Thermographic evaluation and analysis of a cold-water test: a comparative study between patients with the fibromyalgia syndrome and healthy controls.

Elien DE SCHAMPHELAERE

Promotor: Prof. Dr. Devulder J.
Co-promotor: Dr. Brusselmans

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Master of Medicine in Medicine
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Date 14/04/2013

(signature)

De Schamphelaere Elien

Name (student)

(promoter)
Prof. Dr. Devulder J.
Dr. Brusselmans G.
TABLE OF CONTENTS

FOREWORD .................................................................................................................. VI

ABSTRACT (English) ................................................................................................. 1
ABSTRACT (Nederlands) ......................................................................................... 2

LIST OF FIGURES ..................................................................................................... 3
LIST OF TABLES ......................................................................................................... 4
LIST OF ABBREVIATIONS ......................................................................................... 5

1. INTRODUCTION ...................................................................................................... 6
   1.1. Historical perspective ......................................................................................... 7
   1.2. Etiology ............................................................................................................. 8
   1.3. Pathophysiology .............................................................................................. 8
       1.3.1. Abnormal stress reaction ....................................................................... 8
       1.3.2. Abnormal pain sensitivity ..................................................................... 9
       1.3.3. Autonomic dysfunction ..................................................................... 11
   1.4. Diagnosis ........................................................................................................ 11
   1.5. Therapy ........................................................................................................... 12
       1.5.1. Pharmacologic treatment ...................................................................... 13
       1.5.2. Non-pharmacologic treatment ................................................................. 13
       1.5.3. Education and psychological domains .................................................. 14
       1.5.4. Complementary and alternative medicine ............................................ 14
   1.6. Cold water test ................................................................................................ 15
   1.7. Research question ........................................................................................... 15
2. MATERIAL AND METHODS ......................................................................................... 16
  2.1. Subjects ........................................................................................................... 16
  2.2. Materials ......................................................................................................... 16
  2.3. Methods .......................................................................................................... 17

3. RESULTS .................................................................................................................. 18
  3.1. Describing the test group by analysing the questionnaires (POMS and PainDetect) 18
    3.1.1. PainDETECT ............................................................................................ 18
    3.1.2. POMS ...................................................................................................... 19

  3.2. Describing the test group by body features ...................................................... 20
    3.2.1. BMI ......................................................................................................... 20

  3.3. Temperature differences between FM patients and healthy controls ............... 21
    3.3.1. Basic temperature measurements .............................................................. 21
    3.3.2. Temperature indices .................................................................................. 22
    3.3.3. Right – left ear temperature differences ................................................... 23

  3.4. Experimental results .......................................................................................... 24
    3.4.1. Immersed time ......................................................................................... 24
    3.4.2. Development of NRS score ..................................................................... 24
    3.4.3. Comparison of NRS score between FM patients vs. healthy controls ....... 26
    3.4.4. Temperature decrease .............................................................................. 26
    3.4.5. Cool-down rate ....................................................................................... 27
    3.4.6. General recuperation ............................................................................... 28
3.4.7. Recuperation during 0-20 minutes ................................................................. 29
3.4.8. Recuperation during 0-5 minutes ....................................................................... 29
3.4.9. Recuperation during 5-20 minutes .................................................................... 30
3.4.10. Recuperation after 20 minutes compared with basal temperature .......... 30
3.4.11. Warm-up rate .................................................................................................. 31
3.4.12. Vital parameters during the experiment ............................................................. 33

4. DISCUSSION ........................................................................................................... 34

5. CONCLUSION .......................................................................................................... 37

ACKNOWLEDGEMENTS ............................................................................................ 38

REFERENCES ............................................................................................................. 39
FOREWORD

For the last two years I have continuously kept on working on this thesis. Firstly by doing all the experiments, secondly by analyzing all the data and finally by writing down the results of my investigation. I realized and experienced how interesting scientific research can be. The combination of personal contact, in particular with the group of patients, and the scientific side of statistic analysis of data I found through research and eventually writing them down, has been a great experience to me. My interest in scientific research is strongly encouraged and considerably grown in the course of this study.

I would like to thank everybody who supported me in the last two years.

In particular I wish to thank my mentor, Dr. Brusselmans. Whenever I had questions or whenever I got stuck with my data, she was there to consider the problem and to stimulate me in the process of searching and finding a solution.

I also want to say thanks to my parents for giving me the opportunity to study medicine and for being my biggest “frontline” supporters.

Finally I’d like to thank my boyfriend for his never-ending support.

I tried to paint a picture of how I really feel. But I could not find the colors to make it all seem real. Not one color was hot enough, to show the burning pain. Not one color bright enough, to wince me back again. Not one color was dark enough, to show the isolation. In the end I saw one thin line worn, frayed and almost broke. To my mind, that one thin line is a single thread of hope.

- A Picture of Pain, Bear Peterson
ABSTRACT (English)

Aim and backgrounds The aim of this study is to examine differences between the nervous system of patients with the fibromyalgia syndrome (n=23) and healthy controls (n=15). Because one of the features of the autonomic nervous system is the regulation of body temperature, we set up a cold-water experiment.

Methods Twenty-three female patients with the fibromyalgia syndrome and 15 female controls in general good condition, were recruited. Different questionnaires (PainDETECT and POMS) were filled up. All patients and controls underwent a cold-water immersion experiment. They were asked to put their forearm into cold water as long as possible. Skin temperature and the recuperation process was recorded by a thermographic camera. The results of the questionnaires and the cold water experiment were analyzed and compared by use of statistical package, SPSS.

Results At baseline conditions a significant difference was found in the following parameters : body mass index (p=0.011), body temperature (p=0.027), forearm thermography (p=0.018), peripheral (forearm thermography) / central (ear temperature ) (p=0.033), left – right ear difference (p=0.018). During the experiment the following parameters were found significantly different : immersed time (p<0.001), temperature decrease (p<0.001), cool-down rate (p<0.001), recuperation between 0 and 20 minutes (p<0.001), recuperation between basal temperature and 20 minutes (p<0.001).

Conclusion This study showed an abnormality in the autonomic nervous system in baseline conditions. The cold water test wasn’t able to show the expected difference in autonomic nervous system response between FM patients and healthy controls.
ABSTRACT *(Nederlands)*

Doel: Deze studie werd ontwikkeld met als onderzoeksvraag het al dan niet aanwezig zijn van een verschil in werking van het autonoom zenuwstelsel tussen patiënten met fibromyalgie (n=23) en gezonde controles (n=15). Aangezien één van de belangrijkste functies van het autonoom zenuwstelsel de regulatie is van lichaamstemperatuur, werd dit verschil onderzocht d.m.v. een koude experiment.

