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Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

Interoception and proprioception: a pilot study to compare patients with fibromyalgia and a healthy control group

Lore Corstjens
Marlies Cuypers

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

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dr. Stef FEIJEN

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Research context

This master's thesis is part of the research field 'Pain, fatigue and somatically unexplained physical symptoms', which is inherent to the master's program Rehabilitation Sciences and Physiotherapy at the University of Hasselt. The study was conducted within the larger context of the study: "Interoception and proprioception in patients with fibromyalgia" (B1152022000007). The objective of this study is to compare interoceptive accuracy, sensibility and awareness, and proprioception in patients with FM to a healthy control group. Secondly, the aim is to assess the correlation between interoceptive accuracy, sensibility and awareness, and the correlation between conscious and unconscious proprioception.

Understanding the concepts of interoception and proprioception in FM is central to integrative research concerning FM and its influence on the musculoskeletal system. Furthermore, interoceptive treatment protocols can potentially be translated into proprioceptive treatment protocols and vice versa.

Two Rehabilitation Sciences and Physiotherapy students administered the study, with the support of Prof. Dr. K. Bogaerts, Dr. S. Feijen, Dr. M. Van Den Houte and Dra. I. Ramakers in collaboration with REVAL Health and Rehabilitation Psychology Research Group,
Faculty of Rehabilitation Sciences UHasselt, the Multidisciplinary Expertise Center Tumi Therapeutics (Heusden-Zolder, Belgium), Reuma Clinic (Genk, Belgium), and Reumacentrum Genk (Genk, Belgium).

The searchable research question was determined by the students in consultation with the supervisor and co-supervisor. The method and study design were determined by the co-supervisor, therefore the students didn't have any part in determining these constructs as the study was part of an ongoing research project. The recruitment of the patients, data acquisition, statistical analysis and interpretation were performed by the students with the support of Dr. M. Van Den Houte and Dra. I. Ramakers. The academic writing was accomplished by the students, they both worked equally and simultaneously on the study, constantly reviewing each other's work, in order to make it cohesive.

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1. Abstract

Background: Interoception is more and more viewed from an inclusive point of view, where proprioception is part of interoception. Previous research revealed disrupted interoception in patients with fibromyalgia (FM). Research concerning proprioception in patients with FM is inconclusive. Additionally, the two concepts were not viewed in the same context before.

Objectives: To compare interoceptive accuracy, sensibility and awareness, and conscious and unconscious proprioception in patients with FM to a healthy control group, and to assess the correlation between interoceptive aspects and between proprioceptive aspects.

Methods: Proprioception was measured by a muscle vibration task and a head repositioning accuracy task. Subsequently, interoception was assessed, using the following measures: the Respiratory Occlusion Discrimination task to assess interoceptive accuracy, the Visual Analogue Scale to measure interoceptive awareness, and two self-reported questionnaires (Interoceptive Sensitivity and Awareness Questionnaire and Three-domain Interoceptive Sensations questionnaire) for interoceptive sensibility.

Results: No significant differences were found between the patient group and the healthy control group for interoceptive tasks or proprioceptive tasks. For interoception, no significant correlations were found between any aspects in the FM group. No significant correlations for the proprioceptive tasks were found in either of the groups.

Conclusion: No significant differences between the patient group and the healthy control group concerning the aspects of interoception and proprioception were found. The measures didn't significantly correlate in either group. Further research in the overreaching study is needed as the sample size in this study was too small to provide anything but preliminary results.

Keywords: interoception, proprioception, fibromyalgia

2. Introduction

About 40-49% of all patients in primary care present with medically unexplained symptoms (MUS) (Haller et al., 2015). These symptoms can occur as clusters, where they are referred to as functional syndromes such as fibromyalgia (FM). FM is described as a disorder where the patient experiences chronic widespread pain which cannot be explained by other disorders (Hulens et al., 2018). Using the diagnostic American College of Rheumatology (ACR) criteria (Wolfe et al., 2010, 2016), FM reaches a prevalence of 2-3% worldwide, making it the third most common musculoskeletal condition, after low back pain and osteoarthritis (Sarzi-Puttini et al., 2020). The impact of FM on quality of life is significant (Arnold et al., 2008), as it is common for FM patients to report loss of function and work disability due to pain, fatigue, and weakness (White et al., 1999). Even though the exact mechanisms behind FM are unknown, etiological hypotheses are the development of chronic pain due to central sensitization (Van Oosterwijck et al., 2013; Chinn et al., 2016), altered pain processing (Gracely et al., 2003), decreased connectivity within the pain network (Jensen et al., 2012; Flodin, et al., 2014), increased sympathetic activity (Meeus et al, 2013; Martinez-Martinez et al., 2014) and genetic predisposition (Lee et al., 2012). Additionally, interoceptive dysfunction is more and more accepted as an important component of somatoform disorders, such as FM (Khalsa et al., 2018).

“Interoception refers to the process by which the nervous system senses, interprets, and integrates signals originating from within the body, providing a moment-by-moment mapping of the body’s internal landscape across conscious and unconscious levels'' (Khalsa et al., 2018, pp. 1-2). Garfinkel et al. (2015) proposed a framework identifying three aspects of interoception: interoceptive accuracy, interoceptive sensibility and interoceptive awareness. Firstly, interoceptive accuracy refers to “the objective accuracy in detecting internal bodily sensations'' (Garfinkel et al., 2015, p. 67). Secondly, interoceptive sensibility is defined as “the self-perceived dispositional tendency to be internally self-focused and interoceptively cognisant” (Garfinkel et al., 2015, p. 67). Thirdly, interoceptive awareness is described as “the metacognitive awareness of interoceptive accuracy” (Garfinkel et al., 2015, p. 67).

Bogaerts et al. (2010) found significantly lower interoceptive accuracy in high MUS reporters during a rebreathing test. Furthermore, persons with a greater number of MUS, appear to

have a lower interoceptive accuracy (Bogaerts et al., 2008; Weiss et al., 2014). Additionally, patients with widespread pain present with significantly distorted interoceptive accuracy compared to a healthy control group (Di Lernia et al., 2016). However, research is inconclusive, as some studies are reporting no differences in patients with somatoform disorders (Schulz et al., 2022), nor in high symptom reporters (Schulz et al., 2020).

Even though there is no consensus around the scope of interoception, in an inclusive manner proprioception ought to be a part of interoception (Ceunen et al., 2016). Proprioception is defined as the sense of body position and movement (Tuthill & Azim, 2018). Proprioceptive information is obtained through input from both proprioceptors and different mechanoreceptors located in the skin, muscles, and joints (Proske & Gandevia, 2012). There are two levels of proprioception: conscious proprioception which is voluntary, and unconscious proprioception which is reflex-initiated (Laskowski et al., 2000).

