirable to describe a pain phenomenon with words or with numbers? Different questions need different methods to find good and valid answers (16:25).

There are two main research methods in modern research and these methods have important distinctions, both in application and in theory (16:25). The two evaluated types are the quantitative method the qualitative method. Quantitative method usually has a hypothetic-deductive method as a foundation, which involves a theory with a hypothesis that can be tested (16:26). Most hypothesises is tested in an empirical manner, which means that the hypothesis goes through an evaluation based on lived experiences, observations and experiments (16:24). These evaluations accumulate into numbers or data sets that describe the phenomenon, which can give a quantifiable answer considering the hypothesis (16:25). The different numbers or data sets need different tests, based on the design (16:26). These tests will accumulate into results that may or may not confirm the hypothesis. Qualitative method often gathers a lot of information from few participants (16:27). It focuses on why things are how they are, and describes phenomenon with words (16:27). A simplified description of the difference between quantitative and qualitative method is that quantitative method describes the phenomena with numbers, while qualitative method describes it with words (16:25).

In this pilot study a quantitative method was used, and the subjects pain experience was quantified. It was designed as a RCT, it differs from other quantitative designs with the criterions of randomised selection of subjects within the population investigated, as well as randomised distribution of participants to control and intervention group (7:71). Furthermore, a pain education course was held for the intervention group, which was the specific intervention in relation to testing the hypothesis. A CPT was then used as source to inflicting a nociceptive stimulus under controlled circumstances, and a Numeric Rating Scale (NRS) was used to quantify the subjects experienced level of pain. This was what formed the fundamental design of the study.

A pilot study has an intention of testing the validity and reliability of the method and design, it is done in a small scale to see if there is any flaws in the design, and if the method is suitable for further research in a bigger scale (6:73). This study had therefore of a design that had not been used before, and the goal was therefore to test it in practise. Because it is done in a small scale, a pilot study cannot make conclusions valid for a bigger population, only assumptions can be made.

2.2 Justification of method

A typical qualitative method would use an interview to collect information on experienced pain level within subject (16:27). An interview could be done both before, under, and after a noxious stimulus. By interviewing participants from both intervention and control group, it could be analysed for differences in the results. This method would give a good description of experienced pain within participant in the two groups, a description more complex than numbers. Though, this example of a qualitative method cannot describe results for a bigger population; it can only answer for the subjects participating the study. To find the truth for a bigger population, a lot more subjects need to be tested to be able to generalise the hypothesised result, that possessing knowledge of pain physiology affect the pain experience.

A quantitative method is more suitable for effectively testing a bigger sample of a given populations, and therefore also to get results that are valid to generalise to count for that population (16:27). One can then see if knowledge of pain can help a vast spectre of the population, with different background, ethnicity, age and size. One would only need a sample size that statistically covers all the spectres of the population. The more heterogeneous the group becomes, the bigger the sample needs to be (16:50). Therefore, this pilot study investigated the quantitative method, so that one could do an evaluation and draw an assumption valid for a bigger population. Besides the ability to generalize results, economics and time efficiency also made the quantitative method more suitable than the qualitative one.

2.3 Method with protocol

It was collected a sample of 23 subjects, all students from the Norwegian University Campus Kristiania. In the process of collecting volunteers, lectures were visited, and the essence of the research was explained to the classes. A lot of time was used to collect volunteering test subjects. Inclusion and exclusion criterions were set for the subjects to fulfil, and they were asked to sign a paper that stated.

Table 1 - Inclusion criteria

Age	18 – 25
BMI	18 - 25
Occupation	Students at campus Kristiania

Table 2 - Exclusion criteria

Pain	On-going, chronic
Psychological illness	Depression, anxiety exc.

The volunteering test subjects were random assigned to either the intervention or the control group. An easy randomisation was done, whereas subjects name were written on pieces of paper and then mixed. Half of the pieces were randomly picked, forming the control group, while the last half formed the intervention group.