*Materiaal en methode* Driëntwintig vrouwelijke patiënten met fibromyalgie en 15 gezonde vrouwelijke vrijwilligers in algemeen goede gezondheid werden geïncludeerd in de testgroep. Verschillende vragenlijsten (PainDETECT en POMS) werden afgenomen. Alle patiënten en controles ondergingen het koud-water experiment. Aan iedere vrouw werd gevraagd haar arm, vanaf de vingers tot aan de elleboog, in het koude water onder te dompelen tot de pijn ondraaglijk werd. Nadien werd de huidtemperatuur en het herstelproces nauwkeurig opgenomen met de thermografische camera. De resultaten van de vragenlijsten en experimenten werden opgenomen in een database en verwerkt d.m.v. een statistisch pakket, SPSS. Een vergelijkende studie tussen beide groepen werd gesteld.

*Resultaten* Tijdens basale omstandigheden werd een significant verschil gevonden in volgende parameters: BIM (body mass index), lichaamstemperatuur *(p=0.027)*, voorarm thermografie *(p=0.018)*, perifeer (voorarm thermografie) / centraal (oor temperatuur) *(p=0.033)*, links-rechts oor temperatuur verschil *(p=0.018)*. Tijdens het experiment werd in volgende parameters een statistisch significant verschil vastgesteld: ondergedompelde tijd *(p<0.001)*, temperatuurdaling *(p<0.001)*, afkoelsnelheid *(p<0.001)*, herstel tussen 0 en 20 minuten *(p<0.001)*, herstel tussen basale temperatuur en 20 minuten *(p<0.001)*.

*Conclusie* De studie kon een duidelijk verschil aantonen tussen beide groepen in basale omstandigheden. Het koud-water experiment kon niet de verwachte verschillen in de werking van het autonoom zenuwstelsel tussen fibromyalgie patiënten en gezonde controles aantonen.
LIST OF FIGURES

Figure 1 Pathophysiology of pain. .......................................................................................... 10
Figure 2 Location of 18 fibromyalgia tender points. ................................................................. 12
Figure 3 Use of medication within the FM patients group. ....................................................... 16
Figure 4 Describing the total PainDETECT score within the FM group. ................................. 19
Figure 5 Describing the difference in POMS between the FM patients and healthy controls. 19
Figure 6 Describing BMI index within the FM patients group. .................................................. 20
Figure 7 Describing BMI index within the healthy controls group ........................................... 20
Figure 8 Body temperature between FM patients and healthy controls. ................................. 21
Figure 9 Average ear temperature between ............................................................................. 21
Figure 10 Forearm thermography in basal conditions between FM patients and healthy controls........................................................................................................................................... 22
Figure 11 P (forearm) / C (ear) index between FM patients and healthy controls................. 22
Figure 12 P (axilla) / C (ear) index between FM patients and healthy controls. .................... 23
Figure 13 Right – left ear temperature difference between FM patients and healthy controls. ........................................................................................................................................... 23
Figure 14 The difference in immersed time between FM patients and healthy controls........ 24
Figure 15 The development of NRS score of FM patients during the experiment. ................. 25
Figure 16 The development of NRS score of healthy controls during the experiment. .......... 25
Figure 17 Temperature decrease between FM patients and healthy controls. ....................... 26
Figure 18 The relation immersed time - decrease in temperature of FM patients...................... 27
Figure 19 The relation immersed time - decrease in temperature of healthy controls. ............ 27
Figure 20 General recuperation of temperature after the immersion during the next 20 minutes between FM patients and healthy controls. ......................................................................................... 28
Figure 21 The development of the recovery (T0-T5) of FM patients. ...................................... 29
Figure 22 The development of the recovery (T0-T5) of healthy controls. ............................... 30
Figure 23 Progress of temperature during the experiment. .................................................... 31
Figure 24 The progress of recovery (T5-T20) of FM patients. .................................................. 32
Figure 25 The development of recovery (T5-T20) of healthy controls. .................................... 32
Figure 26 The evolution of RR during the experiment. .............................................................. 33
Figure 27 The evolution of pulse during the experiment (average pulse). ............................... 33
LIST OF TABLES

Table 1 Common symptoms presented by patients with FM.......................................................... 6
Table 2 “Stressors” Capable of Triggering FM and Related Conditions........................................... 8
Table 3 Treatment goals in FM therapy............................................................................................... 12
Table 4 European League Against Rheumatism recommendations for FM treatment, including both medication and non-pharmacologic therapies................................................................. 14
Table 5 Describing the features of PainDETECT by FM patients......................................................... 18
Table 6 Averages of NRS score by FM patients and healthy controls.................................................. 26
Table 7 Average temperature progress during the experiment............................................................. 28
Table 8 Progress of temperature during the experiment................................................................. 31
Table 9 The evolution of RR during the experiment (average RR)................................................... 33
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>IBS</td>
<td>Irritable Bowel Syndrome</td>
</tr>
<tr>
<td>TMD</td>
<td>TempoMandibular Disorder</td>
</tr>
<tr>
<td>ACR</td>
<td>American College of Rheumatology</td>
</tr>
<tr>
<td>HPA</td>
<td>Hypothalamic-Pituitary-Adrenocortical</td>
</tr>
<tr>
<td>LC-NE</td>
<td>Locus Ceruleus/NorEpinephrine</td>
</tr>
<tr>
<td>CSF</td>
<td>CerebroSpinal Fluid</td>
</tr>
<tr>
<td>EAA</td>
<td>Excitatory Amino Acids</td>
</tr>
<tr>
<td>PTN</td>
<td>Pain Transmission Neurons</td>
</tr>
<tr>
<td>NO</td>
<td>Nitric Oxide</td>
</tr>
<tr>
<td>ANS</td>
<td>Autonomic Nervous System</td>
</tr>
<tr>
<td>HRV</td>
<td>Heart Rate Variability</td>
</tr>
<tr>
<td>NSAID</td>
<td>Non-Steroidal Anti-Inflammatory Drugs</td>
</tr>
<tr>
<td>EMG</td>
<td>ElektroMyoGraphy</td>
</tr>
<tr>
<td>CBT</td>
<td>Cognitive Behavioral Therapy</td>
</tr>
<tr>
<td>SSRI</td>
<td>Selective Serotonin Re-uptake Inhibitor</td>
</tr>
<tr>
<td>POMS</td>
<td>Profile Of Mood Scale</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for Social Sciences</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>RR</td>
<td>Riva Rocci, Blood Pressure</td>
</tr>
<tr>
<td>NRS</td>
<td>Numeric Rating Scale</td>
</tr>
</tbody>
</table>
1. INTRODUCTION

Fibromyalgia (FM) is estimated to affect 2% of the European population, most of them are females. This makes it one of the most common chronic widespread pain disorders. It is the second most common disorder observed by rheumatologists. A substantial subpopulation of patients first present en seek ongoing care in the primary care setting (1). FM is seen as a syndrome marked by chronic widespread pain and multiple symptoms, including fatigue, sleep disturbances, cognitive dysfunction, and depressive episodes. Some neurologic symptoms like paresthesias, blurred vision, numbness, and weakness, are often reported by FM patients (2). Disorders associated with FM are chronic fatigue syndrome, irritable bowel syndrome (IBS), irritable bladder syndrome or interstitial cystitis, and temperomandibular disorder (TMD). Patients with FM complain of hyperalgesia (heightened pain response to normally painful stimuli) and/or allodynia (pain responses to normally non painful stimuli). The causing stimuli can be heat and cold, as well as mechanical and ischemic pressure (2). Responses as hyperalgesia and allodynia suggest that patients with FM have a fundamental problem with pain or sensory processing rather than an abnormality confined to the region of the body where pain is experienced (3).