Individuals with MUS have also been the subject of increasing research on proprioception in recent years. Van Ravenzwaaij et al. (2010) concluded that disrupted proprioception could be one of the mechanisms behind physical symptoms in patients with MUS. In several studies, individuals with FM were found to have impaired trunk and neck position sense (Celenay et al., 2019; Vaillant et al., 2017; Gucmen et al., 2022, see for a review: Ramakers et al., 2022). However, other studies reported no differences in knee joint repositioning (Nijs et al., 2006; Ulus et al., 2013) and upper body-related repositioning accuracy (Bardal et al., 2016; Brun et al., 2020) between FM and a healthy control group.

Understanding the concepts of interoception and proprioception in FM is central to integrative research concerning FM and its influence on the musculoskeletal system. The goal of the present study is to assess interoceptive accuracy, sensibility and awareness, and conscious and unconscious proprioception in patients with FM and a healthy control group, and to assess the correlation between interoceptive aspects and between proprioceptive aspects. We expect to find a disrupted interoception and proprioception in patients with FM compared to a healthy control group, a good correlation between the three aspects of interoception, and no correlation between conscious and unconscious proprioception.

3. Methods

3.1 Participants

Patient group

Patients were recruited via Tumi Therapeutics (Heusden-Zolder, Belgium), Reuma Clinic (Genk, Belgium), and Reumacentrum Genk (Genk, Belgium). Diagnosis was based on the ACR criteria, which consisted of the following three criteria: 1) pain reported in at least seven of the eleven described body regions (Appendix 1) and a score of at least five out of twelve for symptom severity, or pain in three to six described body regions and a score greater than nine for symptom severity, 2) symptoms have to be present for at least three months and 3) the symptoms cannot be explained by another somatic disorder (Wolfe et al., 2010, 2016). Exclusion criteria for the patients were: 1) pregnancy, 2) age younger than 18 years old or older than 65 years old, 3) presence of a chronic (symptoms have to be present for at least 3 months) organic condition (e.g. epilepsy, rheumatoid arthritis, asthma, diabetes, etc.) or an acute illness (a fever, the flu, etc.), 4) any neck complaints at the moment of the testing that aren't related to their current diagnosis of FM, 5) a recent whiplash trauma (less than 3 months ago or more than 3 months with currently present symptoms), 6) diagnosis of organic explained vestibular or neurological conditions, 7) recent orthopedic injury of the lower limbs (e.g. an acute ankle trauma) that can affect balance, 8) BMI > 30.

Healthy control group

The healthy control group was recruited through local advertisement. If interested, potential participants could contact the researcher, to receive information and informed consent online (Appendix 2). Additionally, a link to the Checklist for Symptoms in Daily Life (CSD) (Walentynowicz et al., 2018) and a couple of demographic questions were sent to them via Qualtrics. They consented to participate in the study before filling in the questionnaires. Healthy individuals were recruited to individually match the patient group regarding the following criteria: 1) age group (per five years), 2) gender (X included), 3) educational level, 4) BMI (per 3 points). Additionally, the aim is to recruit participants with few disorders in daily living. Therefore, the healthy control group will be screened using the CSD (Walentynowicz, et al., 2018). Participants will only be included when they score lower than 100 on this questionnaire. Exclusion criteria for the control group were the following: 1) pregnancy, 2) younger than 18 years old or older than 65 years old, 3) depressive

episodes, anxiety disorder, eating disorder, drug abuse, psychotic disorders or a psycho-organic disorder, all of them diagnosed with DSM-V (MINI), 4) presence of a chronic (symptoms have to be present for at least 3 months) organic condition (e.g. epilepsy, rheumatoid arthritis, asthma, diabetes, etc.) or an acute organic condition (a fever, the flu, etc.), 5) persistent bodily complaints (e.g. hyperventilation, long-lasting COVID, chronic pain, chronic fatigue, chronic tinnitus, etc.), 6) any kind of neck complaints, 7) a recent whiplash trauma (less than 3 months ago or more than 3 months with currently present symptoms), 8) diagnosis of vestibular or neurological conditions, 9) recent orthopedic injury of the lower limbs (e.g. an acute ankle trauma) that can affect balance, 10) BMI > 30. Since a psychiatric disorder is one of the exclusion criteria, the MINI was administered to explore any undiagnosed psychiatric disorders (Overbeek et al., 1999).

3.2 Procedure

Participants went through a research protocol, consisting of five parts, approved by the ethics committee. To begin with, all participants gave consent before any data was gathered. Interoceptive measures were recorded, using the following measures: Respiratory Occlusion Discrimination (ROD) task (Van Den Houte et al., 2021) to assess interoceptive accuracy, the Visual Analogue Scale to measure interoceptive awareness, and two questionnaires (Interoceptive Sensitivity and Awareness Questionnaire (ISAQ) (Bogaerts et al., 2021) and Three-domain Interoceptive Sensations questionnaire (THIS-q) (Vlemincx et al., 2021) for interoceptive sensibility. At the beginning of these questionnaires, the participants were asked to fill in some demographic questions, the following aspects were included: year of birth, length, weight, sports activities, highest level of education, medication use, presence of any medical disorders, smoking behavior, alcohol use and past COVID infections. Two proprioception tasks were administered in a randomized order: a muscle vibration task and a head repositioning accuracy task (HRAT). A detailed description of the used tests can be found in the following paragraphs.

Respiratory occlusion discrimination task (ROD-task) (Van Den Houte et al., 2021)

The respiratory occlusion discrimination task (ROD-task) is a test to measure interoceptive accuracy in the respiratory domain (Van Den Houte et al., 2021). During this task, the participant was asked to breathe in a device that administers occlusions between 260 ms and