This study was planned and executed by two research conductors. The study was executed with single blinding, whereas the research conductor in charge of the CPT execution and data gathering was not familiar with which group the participants belonged to.

Three pain education courses were set to three alternative dates. Participants in the intervention group were contacted through text messages by phone, and they where asked to participate the course suitable for them. Each of the three courses consisted of 2-7 participants, and the research conductor used approximately 35 minutes to complete each course. The courses took place in a classroom at Campus Kristiania.

Six participants decided to back out, and the 16 participants remaining got exposed to the CPT in randomly fashion within a period of four weeks after the pain education course. Individual agreements on time and date for execution were done, so every subject could participate a time suitable for them.

CPT is a tool that can be used both for applying pain and for measuring pain. When used only to apply pain, an external tool is necessary for addressing pain. When the CPT is used to measure pain, it is measuring threshold and tolerance. Subjects' hand is put in water with low temperature, to activate nociceptive nerve fibres. In this study a bucked made of aluminium metal was used. It had an oval shape, and had a total volume of six litres. To keep a stable temperature cold water from the tap was used, with ice that covered the water surface. The bucked was approximately half full, and had about three litres of water plus ice. To monitor the temperature, it was used a simple, digital thermometer, which had its measuring part submerged about two centimetres under the water surface. This was evaluated as the height of where most of the hand of the subject was positioned during the test.

NRS is a tool for quantification of pain (18). It is a form with a straight line, marked with numbers, from 0 to 10. 0 equals to no pain, and 10 equals to worst imaginable pain (18). The NRS-form used in this study was an A4 sheath of paper with six identical numeric rating scales. Candidate number was filled in on the form. The NRS was explained to the participants in Norwegian, and it was explained as followed;

> "*Experienced pain shall be measured by using a NRS. NRS, Numeric Rating Scale, is a tool to measure experienced intensity of pain. Zero equals to no pain, and ten equals to worst pain imaginable. The NRS-form will map your personal experience of pain during the test."*

When all participants had executed the CPT and ranged their pain experienced, analysis of data begun. SPSS (formerly called Statistical package for the Social Sciences) was used to run different tests.

2.4 Data collection

All 16 participants went through the CPT procedure one by one. The CPT was performed in a quiet room with minimum of noise or other disturbing factors. Outer stimuluses' were tried held on a minimum level for all participants.

As soon as each subject entered the test room, the subject was read the standardised information form and asked if it was understandable. They were all given the exact same information. Research conductor acted neutral, and informed that no communication was allowed during the test. The subjects were asked to start the test by immerse their hand into the water when they felt ready. They where asked to use their dominant hand, and to keep it in the water for as long as possible up till a maximum time of five minutes. The water had a temperature of 2-4°C. The subjects were asked to take a mark on the NRS-form they had in front of them at given times during the test. They were noticed every time they should take a new mark. The times set for marking the NRS-form were; the moment they lowered their hand in the water, every 60 seconds during the test, and at the exposure time of the CPT, which was set at five minutes. The subjects were reminded of when to set a mark on the NRS-form during the CPT.

Results from the NRS-form were the foundation in the analysis, to see whether there was an effect between the two groups or not. In other words, the NRS measures was used to assess the pain experience from the moment the subjects were exposed to the stimulus, and at every 60 seconds until five minutes were reached, or until they cancelled. The information accumulated from the NRS-form was all that was used to evaluate the subject's pain experience.

2.5 Analysing methods

> *A trial run of the analysis of results should always be accomplished in the pilot study. The researcher can see whether the items can be analysed in a meaningful way and then ascertain whether some changes are warranted for easier analysis. This is one of the most profitable outcomes of the pilot study* (6:279).

The analysis of data was done by using the statistical program SPSS. The data from the two groups was plotted in a graph to control for a normal distribution. When normal distribution was concluded, the data was analysed by using multivariable linear regression tests. To keep the level of analysis at an understandable level, it was decided to look at differences in only two of the measures (out of a total of six measures per subject) between the intervention group and the control group. It was therefore decided to use the NRS measures from the first minute and the fifth minute, in relation to the baseline. The ranged level of pain from the first measure was set as baseline.