Table 1 Common symptoms presented by patients with FM (4).

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain complaints</td>
<td></td>
</tr>
<tr>
<td>– Low back pain</td>
<td>63</td>
</tr>
<tr>
<td>– Headaches</td>
<td>47</td>
</tr>
<tr>
<td>– Arthritis</td>
<td>46</td>
</tr>
<tr>
<td>– Muscle spasm</td>
<td>46</td>
</tr>
<tr>
<td>– Jaw pain</td>
<td>29</td>
</tr>
<tr>
<td>Neurologic and sensory disturbances</td>
<td></td>
</tr>
<tr>
<td>– Tingling</td>
<td>46</td>
</tr>
<tr>
<td>– Numbness</td>
<td>44</td>
</tr>
<tr>
<td>– Restless legs</td>
<td>32</td>
</tr>
<tr>
<td>– Tinnitus</td>
<td>30</td>
</tr>
</tbody>
</table>
1. INTRODUCTION

<table>
<thead>
<tr>
<th>Gastrointestinal complaints</th>
<th>44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritable bowel syndrome</td>
<td></td>
</tr>
<tr>
<td>Bloating</td>
<td>40</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Constitutional symptoms</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic fatigue</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychological symptoms</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other symptoms</th>
<th>37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus problems</td>
<td></td>
</tr>
<tr>
<td>Tooth problems</td>
<td>32</td>
</tr>
<tr>
<td>Bladder problems</td>
<td>26</td>
</tr>
<tr>
<td>Rashes</td>
<td>25</td>
</tr>
</tbody>
</table>

1.1. Historical perspective

Although the term “fibromyalgia” (FM) is relatively new, the condition has been described in the medical literature for several years. Sir William Gowers coined the term “fibrositis” in 1904. The current concept of FM was established by Smythe and Moldofsky in the mid-1970s, with the term “fibromyalgia”. This reflects the increased evidence that this syndrome represents an abnormality of pain processing (–algia) rather than an inflammation of connective tissues (“itis”). The next advance in FM was the development of criteria for the syndrome by the American College of Rheumatology (ACR), which were published in 1990. The criteria required: “tenderness on pressure (tender points) on at least 11 of 18 specified sites and the presence of widespread pain for more than 3 months for diagnosis. Widespread pain is defined as axial pain, left- and right-sided pain, and upper and lower segment pain” (5). Major advances in understanding FM occurred after medical researchers realized that this syndrome is not caused by peripheral damage or inflammation. Instead they began to explore the central neural mechanism of the most common symptoms reported by many patients (3). In 2010, the ‘revised’ criteria for diagnosis of FM were published by the same group of authors as the original criteria of 1990. The revised criteria are based on a widespread pain index (ACR criteria) and a symptom severity scale (6).
1. INTRODUCTION

1.2. Etiology
The underlying mechanisms responsible for symptom expression in FM and related disorders are complex and multifactorial (3). The etiology of FM includes abnormalities in the neuroendocrine and autonomic nervous systems, genetic factors, psychosocial variables, and environmental stressors (2). Pain threshold studies show that patients with FM perceive pain at a lower threshold than healthy controls, for example the pain response to pressure on some area of the body (7).

Table 2 "Stressors" Capable of Triggering FM and Related Conditions (3).

<table>
<thead>
<tr>
<th>Stressors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral pain syndromes</td>
</tr>
<tr>
<td>Infections (e.g., parvovirus, Epstein-Barr virus, Lyme disease, Q fever)</td>
</tr>
<tr>
<td>Physical trauma (e.g., automobile accidents)</td>
</tr>
<tr>
<td>Psychological stress/distress</td>
</tr>
<tr>
<td>Hormonal alterations (e.g., hypothyroidism)</td>
</tr>
<tr>
<td>Drugs</td>
</tr>
<tr>
<td>Vaccines</td>
</tr>
<tr>
<td>Certain catastrophic events (war, but not natural disasters)</td>
</tr>
</tbody>
</table>

1.3. Pathophysiology

1.3.1. Abnormal stress reaction
Some authors have proposed that disruptions in response to stress may be an important mechanism generating pain and other symptoms in FM. The principal components of the human stress response are the hypothalamic-pituitary-adrenocortical (HPA) axis and locus ceruleus/norepinephrine-sympathetic (LC-NE) system. Although results of studies examining HPA axis function in patients with FM are inconsistent, with both HPA axis hypoactivity and hyperactivity identified (6).
1. INTRODUCTION

1.3.2. Abnormal pain sensitivity

On the molecular level, patients with FM show changes in levels of neurochemicals and receptors associated with increased signalling in ascending (pro-nociceptive) pathways and decreased signalling in descending (anti-nociceptive) pathways (8). The increased signalling in ascending pathways (pro-nociceptive pathways) is indicated by increased levels of neurotransmitters in the cerebrospinal fluid (CSF). The neurotransmitters of the pro-nociceptive pathways include substance P, nerve growth factor, and brain-derived neurotrophic factor. A study showed the presence of higher levels of these neurotransmitters in the CSF of patients with FM compared to healthy controls. Additionally, levels of glutamate and other excitatory amino acids have been shown to be elevated in the CSF of individuals with FM. Glutamate acts on N-methyl-D-aspartate receptors and produces increased central pain “wind up”. After repeated painful stimulation this phenomenon causes progressively increased central pain amplifications, which results in greater hyperalgesia and allodynia. Beside the increased signalling of the ascending pathway, the activity of descending (anti-nociceptive) pathways is decreased. This can be evidenced by lower CSF levels of metabolites of neurotransmitters of the descending pathways, including serotonin, norepinephrine and dopamine (1).
Figure 1 Pathophysiology of pain (2).