620 ms. Within each inspiration, two occlusions were inflicted (occlusion interval = 300 ms), of which one is the reference occlusion (440 ms) and one is the test occlusion (longer or shorter than 440 ms). The breathing pattern was visually analyzed by the researcher, who manually inflicted the occlusions at the beginning of the respiration, leaving at least one occlusion-free breath between two trials. The participant's capacity to detect differences in length between two occlusions was measured using a transformed adaptive staircase procedure (Leek, 2001). A two-down one-up procedure was used in this study, meaning that two correct answers are needed to make the distinction between test and reference stimulus smaller and thus more difficult to detect. However, only one incorrect answer led to the use of a greater difference between the two stimuli. This approach allows calculation of the just noticeable difference (JND), or in other words the smallest possible difference between the test stimulus and the reference stimulus where the participant can still distinguish both stimuli about 70.7% of the time (Levitt, 1971). In this study, two staircases were used: an upward staircase where the test occlusions are shorter than the reference occlusion, and a downward staircase where the test occlusions are longer than the reference occlusion. The upward staircase started with a test occlusion of 260 ms, while the downward staircase started with a 620 ms test occlusion. Step size refers to the amount by which the test occlusion length is decreased or increased when giving a wrong answer or giving two correct answers in a row. Both experiments started with a 30 ms step size, but in spite of that, it was variable throughout the whole experiment, as the step size was decreased with 5 ms at every reversal until the minimal stepsize (5 ms) was reached. The experiment ended when both staircases reached six reversals. A reversal can be defined as a change of direction in the staircase, e.g. when an incorrect answer is given after a series of correct answers, the difference between the test and reference occlusion will increase again instead of continuing to decrease. In case one of the staircases reach a total of six reversals before the other one, this staircase was represented but not included in the analysis. JND was measured by averaging the differences between test and reference lengths of the trials where a reversal occurs.

Visual Analogue Scale (VAS)

After indicating which occlusions were thought to be longer, the participants were asked to indicate how sure they were about the correctness of their answer on a ten-point VAS. These scores were, together with the interoceptive accuracy scores, used in a ROC analysis to calculate interoceptive awareness.

Questionnaires: Interoceptive Sensitivity and Awareness Questionnaire (ISAQ) and Three-domain Interoceptive Sensations questionnaire (THIS-q)

The ISAQ is a valid and reliable self-reporting questionnaire, developed by Bogaerts et al. (2021). It measures sensitivity and attention to interoceptive signals of a broad range of bodily systems, such as respiratory, cardiovascular, gastrointestinal, thermoregulatory, energy, mouth and throat, postural, and cerebral areas. The questionnaire consists of 17 statements divided over the three following subscales: 1) sensitivity to neutral bodily sensations, 2) attention to unpleasant bodily sensations, and 3) difficulty disengaging from unpleasant bodily sensations. Responses to the 17 statements are provided on a 5-point Likert-scale, ranging from 1 (“strongly disagree”) to 5 (“strongly agree”). Reliability of the first two subscales is acceptable, in contrast with the third subscale’s reliability, which is poor (Bogaerts et al., 2021). The THIS-q was developed by Vlemincx et al. (2021). It is like the ISAQ, a valid and reliable self-reporting questionnaire, however, the number of included bodily systems is more limited (Vlemincx et al., 2021). It assesses the perception of sensations of the respiratory, cardiac, and gastroesophageal systems. The questionnaire consists of 28 neutrally described statements regarding the three previously mentioned bodily systems. Again, a five-point Likert-scale was used, ranging from 1 (“never”) to 5 (“always”). Both questionnaires are available and valid in Dutch.

Muscle vibration task

Unconscious proprioception was examined through the use of vibration to stimulate the muscle spindles of the lumbar multifidus and the triceps surae bilaterally following the method of Claeys et al. (2015). Muscle vibration stimulates the type Ia afferents and thus induces a muscle-lengthening illusion (Goodwin et al., 1972). In healthy individuals, this will result in a compensatory displacement of the center of mass (COM) in a backward direction for the triceps surae, and a forward direction for the lumbar multifidus (Brumagne et al., 2004,

2008). The excursion of the COM was assessed by a force plate (AMTI, USA, 500Hz). The vibration was induced using one or two vibrators (Maxon motors, Switzerland) for the lumbar multifidus and the triceps surae respectively, with a frequency of 60 Hz, and an approximated amplitude of 0.5 mm. Vibrations were started 20 seconds after the start of the trial and were applied for 15 seconds. Altogether, four test conditions were administered, consisting of two different placements of the vibrations (lower back and muscle-to-tendon transition of the triceps surae) and two different surfaces (stable surface and unstable surface, using a foam). Using the unstable surface, healthy people's central nervous system (CNS) will upregulate proprioceptive signals of the lower back muscles, and downregulate the signals of the ankle muscles, enabling a more trunk-directed strategy (Brumagne et al., 2008). Additionally, several studies found a more ankle-focused approach in people with low back pain (Brumagne et al., 2004; Claeys et al., 2011).

Head repositioning accuracy task

The head repositioning accuracy task was administered to assess conscious proprioception (Revel et al., 1991). The participant sits in a chair, is blindfolded and a headlamp is placed on his head directed at a target 90 cm in front of him. Then he was asked to look straight ahead, keep his head in a neutral position and memorize this position, this point was marked by the researcher. Subjects then actively rotated their head and thereafter moved back to the initial position. The place where the participant stops was indicated on the target. Then the head was passively placed back in the initial neutral position by the researcher. This procedure was repeated five times for the right side and five times for the left side. Lastly, the average deviation from the initial target related to the neutral position was calculated, which could be used to estimate proprioceptive accuracy of the neck.

3.3 Data analysis

Interoceptive accuracy was quantified through the performance on the ROD task. The average difference between the test lengths and the reference length of the trials, in which a reversal occurs, was calculated as the JND using MatLab. Interoceptive sensitivity was measured as the score on the ISAQ and the THIS-q. Lastly, interoceptive awareness was calculated by receiver operating characteristic (ROC) curve analysis, using SAS 9.4. This score reflects the relationship between the correctness of trials on the ROD task and scores on the VAS scale

that measures certainty of response. Correct decisions on the ROD task were used as the state variable, with certainty ratings as the test variable. The area under the curve is a precise measure of how accurately the certainty ratings predict performance on the trials and is therefore a good measure of interoceptive awareness (Bekrater-Bodmann et al., 2020).

Proprioceptive accuracy was quantified through 2 tests: the head repositioning accuracy task and the muscle vibration task. In the head repositioning task, the proprioceptive accuracy of the neck was quantified as the mean deviation from the reference point. In the task that measures the effect of muscle vibrations on COM excursion the absolute value of the mean COM displacement of the ankle divided by the absolute value of the mean COM displacement of the ankle and back (|ankle|/(|ankle|+|back|) represents the proprioceptive accuracy for this task. A score of 1 corresponds to 100% proprioceptive dependence on the ankle muscles, while a score of 0 means 100% dependence on the lumbar multifidus.