Two multivariable linear regression tests were used to look for significant differences between the two groups at two respective measures. *Body Mass Index* (*BMI*), *Gender*, *Age*, and *Group* were set as independent variables. The independent variables besides *Group*, contributed to adjusted results. The dependent variable was subjects ranged level of pain on the NRS-form. The first multivariable linear regression test was between the two groups, and compared them by the variance of the dependent variable, using the one-minute measure in relation to the baseline. In other words: the one-minute measure in relation to baseline in control group was compared to the equivalent measure in the intervention group. At the

second test, where the independent variables were the same, the dependent variable was the fifth-minute measure in relation to baseline. The variance within the group was then compared between the two groups. It was then possible to see how different the two groups experienced pain. Two individuals did not finish the test, and were therefore excluded from the data analysis.

To show the results as descriptive statistic, the data was plotted in a dot graph diagram with a mean value of all the six NRS measures from each subject, comparing the two groups. As well as the mean, the dot graph showed the 95% confidence interval for each of the six measures.

To check if independent variables influenced or disturbed more than others, there was done a "crude" multivariable linear model regression test for each independent variable against the dependent variable. It was taken a multivariable linear regression test with only *Group* as a constant against the dependent variable. The P-value was then compared to the equivalent P value for *Group* in the multivariable regression test, which also had the other independent variables in the same test (*BMI*, *Age*, and *Gender*). If the two P-values are fairly similar, it can be concluded that the *Group* constant does not inflict or disturb the results more than what is expected. The same procedure was done for *BMI*, *Age*, and *Gender*.

2.6 Intervention group and the pain education course

To assure validity and reliability in relation to the factor manipulated in the intervention group, some learning goals about acquired pain knowledge were established. Therefore the subjects had to achieve knowledge about and understanding of the topics in *Table 3* before executing the CPT:

Table 3 - Learning goal: subjects were introduced to four main topics prior to CPT

Topic	About- and functions of pain	Basic Neurophysiology	Pain and tissue damage	The Body-Self Neuromatrix
Learning goal	Know WHO´s definition of pain	Know of the role of nociception	Understand that pain can occur without tissue damage	Be familiar with the concept of the neuromatrix
	Understand how pain works as a protective mechanism	Know of the role of the spinal cord and the brain in relation to nociception	Understand that tissue damage can occur without pain	Be familiar with the concept of a neurosignature
	Understand that pain is a individual experience produced by the brain	Be familiar with the route of a danger signal	Know how nociception is one out of many inputs generating pain	Knowledge about pain as a multifactorial experience
	Know of essential factors in relation to the brains production of pain	Understand basics on the concept of neuroplasticity	Understand that pain relies on the brains interpretation of threat	Know about the role of cognitive-related brain areas, sensory signalling systems, and emotion-related brain areas when it comes to pain production

For the intervention group to achieve knowledge and understanding of the content in *Table 3*, and to reach the goals set for them, an education course was executed. The course was held in groups of 2-7 participants at the time, and lasted for approximately 35 minutes. A Power Point presentation was used to show the content, while a lecturer went through the content. Metaphors were used while explaining. The content was adapted to a basic level, suited for population without possessing knowledge of pain and its physiology. The participants were encouraged to participate with questions when desired. The main goal was that they would establish basic knowledge about pain and how it works, so that they would possess more knowledge about pain than what is expected from the average population.

3.0 Ethics

The guidelines of the International Association for the Study of Pain (IASP) were used as a tool to evaluate the ethics (19).The Nuremberg Code was also followed to ensure the ethics in this research (20). The participants in this study were influenced by a nociceptive stimulus from a CPT, which is a common used tool to produce pain in research (9). Teachers and professors at The Norwegian University College of Health Science were used as an external committee to evaluate ethics in this research, and they approved.