(A) In the classic model of acute pain, painful stimuli are transmitted from the periphery to the dorsal horn via the primary afferent fibers (A-δ and C nerve fibers) and from the dorsal horn to the brain via the spinothalamic tract. Pain perception is modulated through the activation of descending inhibitory pathways and the release of neurotransmitters such as norepinephrine, serotonin and opiatelike substances (endorphins). (B) In the dorsal horn, incoming afferent pain signals cause the release of substance P and excitatory amino acids (EAA), which bind to activate postsynaptic receptors on the pain transmission neurons (PTN). Glia are present but quiescent. (C) With intense or prolonged exposure to painful stimuli, incoming afferent signals are increased, and presynaptic release of substance P and EAAs is enhanced. An influx of calcium increases the production of nitric oxide (NO), which diffuses out of the PTN and causes the PTN to become hyperexcitable and further enhances the presynaptic release of EAAs and substance P. Glia cells become hyperexcitable and further enhances the presynaptic release of EAAs and substance P. Glia cells become activated and release substances that further increase presynaptic release and postsynaptic hyperexcitability (2).
1. INTRODUCTION

1.3.3. Autonomic dysfunction
Several biological abnormalities have been described in FM patients, including dysfunction of the autonomic nervous system (ANS) (9). The ANS is the main regulatory system of the body in charge of maintaining essential involuntary functions. These functions are the so called vital signs, including blood pressure, pulse, respiration, and temperature. The ANS maintains the function of all internal organs. The heart rate, intestinal motility, urination, sexual activity, and many other variables are all regulated by the ANS (10). Abnormality of the ANS has been documented in conditions such as irritable bowel syndrome, chronic fatigue syndrome and migraine headache (11). FM is often associated with these conditions, suggesting a similar pathophysiology. Several studies examined the ANS of FM patients. Some studies reported increased autonomic activity measured by elevated skin conductance, heart rate (12) and blood flow (13). A 24h HRV analysis in a circadian-variation study showed an increased nocturnal predominance of the low-frequency band oscillations. This suggests an exaggerated sympathetic modulation of the sinus node (14). Impaired sympathetic reactivity to orthostatic stress is also seen in FM patients (15). FM patients are hyporeactive to various sympathetic stimuli such as auditory stimulation test, cold presser test at 10 and 4°C (16) and gravitational stress using tilt table (17). FM appears to be a situation of autonomic dysfunction. Both the sympathetic limb, functioning as “fight or flight reaction”, and the parasympathetic limb, functioning as “rest and digest”, are differentially involved. Dysfunction of the ANS can also explain the diverse clinical manifestations of the syndrome such as sleep disorders, anxiety, Raynaud’s-like phenomenon, Sicca symptoms and intestinal irritability (11).

1.4. Diagnosis
Diagnostic criteria were established by the American College of Rheumatology (ACR): “1. pain must be chronic, persisting ≥ 3 months, 2. pain must be widespread, 3. pain must affect both sides of the body, 4. pain must affect areas above and below the waist, 5. axial pain must be present; and 6. at least 11 of 18 tender points must be painful to ~ 4 kg of pressure”.
Although meeting the ACR criteria helps ensuring the diagnosis of fibromyalgia, diffuse pain may occur with several other medical conditions. A careful history and examination is required to exclude these potentially correctable medical conditions or illnesses that require disease-specific treatments (4), before making a FM diagnosis.
1. INTRODUCTION

1 and 2: occiput; 3 and 4: trapezius; 5 and 6: supraspinatus; 7 and 8: gluteal; 9 and 10: lower lateral cervical; 11 and 12: 2nd costochondral junction; 13 and 14: lateral epicondyle; 15 and 16: greater trochanter; 17 and 18: medial knee fat pad. (5).

Figure 2 Location of 18 fibromyalgia tender points.

1.5. Therapy

Many patients experience FM as a stressful syndrome as its etiology is complex and not fully understood. Treatment isn’t standardized yet and often ineffective. FM is a syndrome with an unpredictable disease course, so that patients have to deal with lot of uncertainty about their future. The aim of treating FM is to decrease pain and increase function. The most benefits are seen by use of a multimodal therapeutic strategy which, in most cases, includes pharmacologic and non-pharmacologic interventions (18).

Table 3 Treatment goals in FM therapy (19).

<table>
<thead>
<tr>
<th>Overall Treatment goals in Fibromyalgia Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reduce pain and tenderness</td>
</tr>
<tr>
<td>• Ameliorate multidimensional symptoms, including :</td>
</tr>
<tr>
<td>- Fatigue</td>
</tr>
<tr>
<td>- Cognitive impairment</td>
</tr>
<tr>
<td>- Disrupted sleep</td>
</tr>
<tr>
<td>- Mood and anxiety symptoms</td>
</tr>
<tr>
<td>- stiffness</td>
</tr>
<tr>
<td>• Restore functionality and improve quality of life</td>
</tr>
</tbody>
</table>

1. INTRODUCTION

1.5.1. Pharmacologic treatment
FM had been treated by a wide range of drugs including antidepressants, opioids, nonsteroidal anti-inflammatory drugs (NSAID), sedatives, muscle relaxants, and anti-epileptic agents. Only a few have shown to have clear-cut benefits in randomized controlled trials. The benefit of NSAIDs has generally been disappointing (18). Both antidepressants and neuromodulating anti-epileptics showed substantially benefits of FM symptoms in patients. Dual-action antidepressants like SNRI’s (selective serotonin and noradrenal re-uptake inhibitor) affect both serotonin and norepinephrine transmission. This offers effective analgesia as well as improvement in mood disorders. Among antidepressants SSRI’s provide the best efficacy and tolerability for FM (4).

1.5.2. Non-pharmacologic treatment
As FM patients are treated by the use of multimodal strategy, non-pharmacologic treatment is implemented too. The non-pharmacologic treatments linked to improvement of FM are aerobic exercise and strength training. FM is most effectively treated with fitness and strengthening exercise. Evidence-based guidelines by the Ottawa Panel for non-pharmacologic treatment of FM, based on findings of randomized and controlled trials can be summarized as:

- The Ottawa Panel has found emerging evidence to support the use of aerobic fitness programs for the overall management of FM. Most improvements were found by restoring quality of life. Aerobic fitness exercises were found to increase endurance. This, in turn, improved greatly the everyday functionality of patients (20).
- The Ottawa Panel has found emerging evidence to support the use of strengthening exercises as part of the overall management of FM. Improvements were seen for muscle strength, quality of life and decrease in depression (21).

The Ottawa panel concluded: “Due to the vast variability in FM symptoms, patients would likely function best with a highly individualized program that incorporates multiple treatment regimens” (20-21)
1. INTRODUCTION

1.5.3. **Education and psychological domains**

Patient education has the aim of reducing anxiety, increasing treatment compliance, improving coping behaviours and self-efficacy. Moreover it draws away the attention from symptoms and moves the attention toward improved functioning and quality of life. Therapy dealing with the interrelationships between the physical and psychological aspects of the illness supports great benefits for FM patients. Psychophysiological therapy is based on two principle approaches, such as EMG biofeedback, and cognitive-behavioural therapy (CBT). CBT leads to improvements in pain, other clinical symptoms, functional disability, pain behaviour, and tender point measures (18).

1.5.4. **Complementary and alternative medicine**

Complementary and alternative medicine is often used by FM patients in addition to conventional treatments. Most of the studies of alternative medical systems (homeopathy), energy therapies (magnetic therapies), and mind-body interventions (biofeedback, relaxation, and hypnotherapy) are methodologically flawed. Definite conclusion can’t be drawn as to their usefulness. Acupuncture, nutritional supplementation and massage therapy have shown a moderate evidence of effectiveness (18).

**Table 4** *European League Against Rheumatism recommendations for FM treatment, including both medication and non-pharmacologic therapies* (4).