Statistical analysis was conducted using the software program JMP PRO 16 (significance level: $p = .05$). Descriptive statistics (mean value and standard deviation) were calculated for age, gender and BMI. For interoceptive performance on the ROD task, VAS, ISAQ and THIS-q, normality was verified using the Sharpiro-Wilk test. Significant differences in performance were measured by t-tests. The JND on the ROD task, the scores on the ISAQ and THIS-q, and the ROC curve analysis were used to calculate Pearson's correlation between these tasks in case of a normal distribution. When comparing a task that was not normally distributed, the Spearman's correlation was used. For the proprioceptive performance on the postural control task and head repositioning accuracy task, normality was verified using the Sharpiro-Wilk test. Significant differences in performance were measured by t-tests. Average deviation from the reference point of the HRAT and the absolute value of the mean COM displacement of the ankle and back on the muscle vibration task were used to calculate the Pearson correlation between these tasks. Detailed statistical decision-making processes can be found in appendix 3.

4. Results

4.1 Sample characteristics

The average age of the patient group (n = 7) was 41.83 years (SD = 11.94; range: 28-59). The sample consisted of five females and one male. The gender of one participant was not known, as the demographic data of this patient was missing. The mean BMI was 22.12 kg/m² (SD = 2.54; range: 19.00-25.02). The average age of the control group (n = 4) was 46.75 years (SD = 6.02, range: 39-52). The healthy control group consisted of four females and no males. The mean BMI was 21.32 kg/m² (SD = 3.40; range: 17.40-25.90).

4.2 Interoception

Interoceptive accuracy

The average JND of the patient group (n = 6) on the ROD-task was 78.89. The healthy control group (n = 2) had an average JND of 83.54. No significant differences between the patient group and healthy control group were found on the ROD task (p_{ROD} = .74).

Interoceptive awareness

The area under the curve (n = 6), for calculating interoceptive awareness, was .59 on average in the patient group. For the healthy control group (n = 1), the only obtained value was .77. No statistical analysis could be carried out for the ROC curve analysis, as there was only one value available.

Interoceptive sensibility

Regarding interoceptive sensibility an average score of 54.6 was found for the ISAQ (n = 5), and 86.5 for the THIS-q (n = 4). Regarding interoceptive sensibility, an average score of 52.8 was found for the ISAQ (n = 4), and 93.3 for the THIS-q (n = 4). No significant differences could be observed in the ISAQ between the patient group and the healthy control group (p_{ISAQ} = .57). No statistical analysis for the THIS-q could be carried out, as there was only data obtained of one matched pair.

Correlation of interoceptive aspects

No significant correlations could be found between any of the aspects of interoception in patients with FM (table 1). Due to the limited data from the healthy control group, again no analysis could be carried out.

Table 1

Correlations between aspects of interoception in patients with FM

Compared aspects	n	Correlation		*p*
		Pearson	Spearman	
JND and AUC	6	-.40	/	.429
JND and ISAQ	4	.16	/	.839
JND and THIS-q	3	/	-.50	.667
AUC and ISAQ	4	-.85	/	.154
AUC and THIS-q	3	/	.50	.667

Note. : JND = Just notable difference; AUC = Area Under the Curve;
ISAQ = Interoceptive Sensitivity and Awareness Questionnaire;
THIS-q = Three Domain Interoceptive Questionnaire.

* $p < 0.05$.

4.3 Proprioception

Muscle vibration task

The scores of patients with FM (n = 7) on the muscle vibration task on a stable foundation averaged 87.58%. On the unstable foundation (n = 6), the average score was 51.39%. The average score of a healthy control group (n = 3) on the muscle vibration task for the stable condition was 79.07%. In the unstable condition (n = 4), the average score was 53.08%. No significant difference was found in either condition between patients with FM and a healthy control group ($p_{\text{muscle vibration task, stable}} = .21$; $p_{\text{muscle vibration task, unstable}} = .77$).

HRAT

Patients with FM (n = 6) had an average deviation of 4.90 cm from the reference point. The healthy control group (n = 4) had deviated 6.15 cm from the reference point on average. Data analysis showed no significant difference between patients with FM and a healthy control group (p_{HRAT} = .84).

Correlation of proprioceptive tasks

In the patient group, no significant correlation was found between either of the conditions of the muscle vibration task and the HRAT ($r_{stable,\ 7}$ = -.44; p = .32; $r_{unstable,\ 6}$ = .60; p = .21). Similarly, no significant correlation was found in the healthy control group ($r_{stable,\ 3}$ = .99; p = .10; $r_{unstable,\ 4}$ = .59; p = .41).

5. Discussion

The main objective of this study was to examine the three aspects of interoception following the framework of Garfinkel et al. (2015) and proprioception in patients with FM and compare those results with a healthy control group. A potential correlation between those three aspects and between two proprioceptive tasks was examined. This study is a pilot for a larger ongoing research project concerning interoception and proprioception in patients with FM, where this data will also be used to address a similar research question. Data analysis showed no significant differences between patients with FM and the healthy control group for any of the interoceptive aspects, nor for any of the proprioceptive tests. No correlation was found between the three interoceptive aspects, nor between the proprioceptive tests.

Notwithstanding the current literature is conflicting concerning differences in interception in patients with FM and a healthy control group, very few studies are published to date examining all three aspects of interoception following the concept of Garfinkel (2015) in FM. Data analysis showed no difference in interoception between FM patients and a healthy control group. This finding contradicts other research, as a disrupted interoception in high MUS reporters, based on the Checklist for Symptoms in Daily Life (Bogaerts et al., 2008; Bogaerts et al., 2010), and patients with FM (Duschek et al., 2017) was found in other research. However, in research on interoceptive accuracy that used the Heartbeat Counting Task (HCT), no difference was found between FM and a healthy control group (Rost et al., 2017; Valenzuela-Moguillansky et al., 2017; Borg et al., 2022).

No significant correlations for the different interoceptive measures were found. This is inconsistent with the research of Horvath et al. (2021), who assessed a potential correlation between two different aspects of interoception: interoceptive accuracy using an HCT and interoceptive awareness using confidence ratings for that task with a VAS. A weak correlation between these aspects was found. Nevertheless, in 2018 a study was published stating that the HCT involves mostly non-interoceptive processes, such as the estimation of the heart rate and thus is not an accurate measure of interoceptive accuracy (Desmedt et al., 2018).

Regarding proprioception, there is only limited research conducted in patients with FM. The few studies that have been conducted on the subject report varying results. No significant

differences between patients with FM and a healthy control group were found in this study concerning proprioception.