Subjects may have a natural skepticism to join an experiment that will cause them pain. It was therefore important to have a good step-by-step explanation of how the CPT would be conducted before anyone encountered it. It was also clearly explained that the experiment would be safe and not cause any injury. Research method and risks was also explained in a consent form, which needed to be understood and signed by the participating subjects. There was a continuous evaluation of potential undesirable physical or psychological effects during the research. To ensure a minimum chance of any undesirable effects, there was set a maximum exposure time to the cold water of five minutes. The research conductor was also taking readings of the water temperature during the whole time of exposure. These precautions were necessary to prevent tissue damage or other complications.

The participating subjects had the liberty to escape the painful stimulus if the stimulus exceeds their pain tolerance. The participants were also at any point in the research process able to terminate their self without any justifications.

4.0 Results

4.1 Crude and adjusted data

The first measure was taken the moment the participants put their hand in cold water, and this measure was used as baseline for their pain experience. The analysis evaluated values from two changes, value from the change from baseline to the one-minute measure, and value from the change from baseline to fifth-minute measure. Further was these values compared between the two groups. The results are shown here, whereas data describes intervention group in relation to the control group:

Table 4 – Results from crude and adjusted data

	Change 1	Change 2
Crude	-1.19 B with a P-value of 0.14	0.73 B with a P-value of 0.51
Adjusted	-1.26 B with a P-value of 0.18	1.45 B with a P-value of 0.20

The crude data only considerate *Group* as independent variable when looking at differences in NRS measures between the two groups. The adjusted data has also evaluated BMI, age and gender. Adjusted data has higher statistical power, due to more independent variables contributing to the end result. Although as observed in the analysis of *Change 1*, the P-value increases when adjusted, while it decreases in the analysis of *Change 2*. The results are inconclusive.

4.2 Descriptive statistics

Both groups were put in the same diagram, so differences between intervention and control group could be compared visually. There was observed that the confidence interval from the intervention group overlapped the measures from the control group, which is a clear indication of no significant differences between the two groups, when 95% significance level is used as a standard to evaluate difference between the groups.

Figure 1

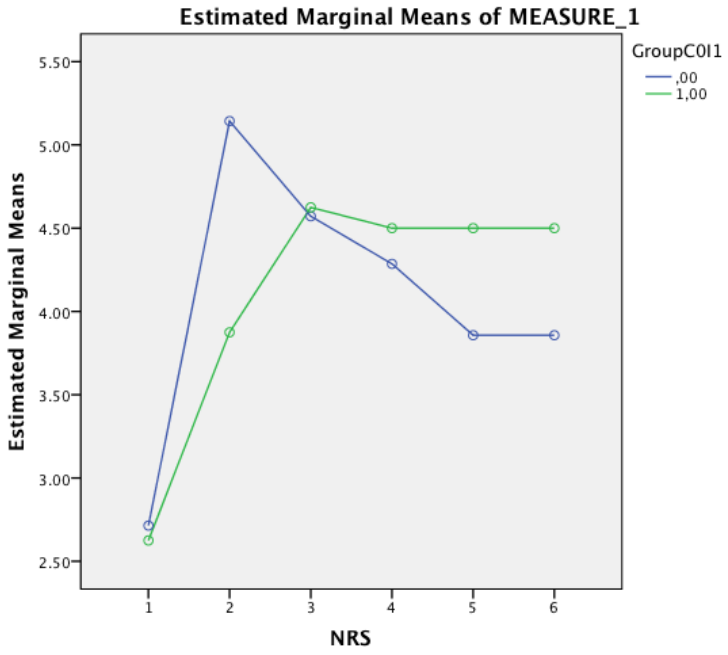

Figure 1 shows the mean value of each of the six measures for both groups, starting with the zero-minutes measure and ending with the fifth-minute measure. The green line is representing intervention group and the blue line is representing control group.
Figure 2