<table>
<thead>
<tr>
<th>Effective medications</th>
<th>Tramadol</th>
<th>Antidepressants</th>
<th>Pramipexole</th>
<th>Pregabalin</th>
<th>Tropisetron</th>
<th>Paracetamol</th>
<th>Acetaminophen</th>
<th>Weak opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective nonpharmacologic treatments</td>
<td>Heated pool treatment with or without exercise</td>
<td>Aerobic exercise</td>
<td>Strength training</td>
<td>Cognitive behavioural therapy</td>
<td>Possibly relaxation, rehabilitation, physical training, and psychological support</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. INTRODUCTION

1.6. Cold water test

The cold water immersion stimulates cutaneous cold-sensitive receptors and nociceptors. The nociceptors evoke an axon reflex and/or a reflex via the central nervous system. The reflex increases skin sympathetic nerve activity to the immersed area in ice-water. This increased sympathetic nerve activity causes first a vasoconstriction of cutaneous blood vessels. Afterwards the vasoconstriction is followed by a vasodilatation (22). The local cold stimulation causes also a reflexive effect on the skin vascular system of the whole body. Cold stimulation has been commonly used for the physiological autonomic function test, such as for stimulation of the sympathetic nerve. Aberrations in the autonomic nerve system function are often observed in patients with fibromyalgia (2).

1.7. Research question

The design of the study aims to show a difference in reaction of the ANS between FM patients and healthy controls, when exposed to a stressor. Because one of the features of the ANS is the regulation of the body temperature, we set up a cold-water experiment. The ANS was challenged under the cold stressor, with a view to see a difference between the reaction of FM patients and healthy controls. Reaction of the body temperature is measured before and after the cold-water immersion. Immediately after the cold-water immersion experiment, we are looking at the recuperation of the forearm temperature in both groups during the following 20 minutes, knowing that the ANS plays a key role in this stadium.
2. MATERIAL AND METHODS

2.1. Subjects
Twenty-three female patients diagnosed with FM participated in this study. The average age was 43 years (range 20-56). They were all patients in the pain clinic at UZGent and all fulfilled the classification criteria for FM proposed by the American College of Rheumatology. (5) Following the manual assessment of tender-points, pressure pain thresholds were determined using a pressure FPK 10 algometer (Wagner Instruments). The average duration of generalized pain was 8,3 years (range 1-35 years). Thirty-five % of the patients were on daily antidepressive medication (25% amitriptyline, 10% SSRI), 50 % of the patients need pain medication on daily basis.

![Use of medication](image)

**Figure 3** Use of medication within the FM patients group.
Fifteen female healthy controls were selected by age. They were asked to be in general good health. Pregnant women were excluded. The average age was 40 years (range 20-56 years). The experiments were approved by the local ethical committee of the UZGhent. All subjects were carefully instructed on the study procedures and gave their informed consent.

2.2. Materials
The thermographic pictures were taken by a computer-assisted infrared thermograph (Thermacam SC300, FLIR, Danderyd, Sweden). This thermographic camera produces a matrix (representing image points) of temperature values. The thermal sensitivity of the thermograph is 0,05°C at 30°C. Body temperature was measured by an ear thermometer.
2. MATERIAL AND METHODS

(Genius 2 IR Tympanic Thermometer) and an electronic thermometer at the axilla (Hantmann Thermoval Basic), on both the left and the right-hand side. Blood pressure and pulse were measured by an automatic monitor type Propaq Encore Welch Allyn. FM tenderpoints were measured by a FPK 10 algometer (Wagner Instruments).

2.3. Methods

The experiment took place at the UZGhent, building 3B2, Multidisciplinary Pain Center (MPC). During the experiment the room temperature was kept at 23°C. The experiment was administered by the same person. Experiments were performed during autumn of 2012. The experiment was based on a cold water test. In this experiment we were interested in the reaction to cold and recovery of the peripheral vasoconstriction after exposure to cold. Patients were interrogated by use of 3 questionnaires, including the PainDetect, the Profile of Mood Scale (POMS) and the American College of Reumatology Criteria of Fibromyalgia (ACR). Controls were interrogated by use of only the POMS. Controls weren’t asked to fill in the PainDETECT or ACR criteria list, because these questionnaires are seen as specific for chronic pain. The control subjects were presumed to be in general good health. Patients and controls were asked to put their forearm into cold water(1°C +/- 0,5°C). The immersed area had to be held as long as possible into cold water with a maximum of 2 minutes (120 seconds). Afterwards skin temperature was measured with an infrared thermograph. There was a thermographic recording before the cold water test, immediately after they came out of the water, and after 1,2,5,10 and 20 minutes of recuperation. The calculation of the thermograms took place after the experiment, by using the software according to the thermographic camera. During the experiment there was a registration of vital parameters (blood pressure and heart rate). A pain score was asked before the experiment, immediately after the cold immersion and at the end of the recuperation (after 20 minutes). All patient and control data were kept in a database. An SPSS 17 Statistics Package for Social Sciences was used for the analyses. Statistical analysis was done using the Student’s T-test with two-tailed significance for the comparison of parametric variables. The non-parametric variables were analyzed with the Mann-Whitney tests. A p value ≤0.05 was considered statistically significant.
3. RESULTS

3.1. Describing the test group by analysing the questionnaires (POMS and PainDetect)

3.1.1. PainDETECT
The PainDETECT questionnaire, which was developed and validated in Germany, incorporates a self-report questionnaire with 9 items. There are 7 sensory descriptor items and 2 items relating to the spatial and temporal characteristics of the individual pain pattern. Its sensitivity and specificity compared to clinical diagnosis is 85% and 80% respectively. PainDETECT is often used for screening of a neuropathic pain component (23). The group of FM patients in this experiment were all asked to fill in the PainDETECT questionnaire (the Dutch version was a translation from the original PainDETECT questionnaire). The questions: “Do you have sudden pain attacks in the area of your pain, like electric shocks? Is cold or heat (bath water) in this area occasionally painful? Does slight pressure in this area, e.g., with a finger, trigger pain?” were answered as the most painful stimuli. All FM patients had a high score for all stimuli.

Table 5 Describing the features of PainDETECT by FM patients.

<table>
<thead>
<tr>
<th></th>
<th>Burning sensation</th>
<th>Tingling/prickling sensation</th>
<th>Light touching</th>
<th>Electric shocks</th>
<th>Cold or heat</th>
<th>Sensation of numbness</th>
<th>Slight pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>3,652174</td>
<td>3,695652</td>
<td>3,695652</td>
<td>4,086957</td>
<td>4,217391</td>
<td>3,826087</td>
<td>4,521739</td>
</tr>
<tr>
<td>Minimum</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Maximum</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>


3. RESULTS

![Graph showing PainDETECT scores](image)

**Figure 4** Describing the total PainDETECT score within the FM group.

The total PainDETECT score can be divided into three categories of pain. Lower than a score of 12 the neuropathic component of pain is unlikely. A score between 12 and 18 is defined as ambiguous, however a neuropathic pain component can be present. A score higher than 18 is likely to have a neuropathic pain component. Within the test group there were 8 patients with an ambiguous result (26% of the total FM patients group). All the other FM patients suffered a clearly neuropathic component of pain.