No correlation was found between the HRAT and muscle vibration task for the healthy control group, nor in patients with FM. This is consistent with the recent research of Horvath et al. (2023) about correlations between different proprioceptive tasks, where is found that proprioceptive accuracy is site and method specific. These findings are in line with the findings of Han et al. (2013), de Jong et al. (2005), and Lowrey et al. (2020), among others. Additionally, the HRAT measures conscious proprioception, while the muscle vibration task assesses unconscious proprioception, these two constructs are processed through different pathways. Conscious proprioceptive signals are processed through the conscious relay pathways (Lundy-Ekman, 2022), while the spinocerebellar tract carries signals regarding unconscious proprioception (Chandar et al, 2014). On the contrary, another study did find a significant correlation between cervical joint position error and standing balance tests in patients with whiplash (Treleaven et al., 2006).

The primary limitation of this study is the limited sample size, resulting from the fact that this study is a pilot study for a bigger project. This resulted in insufficient statistical power to address generalizable results. The study failed to address any significant correlations; the underlying cause is presumably the fact that the results of correlation analysis can also be influenced by limited a sample size. Also, more patients than healthy controls were recruited, thus not every patient would be matched to a healthy control person. The generalizability of the results could be compromised by the absence of males as the matched pairs only consisted of females. Another limitation is that while comparing FM patients' results to those of the healthy control group, the questionnaire's subscales were not taken into consideration. Bogaerts et al. (2022) showed higher scores on only two of the ISAQ's three subscales in FM patients, therefore this seems to be a significant limitation. Future research should take this into consideration. Aside from that, bias might be present due to missing data resulting from technical difficulties. Since this pilot study is part of ongoing psychophysiological research, a great number of questionnaires were conducted to evaluate various psychological variables. Some participants did not complete all of them due to the large number of questionnaires, which resulted in more missing data.

However, due to the fact that interoception, proprioception, and psychological factors were approached from an integrated psychophysiological point of view, this approach is also a strength of this study. Additionally, the research team was composed multidisciplinary and consisted of both physical therapists and psychologists, because this research was conducted in a holistic manner. Despite being time-consuming and causing a small sample size, the tailored matching of the FM patients with the healthy persons reduced the risk of individual variables affecting the results. Furthermore, to measure interoceptive accuracy, this study used the ROD task (Van den Houte et al., 2021) rather than the HCT, which is most often used in recent research (Desmedt et al., 2018, 2020). The ROD task is a promising newly developed task to accurately measure the respiratory interoceptive domain (Desmedt et al., 2023). The ROD task was thoughtfully selected to avoid any kind of bias in measuring interoception, as in 2018 a study was published stating that the HCT involves mostly non-interoceptive processes, such as estimation of the heart rate (Desmedt et al., 2018).

In conclusion, the study didn't find significant differences in interoceptive accuracy, interoceptive sensibility, and interoceptive awareness, nor in conscious and unconscious proprioception between patients with FM and the healthy control group. No correlation was found between the three interoceptive aspects in patients with FM. Regarding proprioception, no significant correlation was found between conscious and unconscious proprioception in patients with FM, nor in the healthy control group. Further research is needed as the sample size in this study was too small to provide anything but preliminary results.

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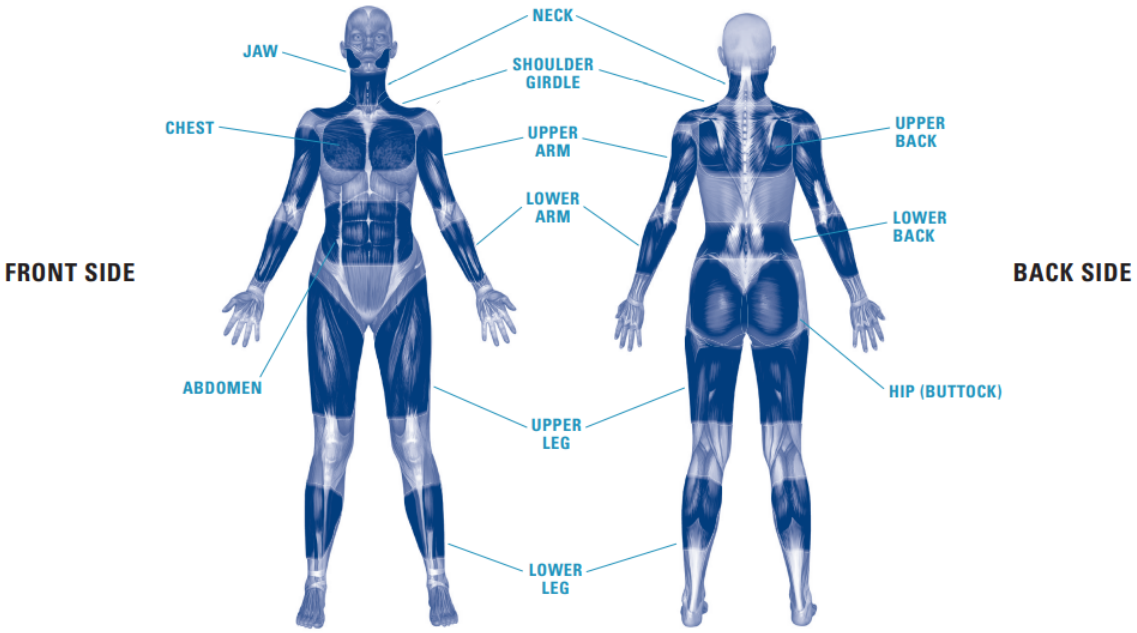
Appendix 1

Identify the areas where the patient felt pain over the past week

❑ Shoulder girdle, left	❑ Lower arm, right	❑ Lower leg, left	❑ Abdomen
❑ Shoulder girdle, right	❑ Hip (buttock), left	❑ Lower leg, right	❑ Neck
❑ Upper arm, left	❑ Hip (buttock), right	❑ Jaw, left	❑ Upper back
❑ Upper arm, right	❑ Upper leg, left	❑ Jaw, right	❑ Lower back
❑ Lower arm, left	❑ Upper leg, right	❑ Chest	



Appendix 2

Msc. Indra Ramakers
Dr. Maaike Van Den Houte
Prof. dr. Lotte Janssens
Prof. dr. Pieter Meyns
Prof. dr. Katleen Bogaerts

Onderzoek naar associaties tussen interoceptie en proprioceptie in een gezonde populatie

DEELNEMERSINFORMATIE (versie 3: 04/01/22)

Vooraleer u toestemt om aan deze studie deel te nemen, is het belangrijk dat u dit formulier leest. In dit informatie- en toestemmingsformulier worden het doel, de procedure, de voordelen, risico's en ongemakken gepaard gaande met de studie beschreven. Ook de voor u beschikbare alternatieven en het recht om op elk ogenblik de studie te verlaten, zijn hieronder beschreven. U hebt het recht om op elk ogenblik vragen te stellen over de mogelijke en/of bekende risico's die deze studie inhoudt.