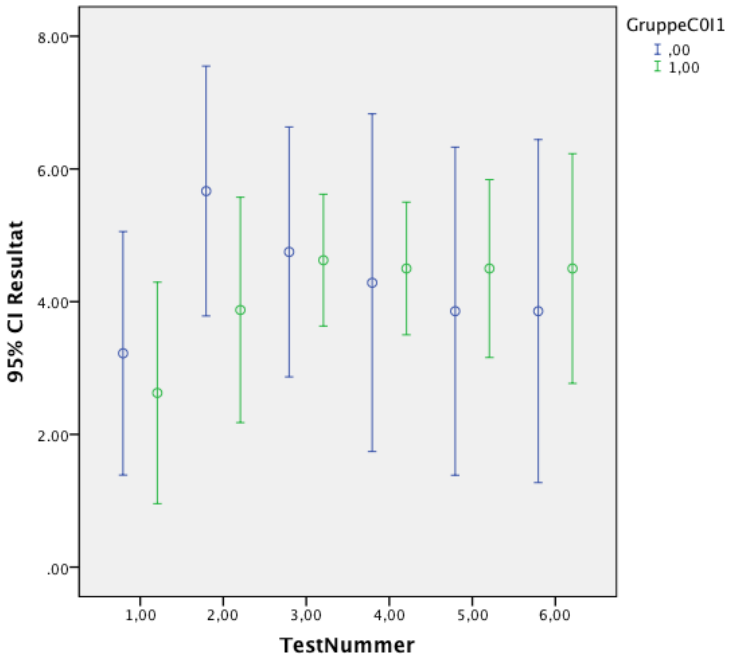

Figure 2 shoes the mean value in six measurements taken between zero and five minutes. Every mean value has also depictured the 95% confidence interval. The big overlap between intervention group and control group, green and blue colors, suggest the lack of significant difference between the groups.

5.0 Discussion

5.1 Discussion of this thesis method and design

One could use a qualitative method to investigate the thesis (16:27). Qualitative method could give a good description of the pain experienced by a subject. A qualitative method often uses interview as a tool to collect information, and this can thereby give tremendous amounts of information about the experienced pain of a subject, both under and after a pain stimulus. This has a very valuable, because, as been discussed, pain is a subjective experience, and there are arguably a lot of aspects and independent variables that the subject is influenced by. This is for instance the different thoughts which the subjects are thinking under and after the pain sensation. A downside of choosing a qualitative method is arguably that it is hard to find a conclusion that can be "the truth" for a bigger population. One can get thorough results from the individuals participating in the study, but it would probably be time consuming, expensive and a lot of work to interview and analyse such an amount of people that one could draw assumptions for a bigger population. Although, if to draw assumptions for a big population is put to side, a qualitative method can analyse the effect of knowledge of pain on the pain experience more thorough and descriptive than the quantitative method used in this thesis.

There was used a quantitative method to do research regarding the hypothesis in the study (16:25). The quantitative method is suitable for research on a big and heterogeneous population (7:42). That arranges for conclusions or assumptions counting for a bigger population (7:37). The quantitative method could further be extended by using a questionnaire and with this get a greater insight in what the subject felt under and after pain, although this

can arguably not compensate for the thoroughness of a good qualitative interview, because of the complexity of pain which is shown in the theory *The Body-Self Neuromatrix* (2:4).

Due to the effort needed to get a random selected sample, and that the goal was to investigate method and design, this study used and was satisfied with a convenience sample (16:49). For a RCT the sample collection should be based on randomisation, so that results can be generalised to count for a bigger population (16:42). The population which results are thought to count for, should also be defined up front, so sample criterion can be established to assure a suitable sample (16:42). A limitation with this study is that the population was not defined, as well as that the sample collection was not sufficient to find results that could be generalised to account for a bigger population.

Sample size should adequately represent the population investigated, and time and cost should also be considered (16:50).A lack in this pilot study is that there where no analysis done for sample size. Sample size is of importance to the validity of analysed results, since a low sample size makes room for results to occur due to chance (16:50). Therefore, the manipulated factor in the intervention group is not necessary the reason for the very weak evidence of difference found between the two groups. For further studies, estimates of required sample size must be done to accomplish a higher level of data validity. Then it may be possible to get significant results which conclusions can be drawn from.