3.1.2. POMS

The profile of mood scale is a widely used instrument designed to assess current mood states. The POMS consists of 32 adjectival items developed to measure 7 aspects of mood (anxiety, tension, depression/dejection, anger/hostility, confusion/bewilderment, vigor/activity, fatigue/inertia and friendship). Responses to each item range from 0 to 4, with higher scores indicating more negative moods over the past week (0 indicates “not at all”, regarding the presence of an adverse mood, and 4 indicates “extremely”) (24). The FM patients had a lower POMS score than the healthy controls, indicating a more depressive, anxious mood. The average POMS of FM patients was -49, of healthy controls it was 0.

![Graph comparing POMS scores](image)

**Figure 5** Describing the difference in POMS between the FM patients and healthy controls.
3. RESULTS

3.2. Describing the test group by body features

3.2.1. BMI

To describe the test group by measuring body features we used the BMI index because this integrates length and weight in one parameter. When we compared the BMI between FM patients and healthy controls we find a significant difference ($p=0.011 (< 0.05)$). This means there were more obese females within the FM patients group than in the healthy controls group. Obesity is associated with increased risk of fibromyalgia, and about 50% patients with fibromyalgia are obese. Moreover, obesity affects symptoms present in fibromyalgia such as physical function and quality of life (25).

![Figure 6 Describing BMI index within the FM patients group.](image1)

![Figure 7 Describing BMI index within the healthy controls group.](image2)
3. RESULTS

3.3. Temperature differences between FM patients and healthy controls

3.3.1. Basic temperature measurements

- **Body temperature**

Body temperature was measured by a digital thermometer at the right axilla. The temperature between healthy controls and FM patients was significantly different ($p=0.027 (<0.05)$). Basal body temperature of FM patients was higher than healthy controls. Average body temperature FM patients = 36.2°C, average body temperature healthy controls = 35.8°C.

![Figure 8 Body temperature between FM patients and healthy controls.](image)

- **Ear temperature**

Ear temperature was measured by an ear thermometer at the right and left ear. An average temperature was measured ((left + right)/2). There was no significantly difference between the average ear temperature of FM patients and healthy controls ($p=0.701 (>0.05$)). Average ear temperature FM patients = 36.8°C, average ear temperature healthy controls = 36.7°C.

![Figure 9 Average ear temperature between FM patients and healthy controls.](image)
3. RESULTS

- Forearm thermography in basal conditions

Forearm thermography was recorded with a thermograph. Temperature was measured by computing the area of the forearm. The temperature was taken under basal conditions, before the experiment took place. The forearm temperature between healthy controls and FM patients was significantly different ($p=0.018 (<0.05)$). Basal forearm temperature of FM patients was higher than healthy controls. Average forearm temperature FM patients = 31.9°C, average forearm temperature healthy controls = 30.9°C.

3.3.2. Temperature indices

- P (forearm) / C (ear) index

The index was measured by creating a new variable, resulting from the quotient forearm temperature divided to ear temperature. Forearm temperature was measured by a thermographic recording, ear temperature was measured by a thermometer in the right and left ear, the average was calculated. The index between healthy controls and FM patients was significantly different ($p=0.033(>0.05)$).

Figure 10 Forearm thermography in basal conditions between FM patients and healthy controls.

Figure 11 P (forearm) / C (ear) index between FM patients and healthy controls.
3. RESULTS

- **P (axilla) / C (ear) index**

The index was measured by creating a new variable, resulting from the quotient axilla temperature divided to ear temperature. Axilla temperature was measured by a digital thermometer, ear temperature was measured by a thermometer in the right and left ear, the average was calculated. The index between healthy controls and FM patients wasn’t significantly different ($p=0.083(>0.05)$). The P(forearm) / C (ear) index of FM patients was approximately equal to the index of healthy controls.

3.3.3. **Right – left ear temperature differences**

A new variable was computed by the difference of the right and left ear temperature. The temperature difference between healthy controls and FM patients was significantly different ($p=0.018(>0.05)$). There was a significant difference of left and right ear temperature between FM patients and healthy controls.

**Figure 12** P (axilla) / C (ear) index between FM patients and healthy controls.

**Figure 13** Right – left ear temperature difference between FM patients and healthy controls.
3. RESULTS

3.4. Experimental results

3.4.1. Immersed time

All subjects were asked to hold the immersed area (right forearm) as long as possible in cold water. After 120 seconds everybody had to pull back their arm out of the cold water. FM patients withdrew their forearm a lot earlier than healthy controls. Within the group of healthy controls there were 7 subjects who reached the 120 seconds. There was significant difference in immersed time between the FM patients and healthy controls ($p \leq 0.001$). FM patients had an average immersed time of 17 seconds. Healthy controls had an average immersed time of 75 seconds.

3.4.2. Development of NRS score

- **FM patients**

  On the graph (figure 15) a significant increase of NRS scores in time is seen. Before the experiment (basal conditions) all the NRS scores were lower than 10. During the experiment there was an increase in scores, but the recuperation occurred in most of the subjects during the following 20 minutes. In contrast to the healthy controls, FM patients didn’t recover complete, a lot of them still had an increased pain score after 20 minutes (due to the cold water immersion). A pain score is a subjective measurement, but can give a general idea of the impact of cold water.

- **Healthy controls**

  On the graph (figure 16) a significant increase of NRS scores in time is seen. In contrast with FM patients a lot of healthy controls had a baseline NRS score of 0. During the experiment a lot of them had an increase in NRS score, but almost all had a total recuperation during the next 20 minutes.
3. RESULTS

**Figure 15** The development of NRS score of FM patients during the experiment.

**Figure 16** The development of NRS score of healthy controls during the experiment.
3. RESULTS

3.4.3. Comparison of NRS score between FM patients vs. healthy controls

There was a significant difference of NRS score between FM patients and healthy controls during the experiment. Statistics were conducted at basal condition, T0 (immediately after the immersion) and at T20 (after 20 minutes of recuperation). At all 3 times there was a significant difference ($p \leq 0.001$).

**Table 6** Averages of NRS score of FM patients and healthy controls.

<table>
<thead>
<tr>
<th></th>
<th>BASAL</th>
<th>T0</th>
<th>T20</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM patient</td>
<td>6,09</td>
<td>8,87</td>
<td>6,35</td>
</tr>
<tr>
<td>Healthy Control</td>
<td>1,40</td>
<td>4,67</td>
<td>0,87</td>
</tr>
</tbody>
</table>

3.4.4. Temperature decrease

All subjects had their own immersed time into the water. First there was looked if the temperature decrease of the forearm in FM patients vs. healthy controls was different. At this point the time of immersion wasn’t included and there was only focussed on the loss of skin temperature during the immersion. This temperature loss between FM patients and healthy controls was compared. A statistic significant difference was found ($p \leq 0.001$). This means that there was a difference in temperature decrease between FM patients and healthy controls. Average temperature loss of FM patients was 13,5°C, of healthy controls it was 17,4°C.