Doel en beschrijving van de studie

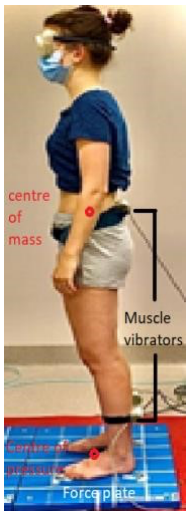
In de wetenschap wordt er aangenomen dat "proprioceptie" (proprioceptie verwijst naar het gevoel van lichaamshouding en beweging, proprioceptie heeft u bijvoorbeeld nodig voor balans) gelinkt is aan "interoceptie" (interoceptie verwijst naar hoe goed mensen zijn in het waarnemen van hun eigen lichamelijke sensaties, bijvoorbeeld voelen hoe vaak uw hart klopt). Het doel van deze studie is om zowel interoceptieve- als proprioceptieve processen in gezonde personen te onderzoeken, en deze onderling te vergelijken met elkaar. Indien u toestemt om deel te nemen aan de studie, zal u gevraagd worden om verschillende vragenlijsten thuis in te vullen (online) en deel te nemen aan 2 testsessies.

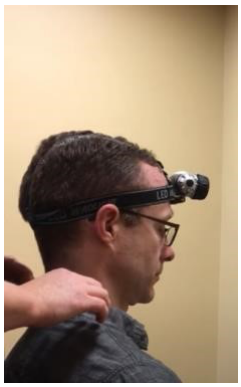
De eerste testsessie zal plaatsvinden in het labo van de faculteit revalidatiewetenschappen van de universiteit Hasselt, te gebouw A in Diepenbeek, duurt circa één uur en bestaat uit:

a) Een taak waarbij spiervibrators worden bevestigd aan de enkels/ onderrug. U zal worden gevraagd om tijdens de vibratie rechtop te staan.

b) Een taak waarbij de nek in een hoek gedraaid zal worden door de onderzoeker waarna u actief terug naar de beginpositie mag draaien. Dit zal meermaals herhaald worden.

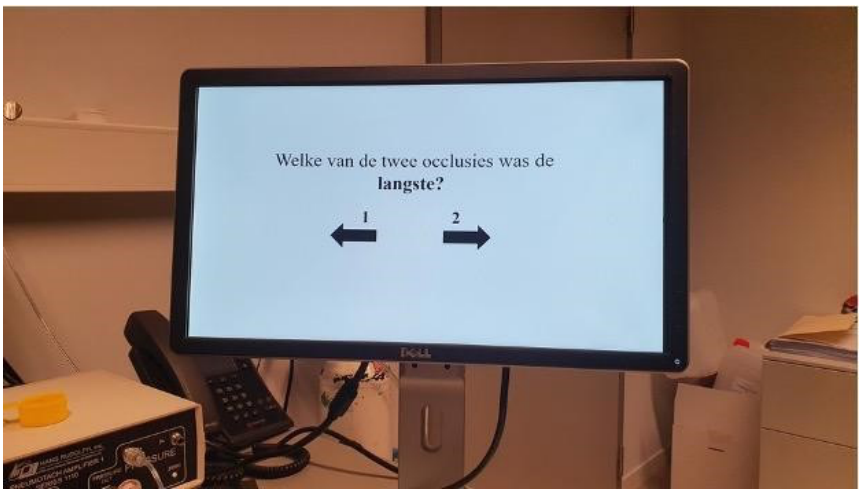
c) Een discriminatie taak die meet hoe goed mensen zijn in het waarnemen van verschillende gewichten. In de taak zal gebruik gemaakt worden van 2 gewichten, u zal deze in uw handen mogen vasthouden. Er zal u nadien gevraagd worden te beoordelen welke van deze 2 gewichten het zwaarste was. Dit zal meermaals herhaald worden.





De tweede testsessie zal plaatsvinden in het Ziekenhuis Oost-Limburg te Lanaken, duurt circa 30 minuten en bestaat uit:

a) Een ademhalingstaak die meet hoe goed mensen zijn in het waarnemen van verschillende ademhalingssensaties. In de taak zal gebruik gemaakt worden van heel korte ademhalingsonderbrekingen (“occlusies”). U zal door een mondstuk ademen terwijl u een neusclip draagt en steeds 2 korte (minder dan 1 seconde) occlusies na elkaar te voelen krijgen. Er zal u gevraagd worden te beoordelen welke van deze 2 occlusies de langste was. Deze occlusies zijn volledig veilig.



Opdrachtgever van de studie

De opdrachtgever van de studie is de Onderzoeksgroep voor gezondheids- en revalidatiepsychologie van de UHasselt.

Vrijwillige deelname
U neemt geheel vrijwillig deel aan deze studie en u hebt het recht te weigeren eraan deel te nemen. Uw beslissing om al dan niet aan deze studie deel te nemen of om uw deelname aan de studie stop te zetten, zal geen enkele invloed hebben op uw verdere behandeling.

Indien u aanvaardt om deel te nemen, zal u deze informatiefolder krijgen om te bewaren en zal er u gevraagd worden het aangehechte toestemmingsformulier te ondertekenen.

U hebt het recht om uw deelname aan de studie op elk ogenblik stop te zetten, zelfs nadat u toestemming tot deelname hebt gegeven. U hoeft geen reden te geven voor het intrekken van uw toestemming tot deelname. Het intrekken van uw toestemming zal geen enkel nadeel of verlies van voordelen met zich meebrengen. Uw beslissing zal geen weerslag hebben op uw medische behandeling.

Risico's en ongemakken
Gezien er tijdens de eerste testsessie gebruikt wordt gemaakt van spiervibraties, bestaat de kans dat de participant hierdoor het evenwicht kan verliezen. Hierdoor zal er steeds een onderzoeker naast de deelnemer staan om een eventuele val ten allen tijden te vermijden. Aan de overige taken zijn zeer weinig tot geen fysieke risico's of ongemakken verbonden. Deze tweede testsessie duurt ongeveer één uur en kan daarom vermoeidheid veroorzaken. Pauzes worden voorzien tussen de verschillende taken.

Aan de tweede testsessie zijn geen fysieke risico's verbonden aan deze studie. Het experiment duurt ongeveer 30 min en kan daarom vermoeidheid veroorzaken. Pauzes van 30 seconden tot 2 minuten worden daarom meermaals voorzien tijdens de testsessies. Er wordt tevens water ter beschikking gesteld voor alle deelnemers tijdens het experiment.

Een mogelijks risico van deze studie is gegevensverlies van de data die we verzamelen.