Low sample size existing of a convenience sample, together with the fact that the participants came from the same school, contributed to a quite homogeneous sample (16:49). There are different ways this may have interfered the results, and may affect the reliability and validity of the result. The sample consisted of healthy students during bachelor education, half of them in marketing and the other half in health. Although the study divided subjects to intervention and control group by randomization, because of the low sized sample there is a chance of ending up with most subjects from health education in the same group. The problem with this chance is the possibility that the students of health already possessed knowledge about the topics in the education program, and therefore did not fit as participants in the control group. It can also be argued that students of health are more physically active, which further can be argued to affect pain tolerance. The homogeneous sample should therefore for further studies be replaced with a more heterogenic one, though representing a defined population.

Considering this study's hypothesis, subjects who are likely to possess the level of knowledge about pain that matches the expected level after completing a pain education course, should be excluded because the interfering influence it will have on the results (16:29,16:46). Inclusion and exclusion criterion for participants were established, but because of the need for participants the criterions were set to a level inferior to optimal. First of all, this study had half of the participants from health education, possibly biased as mentioned above. Secondly, a BMI criterion was set to exclude participants who did not have a BMI within 18-25, though this criterion was removed during the process. Nearly half of the participants had a BMI higher than 25, and because of the need for participants these were not excluded. The inclusion criterions said that participants had to be between 18 and 25 of age, have a good health, and had to be students at Campus Kristiania. The intention of these criterions was to define a suitable sample, and to create reliability. The exclusion criterions were established for reasons of safety, and also to establish some control of the design. For further studies participant criterion need to be better defined and controlled. A limitation with this study´s criterion was that they were not accurate checked for, and some of the participants therefore may have had psychological problems (e.g. anxiety or depression).

Level of subcutaneous fat percentage in participants is a factor worth taking into consideration. It is highly arguably that level of subcutaneous fat is a determent factor in pain experience when exposed to cold. It is determined that subcutaneous fat is the most important factor for insulation in relation to heat loss, it is therefore also likely that subcutaneous fat will protect and function as isolation for nociceptive nerve endings (21:90). This was thought of in advance of the study, and therefore were participants BMI calculated. Though, BMI is not a valid indicator of subcutaneous fat percentage, since it only take individuals height and weight into consideration. BMI is therefor a measurement of low validity considering the thought purpose. BMI within a healthy range was set as an inclusion criterion but as mentioned above, this criterion was subtracted due to the need of participants. For the validity of the results the subtraction of the BMI criterion is arguably not a big limitation, because of the fact that BMI in itself does not reflect subcutaneous fat percentage. A more accurate measure for fat percentage is needed. For further studies are a DXA scan recommended to assess fat percentage of participants, since it is shown to have high accuracy in measuring fat (11).

The content of the pain education course must be valued, where just the essences within each topic were set as limit for acquired knowledge. An assurance of acquired knowledge is recommended for later studies. An example would be to finish the pain education course with an exam, to determine if the knowledge about pain within participants has increased sufficient or not. Both content and duration of the pain education course could have been increased, which likely would have given the participants better conditions for increasing their knowledge and understanding of pain, which would affect the study's validity. The learning goals set for the intervention group should also be accurate specified, to declare necessary level of knowledge for influencing the pain experience. A weakness with this study´s pain education course affecting the reliability is that it had no insurance of the subjects' ability to apply their knowledge. Therefore it is not sure whether the level of knowledge about pain within subjects was sufficient or not, or at which level it was.

"The CPT has been used in many studies of pain, autonomic reactivity, and hormonal stress responses" (9). Von Blayer et.al recommends continuously circulating water and a temperature of 10°C +/- 1°C, when used on children and adolescents (9). The test is used in different studies with different variations, and there is therefore a lack of standardisation in the usage of the CPT (22). It has been concluded that only small differences in temperature can cause a significant difference in pain intensity and tolerance (22). This study had factors that might have affected the test in negative ways, and should be improved for further studies; there were no circulation of water, and therefore the water surrounding the participants´ hand might vary from the temperature showed by the thermometer because of heat from the subjects´ hand; only one thermometer was used, for further study´s it is recommended to have a second thermometer to gain better control; the thermometer used had no decimals, and it is therefore a chance that temperature varied +/- 0.9°C from the number shown on the thermometer.