**Figure 17** Temperature decrease between FM patients and healthy controls.
3. RESULTS

3.4.5. Cool-down rate

At this point a new variable was calculated. This variable included the time of immersion. The cool-down rate was calculated as the quotient of the temperature decrease during the experiment (in degrees) and the time of immersion (in seconds). There was a statistically significant difference in cool-down rate between FM patients and healthy controls (p<0.001). Average cool-down rate FM patients: 1.05 °/S (degrees/second), average cool-down rate healthy controls: 0.34 °/S. While reading this result it became clear that there wasn’t a linear relation between the amount of degrees of cool-down and the time immersed into the water. FM patients, who generally stayed into the water for a shorter time than healthy controls, had a higher cool-down rate. This could be explained in this way that after a certain time the body temperature became used to the cold water and the response of the autonomic nervous system became weaker. Another possible explanation could be that there was a difference of functioning of the ANS in reaction to a cold stressor between FM patients and healthy controls. But an important limitation of this comparison was the difference between time of immersion of both groups. Again, FM patients had in general a shorter time of immersion compared to healthy controls.

![Figure 18](image1.png)  
**Figure 18** The relation immersed time - decrease in temperature of FM patients.

![Figure 19](image2.png)  
**Figure 19** The relation immersed time - decrease in temperature of healthy controls.
3. RESULTS

3.4.6. General recuperation

The progress of recuperation was in general comparable. Healthy controls had a lower temperature after the experiment than FM patients. This could be explained by the fact that FM patients had less temperature loss than healthy controls during the experiment. The first 2 minutes it looked like healthy controls had a faster recuperation than FM patients. From 5 to 20 minutes all subjects seemed to have the same slope of recuperation. Big difference between the slope of both groups were the temperature values. The question whether the velocity of recuperation was different during the first minutes between FM patients and healthy controls, will be investigated in the next steps.

![Recuperation Graph]

**Figure 20** General recuperation of temperature after the immersion during the next 20 minutes between FM patients and healthy controls.

**Table 7** Average temperature progress during the experiment.

<table>
<thead>
<tr>
<th>THERMOGRAM</th>
<th>FM Patients</th>
<th>Healthy Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>31,94°C</td>
<td>30,93°C</td>
</tr>
<tr>
<td>T0</td>
<td>18,48°C</td>
<td>12,92°C</td>
</tr>
<tr>
<td>T1</td>
<td>23,63°C</td>
<td>18,89°C</td>
</tr>
<tr>
<td>T2</td>
<td>24,88°C</td>
<td>21,41°C</td>
</tr>
<tr>
<td>T5</td>
<td>25,92°C</td>
<td>24,23°C</td>
</tr>
<tr>
<td>T10</td>
<td>27,27°C</td>
<td>25,67°C</td>
</tr>
<tr>
<td>T20</td>
<td>28,60°C</td>
<td>27,06°C</td>
</tr>
</tbody>
</table>
3. RESULTS

3.4.7. Recuperation during 0-20 minutes

Table 8 suggests that the biggest difference in the recuperation process was a dissimilarity between T0 and T20 between FM patients and healthy controls. FM patients had an average temperature recuperation of 10.12 ° after 20 minutes, whereas healthy controls had an average temperature recuperation of 14.14°C. This was a significant difference (p<0.001). The limitation about this comparison was the immersed time into the cold water. Healthy controls started their recuperation from 12.92 °C, which is 6° less than FM patients (18.48°C). After 20 minutes the forearm temperature were semi-similar between the two groups. FM patients showed an average temperature of 28.6°C, healthy patients showed an average temperature of 27.06°C. During this 20 minutes healthy controls needed to warm up 6° more than FM patients.

3.4.8. Recuperation during 0-5 minutes

Taking a look at the graphs of FM patients and healthy controls it seemed that FM patients had a heavier response to cold in general during these 5 minutes than healthy controls. For the investigation of this slope the 5 minutes were split into different time periods of 1 minute. The comparison of the first minute (time 0 – time 1) between FM patients and healthy controls couldn’t find anything statistically significantly different. After repeating this procedure for all different time periods, anything statistically different couldn’t be found. FM patients and healthy controls had the same progress of recuperation.

![Figure 21](image.png) The development of the recovery (T0-T5) of FM patients.
3. RESULTS

3.4.9. Recuperation during 5-20 minutes
The recovery progress between 5 and 20 minutes was not significantly different between FM patients and healthy controls. (The tie was split into periods of 1 minute).

3.4.10. Recuperation after 20 minutes compared with basal temperature
To have an idea which impact the cold stressor had on the subjects, the basal temperature (temperature measured before the experiment) was compared to the recuperation temperature after 20 minutes. A statistically significant difference was found ($p=0.018(<0.05)$). FM patients had an average basal temperature of 31,94°C and an average recuperation temperature after 20 minutes of 28,6°C. After 20 minutes their recuperation wasn’t yet fully completed, there was still a deficiency of 3,34°. Healthy controls had an average basal temperature of 30,93 °C and an average recuperation temperature after 20 minutes of 27,06 °C. Their recuperation as well wasn’t fully completed after 20 minutes, there was still a deficiency of 3,87°.
3. RESULTS

Table 8 Progress of temperature during the experiment.

<table>
<thead>
<tr>
<th></th>
<th>Temperature Basal</th>
<th>T0</th>
<th>Temperature decrease after the experiment</th>
<th>T20</th>
<th>Temperature increase after 20 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FM patients</strong></td>
<td>31,94°C</td>
<td>18,48°C</td>
<td>13,46°</td>
<td>28,6°C</td>
<td>10,12°</td>
</tr>
<tr>
<td><strong>Healthy Controls</strong></td>
<td>30,93°C</td>
<td>12,92°C</td>
<td>18,01°</td>
<td>27,06°C</td>
<td>14,14°</td>
</tr>
</tbody>
</table>

Figure 23 Progress of temperature during the experiment.

3.4.11. Warm-up rate

The comparison of the recovery speed between the first minutes and the next minutes, both FM patients and healthy controls had the same pattern. The first minutes both FM patients and healthy controls had a much quicker increase of temperature than the next minutes. The warm-up rate of the first 5 minutes compared with the warm-up rate of next 15 minutes of recovery by FM patients, couldn’t show anything significant different ($p \leq 0.001$). The same result was found with healthy controls ($p \leq 0.001$). FM patients and healthy controls had the same pattern of recovery, quicker during the first minutes and a stagnation later in the recovery process.
3. RESULTS

**Figure 24** The progress of recovery (T5-T20) of FM patients.

**Figure 25** The development of recovery (T5-T20) of healthy controls.
3. RESULTS

3.4.12. Vital parameters during the experiment

- **RR**

During the experiment the vital parameters were recorded. The blood pressure (systolic and diastolic pressure) was measured by an automatic blood pressure cuff. RR was measured in basal conditions and after 1 minute of recuperation. No statistically significant difference could be found. There was a light tendency that the healthy controls had more raise of diastolic and systolic pressure after the first minute of recuperation from the cold water immersion. But this raise wasn’t distinct enough to be statistically significant.

Table 9 The evolution of RR during the experiment (average RR).

<table>
<thead>
<tr>
<th></th>
<th>FM Patients</th>
<th>Healthy Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syst Basal (mmHg)</td>
<td>123,13</td>
<td>128,80</td>
</tr>
<tr>
<td>Diast Basal (mmHg)</td>
<td>81,96</td>
<td>77,76</td>
</tr>
<tr>
<td>Syst T1 (mmHg)</td>
<td>128,00</td>
<td>134,73</td>
</tr>
<tr>
<td>Diast T1 (mmHg)</td>
<td>84,57</td>
<td>85,93</td>
</tr>
</tbody>
</table>

- **Pulse**

The pulse was measured by an automatic cuff. RR was measured in basal conditions and after 1 minute of recuperation. Nothing statistically significant could be found. The only difference between FM patients and healthy controls was the slightly higher pulse of healthy controls after 1 minute of recuperation, but this was too little to be statistically significant.

Figure 26 The evolution of RR during the experiment.

Figure 27 The evolution of pulse during the experiment (average pulse).
4. DISCUSSION

Fibromyalgia appears to be a situation of autonomic dysfunction where both limbs of ANS (sympathetic and parasympathetic) are differentially involved. The aim of the study was to show a difference in function of this ANS. The ANS is the main regulatory system of the body in charge of maintaining essential involuntary functions. These functions are the so-called vital signs, including blood pressure, pulse, respiration, and temperature. We designed a study in which these vital parameters could be measured at rest and after exposure to a stressor, in this study a cold-water test.

At the beginning of the experiment different vital parameters were recorded. Significant differences were found in:

- Basal body temperature (at right axilla)
- Forearm temperature
- The index forearm temperature / ear temperature

This means there is a difference between FM patients and healthy controls in the regulation of their basal temperature. There was also a significant difference found in left vs. right ear temperature between FM patients and healthy controls. Healthy controls had a much more similar temperature at left and right ear whereas FM patients showed much more difference between both ears.

All subjects were interrogated by making use of different questionnaires, before the cold-stressor test was performed. The answers to this POMS questionnaire were significantly different. This can be interpreted as if FM patients have a more depressive and anxious mood than healthy controls. This could be explained by the symptoms of the disease and the frustration resulting from the feeling of ‘not being understood’ by the medical corps and direct environment of the patient.

Secondly the cold-stressor test was performed. All FM patients and healthy controls were asked to put their forearm into cold water, hold it as long as possible and pull it back if the NRS score had reached 9 or 10. Afterwards recuperation of the skin temperature was visualized and analyzed by thermographic recordings. The immersed time into the cold water resulted in a very strong statistically significant difference. FM patients stayed much shorter
4. DISCUSSION

into the cold water as healthy controls. Two possible explanations can be conducted out of this event. Either the FM patients started from a higher NRS score and reached a NRS score of 9 or 10 much faster than healthy controls due to the aberration in ANS, or FM patients perceived the cold water as more painful than the healthy controls. Within the healthy control group there were some subjects who shifted their pain threshold and kept their arm persistently 120 seconds into the cold water. The comparison of decrease of temperature both groups showed during the experiment was statistically significant.

The forearm thermography of healthy controls cooled down a lot more than FM patients. The remark needs to be made that FM patients stayed much shorter into the cold water, so perhaps their bodies hadn’t enough time to cool down as much as the healthy controls did. To take the different immersed times of both groups into account a new variable was computed, defined as the cool-down rate. Looking at the decrease of degrees per second of both groups, a clear statistically difference between both could be observed. It’s necessary to keep in mind, that the physiologic process of cooling down isn’t a linear process on which the body reacts with a constant cool-down rate. Probably the body reacted very heavily the first moments of exposure to the cold stressor, followed by habituation to the cold water and a weaker reaction in the second phase. The cool-down rate of healthy controls was remarkably lower than the cool-down rate of FM patients. The lower rate of healthy controls could be explained by two features: one was the longer immersed time, the second was the normal ANS without any alternations to a cold stressor. FM patients probably stayed too short into the water to be able to see the habituation to the cold.

After the cold-water stressor experiment the recuperation of the forearm was followed during the next 20 minutes. The general recuperation slope showed a similar shape. The temperature immediately after the cold water immersion, was six degrees lower with healthy controls, again it seems necessary to bear in mind that healthy controls stayed significantly longer into the cold water than FM patients. Though looking at the forearm temperature after 20 minutes of recuperation, healthy controls and FM patients had similar forearm temperatures. Consequently healthy controls needed to warm up six degrees more than FM patients during the same 20 minutes. These recuperation temperatures compared to to the basal temperatures before the experiment, suggested that none of the two groups could fully recover. FM patients and healthy controls had different mean cold temperatures after the experiment, but after 20 minutes both groups had similar temperatures. This could suggest that the ANS of FM patients had an aberrant functioning, more specific, worked slower than healthy controls.
4. DISCUSSION

Vital parameters like blood pressure and pulse were measured before and after one minute of the cold-water experiment. Anything significant couldn’t be shown, but there was a slight trend that healthy controls had a more intense response to the cold stressor than FM patients. Systolic and diastolic pressure, such as pulse, increased slightly more with healthy controls.

A few remarks can be drawn from this study. The two groups of subjects were comparable at several points, but due to the study protocol (the difference in immersed times between FM patients and healthy controls), the research question couldn’t be fully examined and answered. We suggest following improvements to the study design:

− The study design could be adjusted to a fixed time for all subjects to keep their forearm into the water. The factor ‘pain’ isn’t that good as motivation to pull the forearm out of the water. By setting a fixed time, we would be more able to compare the physiologic process between both groups, especially the part of the recuperation of the cold stressor. The different times immersed into the water were always a limitation in this study design.

− It should be considered if a thermographic experiment by measuring skin temperature was a good tool to value the autonomic nervous system. In literature most studies investigated the vasomotor response of the autonomic nervous system by using laser Doppler flowmetry (26) or by measuring electrical potentials from electrodes on the foot and hand. (27). On the other hand a study performed in Sweden showed a possibility of measuring the skin temperature by thermography. (28). Another possible parameter to observe the dysfunction of the autonomic nervous system with FM patients was the heart rate variability (9).
5. CONCLUSION

Out of this experiment we can draw a few conclusions:

- The aim of this study (investigate if there was a difference between the autonomic nervous system between FM patients and healthy controls) is partially accomplished. In basal conditions there were some temperature differences between both groups, showing that FM patients have an alteration of function of the ANS.

- Although, once the cold stressor was applied, the expected difference in recuperation did not appear. This could be due to different limitations in the study design:
  - Were skin temperature and changes in this temperature a good parameter to measure autonomic dysfunction?
  - Was the factor ‘pain’ a good motivation to pull the forearm out of the water?

Nevertheless, this study still supports the hypothesis that there is something aberrant within the autonomic nervous system of FM patients. For a better understanding of the syndrome and its features, much remains to be done. This study gives prospects to better skills of defining, diagnosing, understanding and treating FM patients by observing and measuring simple clinical parameters.
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- The use of figure 2: *Pathophysiology of pain*

REFERENCES