In- en exclusiecriteria
U mag, om veiligheids- en methodologische redenen niet deelnemen aan de studie als u aan een van de volgende criteria voldoet:

Exclusiecriteria:

- Zwangerschap
- Jonger dan 18 jaar of ouders dan 65 jaar.
- Geen COVID-19 pas
- Een zelfgerapporteerde psychische aandoening zoals een depressie, burn-out, angststoornis, eetstoornis, middelenmisbruik, psychotische aandoening of persoonlijkheidsstoornis.
- Aanwezigheid van een chronische organische aandoening (Men spreekt van een chronische organische aandoening als deze een periode van minimaal 3 maanden aanwezig is. Voorbeelden zijn: Epilepsie, Hartaandoening, Reuma, Astma, diabetes, etc.) of persisterende lichamelijke klachten (bv. hyperventilatieklachten, langdurige COVID, chronische pijn of vermoeidheid, chronische tinnitus, …)
- Het nemen van antidepressiva, slaap medicatie (benzodiazepines) en angstremmende middelen (anxiolytica)
- Recent whiplash trauma minder dan 3 maanden geleden of langer dan 3 maanden geleden met nog
- steeds aanwezige klachten
- Nekklachten op het moment van testing
- Diagnose van vestibulaire of neurologische aandoeningen
- Recente orthopedische problematiek van de onderste ledematen (bv. acuut enkeltrauma) dat het evenwicht kan beïnvloeden, of van de bovenste ledematen (bv. fractuur of overbelastingsletsel) dat de arm- of handkracht kan beïnvloeden

Voordelen
U zal geen persoonlijk rechtstreeks voordeel halen uit uw deelname aan deze studie. Uw deelname voorziet ons echter van kennis over interoceptie en proprioceptie en zal de domeinen van revalidatiewetenschappen en gezondheidspsychologie verder helpen.

COVID-19
Tijdens het eerste deel van het experiment is er fysiek contact nodig tussen proefpersoon en onderzoeker. Mondmaskers zijn gedurende het volledige experiment verplicht voor beiden. Alle materialen worden na gebruik gedesinfecteerd. Tijdens het tweede deel van het experiment zal de onderzoeker gedurende het volledige experiment een mondmasker dragen. De proefpersoon draagt ook een mondmasker tijdens voorbereiding en afronding, tijdens het experiment zelf zal de proefpersoon door een mondstuk moeten ademen en moet het mondmasker af. De onderzoeker zit op dat moment in een ander lokaal. Het mondstuk wordt per proefpersoon vervangen. Daarnaast wordt het volledige materiaal gedesinfecteerd na gebruik per participant.

Verzekering
Conform de Belgische wet van 7 mei 2004 inzake experimenten op de menselijke persoon, is de opdrachtgever zelfs foutloos, aansprakelijk voor alle schade die de deelnemer en/of zijn rechthebbenden oplopen en die rechtstreeks dan wel onrechtstreeks verband houdt met de studie. De opdrachtgever van deze studie (UHasselt) heeft een verzekering afgesloten die deze aansprakelijkheid dekt. Indien U schade zou oplopen ten gevolge van uw deelname aan deze studie zal die schade bijgevolg worden vergoed conform de Belgische wet van 7 mei 2004.

Vergoeding
Er zullen verschillende bonnen van bol.com van elk 25 euro verloot worden onder de deelnemers. Om kans te maken zal u uw e-mailadres moeten delen via onderstaand formulier.

Bescherming van de persoonlijke levenssfeer
Uitsluitend de onderzoekers verbonden aan dit onderzoek hebben toegang tot alle gegevens die verzameld worden. Ze zijn verplicht tot geheimhouding en stellen zich ook persoonlijk garant dat deze gegevens als zeer vertrouwelijk zullen behandeld worden. Een unieke numerieke code (die op geen enkele manier kan verwijzen naar uw identiteit) wordt aan u toegewezen en zal in plaats van uw naam aan alle informatie en gegevens van uw bijdrage aan deze studie gekoppeld worden, opdat uw identiteit geheim zal blijven. De resultaten zullen anoniem geanalyseerd worden met behulp van de codes die aan iedere deelnemer worden toegewezen en zullen voor de deelnemersgroep als geheel mogelijk gepresenteerd worden op wetenschappelijke vergaderingen of gepubliceerd worden in wetenschappelijke tijdschriften. Persoonlijke informatie over u zal niet gebruikt worden noch doorgegeven op enige manier. De informatie over u zal elektronisch (d.w.z. in de computer) of handmatig verwerkt en geanalyseerd worden om de resultaten van deze studie te bepalen. U hebt het recht aan de onderzoeker te vragen welke gegevens er over u worden verzameld in het kader van de studie en wat de bedoeling ervan is. U hebt ook het recht om aan de onderzoeker te vragen u inzage in uw persoonlijke informatie te verlenen en er eventueel de nodige verbeteringen in te laten aanbrengen. Hierbij worden het medisch beroepsgeheim, de internationale richtlijnen (ICH-GCP) en de Belgische wetgeving nageleefd (o.m. de wettelijke vereisten zoals bepaald in de Belgische Wet van 22 augustus 2002 inzake rechten van de patiënt). Bovendien zijn uw persoonlijke gegevens beschermd door de EU Verordening 2016/679 (Algemene Verordering Gegevensbescherming) of GDPR (General Data Protection Regulation) en de Belgische Wetgeving betreffende de bescherming van natuurlijke personen met betrekking tot de verwerking van persoonsgegevens.

Als u toestemt in deelname aan dit onderzoek, betekent dit dat u ook toestemming geeft voor het gebruik van uw gecodeerde medische gegevens voor de hierboven beschreven doelen en het overmaken ervan aan bovenvermelde personen en/of instanties.

Commissie voor ethiek
Deze klinische studie is beoordeeld door het leidinggevend Comité Medische Ethiek Ziekenhuis OostLimburg en de Universiteit Hasselt, die een definitief gunstig advies gaven voor deze studie op XX/XX/XXXX.

Contactpersonen in geval van vragen in verband met de studie
Als u vragen of opmerkingen heeft over de studie, kan u contact opnemen met:

Indra Ramakers (Psychologe, UHasselt, Lokaal onderzoeker), indra.ramakers@uhasselt.be
Prof. dr. Katleen Bogaerts (klinisch psychologe, UHasselt, hoofdonderzoeker), 011/29.21.27, katleen.bogaerts@uhasselt.be
Comité voor Medische Ethiek UHasselt (CME@uhasselt.be)

TOESTEMMINGSFORMULIER

Onderzoek naar associaties tussen interoceptie en proprioceptie in een gezonde populatie.