The pain intensity rating tool, NRS, which was used in this study, is a widespread tool for quantifying pain intensity in both clinical practice and in research (23,24). When measuring a subjective experience such as pain, it must be noted that a wide variety in results can occur between subjects. Differences in interpretation of the NRS can affect the outcome, and arguably will each subject's distinctiveness also define its experienced pain level. It is nevertheless an important tool to quantify subjects experienced pain intensity, as it has been

showed to have high reliability and validity (24:242). It can further be discussed if NRS is the best method for addressing experienced pain level within subjects, or if other tools are more suitable, e.g; Visual Analog Scale for Pain (VAS Pain) or McGill Pain Questionnaire (24). VAS Pain is fairly similar to NRS, and benefits from a VAS Pain versus NRS is therefore assumed minimal, if some (24:241). The McGill Pain Questionnaire would give a better description of both qualitative and quantitative aspects of the pain experience (24:242). Limitations with the questionnaire would be high level of analysis needed, as well as it is more time demanding than the NRS.

To avoid a potential bias, it was important that the controller in charge of the CPT had not met the participants before, and that he did not know which group the subject belonged to. This type of single blinding makes the results more valid (7:78). Though, a limitation with this study was the fact that all subjects were familiar with the design of the study, as well as which group they belonged to. This may have affected the way they ranged their experienced level of pain during the experiment, an example of the *Hawthorn effect* (6:335). The *Hawthorne effect* is the effect whereas subjects being observed are changing their behaviour because they are being observed (6:335). For further studies it may be beneficial to change the design on this aspect, and a possible solution may be to gather participants to intervention and control group separately. By using such a design subjects can be blinded to the fact that they are being evaluated against another group. Experiment description for participants then need to be addressed, considering ethical aspects. It may be unacceptable to not relieve a full explanation of the study to participating subjects.

With the theory of *The Body-Self Neuromatrix* as a foundation, there may be difficult to find the true value of manipulating cognitive-related brain areas without also controlling for other thought affecting factors (2). To take all these factors into consideration are arguably also impossible, due to the complexity of pain. As tried with this design, manipulating cognitive-related brain areas by increasing knowledge of pain does not control for other factors related to cognitive-related brain areas. When considering emotion-related brain areas, there was not established an evaluation of emotion-related factors within the participants, except the criterion of not having psychological problems. For further studies it may be beneficial to assess more factors in relation to emotion- and cognitive-related brain areas, with validated tools as e.g. Beck Depression Inventory, Beck Anxiety Inventory or Personality Belief Questionnaire (25). The same issue counts for sensory signalling systems, which is thought to be the last of the three contributing inputs when pain is generated. This study with its design only assesses and control for sensory afferents from nociceptive nerve fibres, and participants will always be influenced by other signals through other senses. All external factors should for further studies therefore be put down to a minimum level, so that an effect easier can be controlled for and be awarded the manipulated factor (7:16,16:35).

5.2 Discussion of results from analysis

The results are worth taking into consideration, because even though they were not statistically significant, the sample size was low, and emotion-related conditions were not addressed at all, a very weak difference occurred (P-value 0.18 and 0.20). If the results are linked to the thesis, which has its foundation in *The Body-Self Neuromatrix* theory, there may be a possibility to manipulate cognitive-related brain areas to a certain degree, and from that, affect the output of the neuromatrix, the pain experience. Due to weaknesses in method and design, and the results of very weak evidence, no statistical significant conclusion can be

made. Though, with enhanced design, further studies should be able to better test if knowledge about pain affects the pain experience.

NRS measures from third, fourth and fifth measure were excluded in the multivariable linear regression test. It was done that way due to the high level of analyse needed if all the NRS measures should be included, and the multivariable linear regression test would not be sufficient to analyse these effects. The reason is that there is no linear relationship between the two groups, and that one would take into consideration "clustering effect" and "random effect". One would also need to do measurements between groups and within groups at every single NRS measure. This will create a very big data set, and analysing methods would be on a higher level.

The clustering effect is related to the first measure taken for each participant. This measure will be the basis for their further evaluation of pain level during pain. With stable cold water, the pain level will arguably not have a fast alteration, only a moderate change over time. This causes the measures during the test to be in the area of the first measure, even though the subject ranged the first measure high or low. In other words, a value will have a high chance of being close to the value before. In practice, it will mean that if a subject marked the pain as five on the zero-minute mark, there is a high chance that the next measure will be between four and six. If the zero-minute measure is marked two on the scale, there are a high chance that the next measure are marked between one and three. The effect will cause clusters of results within each subject.

In the crude data analysis, one took a multivariable linear regression test with one independent variable at the time, and used the dependent variable as in the adjusted measurements. This was done to look for confounding variables that may inflict the end results of the adjusted test. The crude results are therefore only used as an analysing method.

Results from the two crude multivariable linear regression tests showed that *BMI* had a very high difference in value (B) between *Change 1* (variance from baseline to the one-minute measure) and *Change 2* (variance from baseline to the fifth-minute measure). This means that *BMI* as an independent variable, worked as a confounding variable, possibly obscuring the result of the dependent variable, ranged pain intensity. *BMI* was never the less used as an independent variable together with *Group*, *Age* and *Gender*. This may have caused an obscured picture of the effect the independent variable intended to manipulate (*Group*), had on the dependent variable (pain intensity) in the adjusted data. The cause of this effect may have inflicted the P-value.

There can be a lot of factors contributing to why there could not be produced any significant results from the statistics in this thesis. A big contributing factor is hypothesized to be the sample size. The sample investigated was quite a homogeneous one, but this factor was not big enough to counterbalance the effect of a small sample size. A high variance in test results caused a high confidence interval that made it an almost impossible task to create significant results with such small groups. Such a high difference in test results was not expected, especially not in the intervention group, which were hypothesised, since they had gone through the pain education course, to experience pain on a more equal level. Though, the intervention group showed a more synonymous rating than the control group. This was expressed unmistakable in the descriptive statistics, where one can observe that every single confidence interval was smaller than in the control group.

It can also be questioned if the results (if some, was very weak) from the study are transmittable to daily life. The participants had the content from the pain education course fresh in memory, as well as they were mentally prepared for the stimuli that they were going to be exposed to. If the result from increased knowledge of pain physiology would help to experience a more rational pain experience in a study of this design, further studies should aim on; longer intervals between education and CPT exposure, to see if an increase in knowledge of pain physiology has an impact on pain experience in the long run. The limiting factor that subjects are mentally aware and prepared for the stimuli is difficult to avoid due to ethics. The study´s design is partly limiting itself this way, because the subjects are aware that they will be applied a painful stimuli, which is rarely transmittable to real life pain experiences. The unexpected aspect with real life experienced pain will in a study of this design be difficult to recreate.

6.0 Conclusion

When looking at the results, there is not a statistical significant difference between the two groups. One can only see a trend in the data, which shows with very weak evidence that possessing knowledge of pain processing affect the pain experience.

Based on the statistics and the evaluation of method and design, there can be concluded that there needs to be changes for further studies. A RCT should be able to investigate for an effect of possessing knowledge of pain physiology in relation to pain experience, by using the base of this study with some improvements. NRS worked to quantify pain, and the CPT worked to induce pain. The pain education course needs some improvements regarding content and goal. Participant criterions need to be better established. Suggestions discussed for controlling other factors hypothesised to affect the pain experience, should be tested. Though, as pain is a multifactorial experience, it will be hard to control for all these factors. Analysing method suited to control for more variables is recommended.

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