Deel enkel bestemd voor de proefpersoon:

Hierbij bevestig ik, ondergetekende (naam & voornaam) _____ dat ik over de studie ben ingelicht en een kopie van de "Informatie voor proefpersonen" en het "Toestemmingsformulier" ontvangen heb. Ik heb de informatie gelezen en begrepen. De onderzoeker heeft mij voldoende informatie gegeven met betrekking tot de voorwaarden en de duur van de studie, én de mogelijke risico's en ongemakken die gepaard gaan met mijn deelname. Bovendien werd mij voldoende tijd gegeven om de informatie te overwegen en om vragen te stellen, waarop ik bevredigende antwoorden gekregen heb.

- Ik heb begrepen dat ik mijn deelname aan deze studie op elk ogenblik mag stopzetten, zonder dat dit mij enig nadeel kan berokkenen.
- Ik ga akkoord met de verzameling, de verwerking en het gebruik van gegevens die tijdens het onderzoek werden verzameld, zoals beschreven in het informatieblad voor de proefpersoon.
- Ik ga akkoord met het gebruik door de opdrachtgever van deze gecodeerde gegevens voor wetenschappelijke doeleinden: de algemene resultaten voor de groep als geheel worden mogelijk gepresenteerd op wetenschappelijke vergaderingen of gepubliceerd in wetenschappelijke tijdschriften. De gegevens zullen niet gebruikt worden voor doelstellingen anders dan deze omschreven in het informatieblad voor de patiënt.
- Ik stem geheel vrijwillig toe om deel te nemen aan deze studie en om mee te werken aan alle gevraagde onderzoeken. Ik ben bereid informatie te verstrekken i.v.m. mijn medische geschiedenis, mijn geneesmiddelengebruik en eventuele deelname aan andere studies.

Datum: _____

Handtekening proefpersoon: _____

☐ Ik wil op de hoogte gehouden worden van de resultaten van dit onderzoek

☐ Ik heb interesse om deel te nemen aan andere onderzoeken van deze onderzoeksgroep, en mag hiervoor gecontacteerd worden.

☐ Ik wil kans maken op één van de waardebonnen van bol.com van 25 euro.

Indien u een van bovenstaande vakjes heeft aangeduid, gelieve dan hier uw e-mailadres in te vullen:
e- mailadres : _____

Deel enkel bestemd voor het onderzoeksteam

Ik, ondergetekende, _____, bevestig hierbij dat

ik, _____ (naam van de proefpersoon voluit) heb

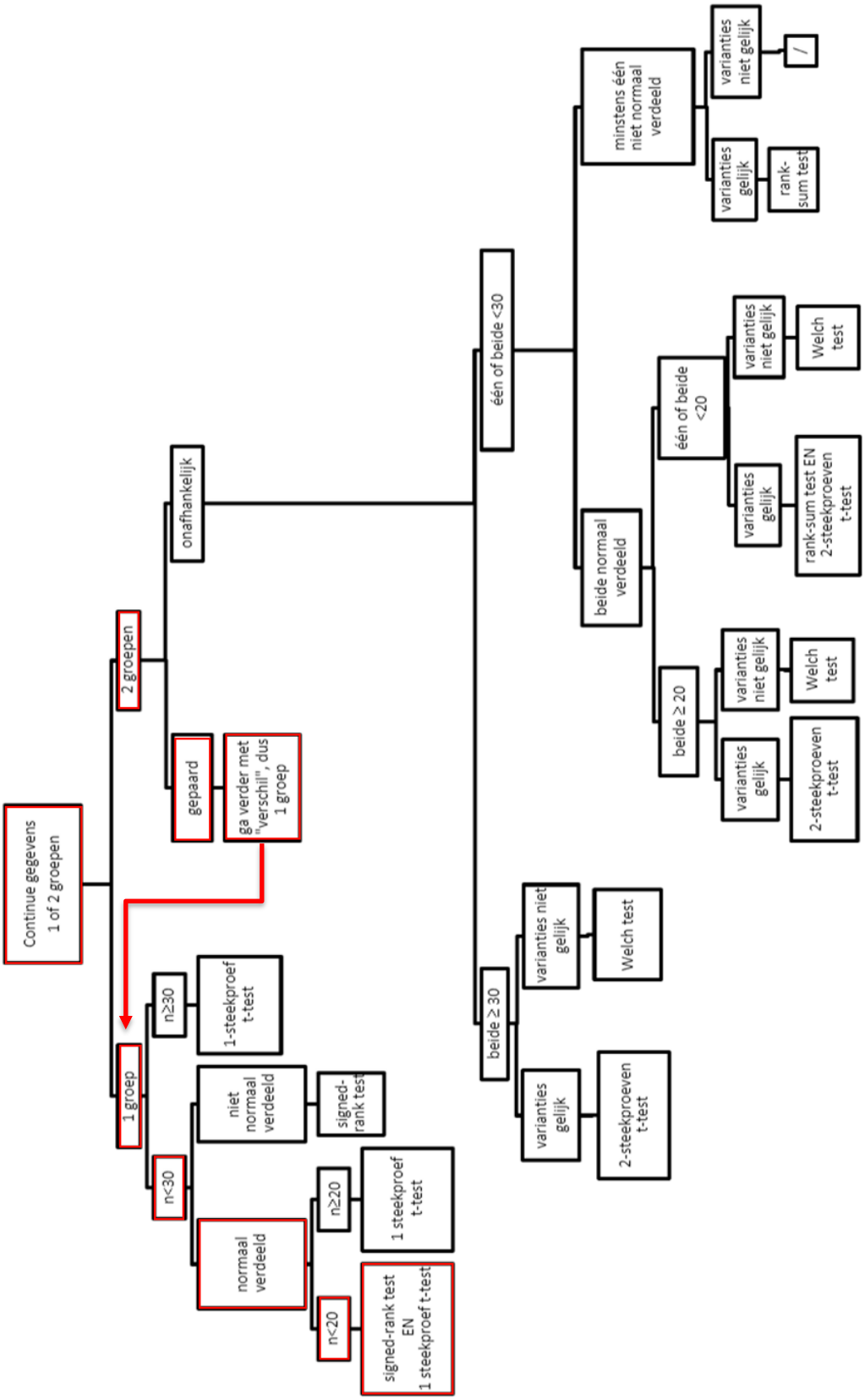
ingelicht en dat hij (zij) zijn (haar) toestemming heeft gegeven om deel te nemen aan de studie.

Datum: _____

Handtekening: _____

Appendix 3

The decision-making process in case of a normal distribution:



The decision-making process in case of a non-normal distribution: