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an experimental study in pain-free subjects

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Original Article

Association between obesity and craniofacial muscles sensitivity: an experimental study in pain-free subjects

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Abstract: The objective of this study was to investigate if any association exists between obesity and muscle sensitivity in the craniofacial region of healthy individuals with different body mass index (BMI). The study was designed as a parallel single blinded investigation approved by the North Denmark Region Committee on Health Research Ethics (N-20180029). Written informed consent was obtained from all participants. Subjects were divided into normal BMI (18.5-24.9 kg/m²) and high BMI (≥ 25.0 kg/m²). Measurement of body composition parameters was followed by pressure algometry applied on skin overlying masseter and temporalis muscles before and after a cold pressor test (CPT). Deltoid muscle was used as a reference point. Statistical analysis was carried out to investigate the difference in mean pressure pain threshold (PPT) values and the conditioned pain modulation (CPM) effect. Forty subjects were included (20 normal BMI and 20 high BMI). No significant difference was found in mean PPT values or mean CPM effect between the BMI groups (PPT: masseter P=0.763, temporalis P=0.425, deltoid P=0.595 and CPM effect: masseter P=0.396, temporalis P=0.463, deltoid P=0.484). Mechanical muscle sensitivity and CPM effect were sex-independent. No influence of BMI was identified on mechanical muscle sensitivity in the craniofacial region of healthy individuals.

Keywords: Obesity, body mass index, craniofacial muscles, pain threshold, pain sensitivity

Introduction

Overweight and obesity are considered multifactorial, complex, and common conditions, which affect more than two billion adults globally [1, 2]. In 2016, the World Health Organization (WHO) stated that 39% of all adults worldwide were overweight, while 13% were people with obesity [3, 4]. In the Scandinavian countries, these conditions are escalating as well, and here the prevalence is even higher with 40-60% [3, 5, 6].

The WHO describes overweight and obesity as: "An abnormal or excessive fat accumulation that presents a risk to health" [6]. They are usually defined by the Body Mass Index (BMI), which is a fast, inexpensive, and easy method when assessing overweight and obesity [6]. A normal BMI is between 18.5 kg/m² and 24.9 kg/m², whereas a BMI between 25.0 kg/m² and 29.9 kg/m² is classified as overweight, and a BMI equal to or greater than 30.0 kg/m²

is considered an obesity status [6-8]. Since BMI does not differentiate between excess fat, lean mass, age, and gender, alternative measurements such as the waist-to-hip ratio (WHR) and body fat percentage are proposed more accurate measures to adjust for different body types [1, 7, 9].

Overweight and obesity have a negative impact on most physiological and biological systems, which eventually leads to several other conditions such as diabetes, cardiovascular, and musculoskeletal disorders [10, 11]. Pain has also been shown highly associated with obesity [12-14], and it is well known that overweight, obesity, and pain all reduce life-quality, and are considered some of the most costly medical problems for society, indicating an important need for further intervention to reverse this development [6, 15]. The cause-effect relation between obesity and pain is not known [12, 16], although several relations have been proposed [12, 16, 17]. One relation states that mechani-

cal loading contributes to tissue damage in weight bearing joints, leading to pain in individuals with obesity [12, 16, 17]. Another proposed mechanism with an effect on the central nociceptive transmission is systemic inflammation, which might explain the occurrence of pain conditions where weight-bearing joints are not involved [17]. Excess accumulation of fat occurs in overweight and individuals with obesity, macrophages enter the adipose tissues, resulting in elevated levels of cytokines, especially interleukin (IL)-6, IL-1 β , and tumor necrosis factor- α , which mediate a systemic inflammatory state [11, 17, 18]. Elevated levels of IL-6 have been shown in different pain conditions such as Tension Type Headache (TTH) and fibromyalgia, leading to aggravation of chronic pain [19]. The systemic inflammatory state is proposed in the literature leading to an increase of general pain sensitivity in both overweight and obese individuals [17]. Few studies have investigated the relation between obesity and craniofacial muscle sensitivity, which may be related to the increased systemic inflammatory state, but further research is needed to clarify [18, 20]. A cause-effect relation could provide better pain management in patients suffering from craniofacial pain leading to increased life-quality.

A study by *Tashani et al.* indicated that individuals with obesity are more sensitive to mechanical stimuli than non-obese individuals, demonstrating that BMI and body fat both influence pain sensitivity in proportion to pressure pain but not to thermal pain [21]. The measurement sites included skin over the thenar eminence, and skin at the suprailiac above the crest of the ilium [21]. On the contrary, *Price et al.* found no difference between obese and non-obese individuals regarding pain sensitivity on the hand and the forehead, i.e. regions with no excessive subcutaneous fat, when inducing thermal and mechanical pain stimuli [22]. To the best of the researchers' knowledge, no other studies investigating mechanical muscle sensitivity in the craniofacial region have yet been carried out. Consequently, further research is needed due to the inconsistency in the literature, as well as the importance of identifying a possible link between craniofacial pain and obesity, in order for clinicians to provide better pain management. Therefore, the current study aimed to investigate the association between obesity

and mechanical muscle sensitivity in a non-weightbearing region, the masseter, and temporalis muscles, of healthy individuals. Pressure algometry was used on skin overlying these muscles to determine mechanical muscle sensitivity before and after a cold pressor test (CPT).

It was hypothesized that 1) mechanical muscle sensitivity is higher in individuals with a BMI ≥ 25.0 kg/m²; and 2) the conditioned pain modulation (CPM) effect is decreased in individuals with a BMI ≥ 25.0 kg/m² compared to individuals with a normal BMI (18.5-24.9 kg/m²).

Material and methods

A parallel group investigator-blinded study was designed to test the hypotheses in healthy subjects with different BMIs. The study was approved by the North Denmark Region Committee on Health Research Ethics (N20180029), and carried out according to the Declaration of Helsinki [23].

Subjects

The sample size of this study was calculated with the effect size identified by *Tashani et al.* who applied a similar methodology [21]. Healthy subjects were recruited via online advertisement (Forsoegsperson.dk and Facebook.com) and through notices at Aalborg University and at other public institutions. Subjects expressing interest to participate in the study received additional information with sufficient time to consider participation. Written informed consent was obtained with giving right to withdraw from the study at any given time without any consequence. Included subjects were healthy men and women of 18-65 years, non-smokers, Caucasian, and with a BMI ≥ 18.5 kg/m². Subjects were excluded if they were pregnant or breastfeeding; had pacemaker; had full-grown beard; lacked the ability to cooperate; performed extreme athletic activities (e.g., bodybuilding); were affected by any neurological, cardiovascular, musculoskeletal, or psychological illnesses; suffered from craniofacial pain, migraine, chronic TTH, new daily persistent headache, or Temporomandibular Disorders (TMD); had dermatological skin conditions, wounds, scars, or skin sensation alteration (e.g., due to a past trauma or operation) in the facial region;

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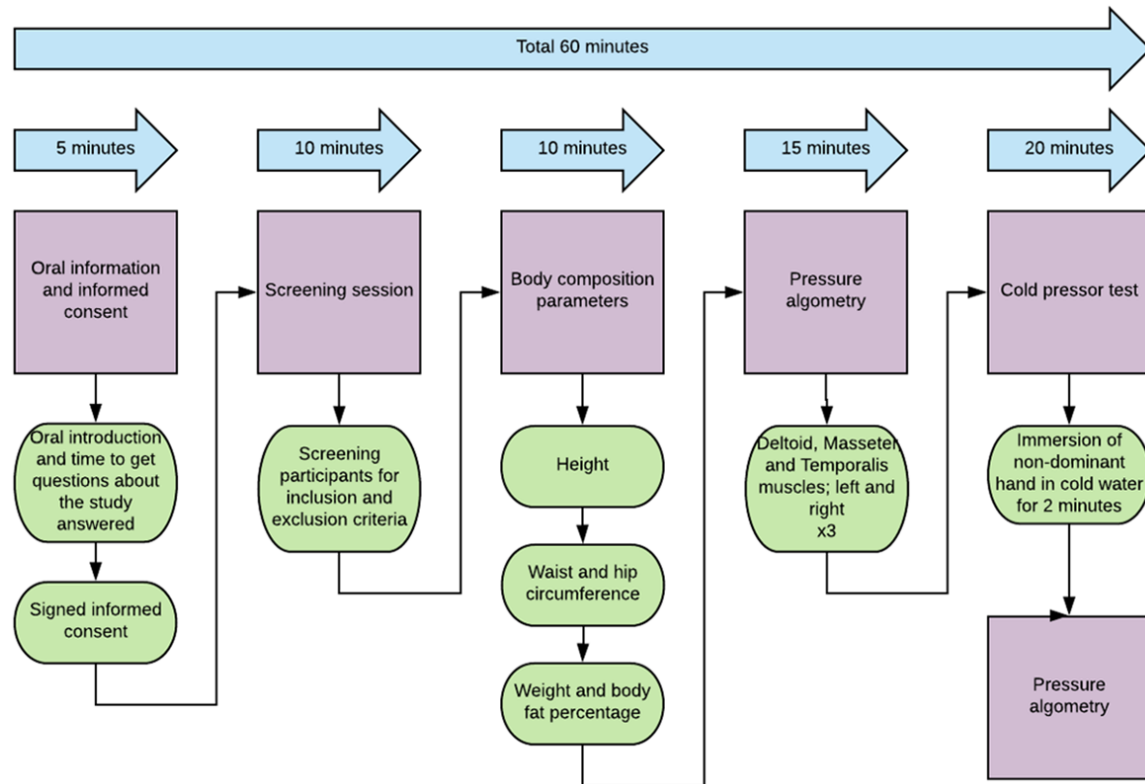


Figure 1. Time-frame of the study session and performed procedures.

experienced chronic pain within the last 3 months or acute pain on the day of the study session; had flu or fever within the last 2 weeks; were addicted to drugs defined as the use of cannabis, opioids, or other drugs; consumed alcohol within the last 24 hours; used medication with impact on the immune system or pain for the last 24 hours, or currently used supplements and medication that are known to affect body weight. Subjects were divided into two groups according to their BMI, high BMI (≥ 25.0 kg/m²) and a normal BMI (18.5-24.9 kg/m²).

Experimental procedure

The experimental session took place in a quiet, spacious, bright room, with a table, two chairs without armrests and wheels, and a blank wall. The session included 5 steps and lasted approximately 60 minutes. Body composition parameters were obtained first and followed by PPT assessment before and after the Cold pressor test (CPT) (Figure 1). All procedures were performed according to standard operating procedures. All data were recorded in case report forms.

Measurement of body composition parameters

Body composition parameters were measured to classify the subjects into two groups, where BMI was used to divide the subjects. Additional parameters were obtained to support the classification. Participants were instructed to wear a loose shirt and a pair of pants when body composition parameters were obtained. Body fat percentage and weight were determined with a SilverCrest Diagnostic Scale (Targa GM-BH, Soest, Germany), which estimates body fat percentage using bioelectrical impedance analysis [7]. Height was measured using a non-elastic measuring tape while the subject was positioned with heels, buttocks, and head against the wall standing on bare feet. Waist circumference was measured with a measuring tape placed at the midpoint between the last rib and the upper edge of the iliac crest, and the hip circumference was assessed around the midline of the greater trochanter. WHR was calculated as waist circumference (cm) divided by hip circumference (cm), while Waist-to-height ratio (WHtR) was calculated as waist circumference (cm) divided by height (cm), and BMI (kg/

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m²) was determined as the weight (kg) divided by the square of the height (m²) [7].

Pressure algometry

Muscle sensitivity to mechanical pressure was assessed by measuring PPT, one of the quantitative sensory tests (QST) [24]. PPT has been altered in a number of conditions such as TMD and TTH and it is considered a valuable measure of muscle sensitivity [25-27].

PPT (kPa) was assessed with a handheld pressure algometer (Somedic Senselab, Södala, Sweden), that could deliver mechanical pressure under controlled conditions with a predetermined slope (30 kPa/sec) [28]. The algometer was equipped with a rubber tip of 1 cm², which was placed perpendicularly on the skin overlying the targeted muscles. The device was calibrated before the study. To define PPT, the subjects were instructed to press a stop button with their dominant hand as soon as the pressure turned into a sensation of pain [29]. The PPT was measured twice, before and after application of CPT, on the skin overlying temporalis, masseter, and deltoid muscles in both right and left sides. The anterior part of the temporalis muscle and the lower prominent region of the masseter muscle were identified by palpation when the subject clenched the teeth. The deltoid muscle was identified five cm below the middle tip of the shoulder, and used as a reference point [30]. The skin surface of the identified muscles were marked with a small piece of 3M medical tape. The PPT was measured three times for those six muscles, without stimulating the same muscle twice in a row. This process ensured that a sufficient washout period was considered between pressure application that may cause temporal summation and muscle sensitization [31]. Furthermore, investigator variability was reduced, as the mean of three measurements from the same muscle was used for further analysis [32].

Cold pressor test

The function of descending inhibitory pain pathways [33] can be investigated experimentally using conditioned pain modulation (CPM), in which a secondary pain stimulus is applied to see how it affects the pain sensitivity to a primary pain stimulus [26, 34]. The importance of investigating the descending inhibitory path-

ways is that in some pain disorders, such as TTH, TMD, and chronic pain in general, the activity of the descending inhibitory pathways has been impaired, resulting in a higher pain sensitivity in affected individuals [26, 34, 35].

CPT is one of the tests that is commonly used to investigate the CPM effect under experimental conditions [15]. The CPM effect was defined as the difference between PPT values before and after the CPT. Subjects were instructed to immerse their non-dominant hand up to the wrist in cold water of approximately 1-4°C for 2 minutes [22, 36]. The subjects were encouraged to keep the hand still during the two minutes. Two minutes were chosen for the CPT, to reduce the risk of tissue damage [37]. The sensation of cold pain was rated by the subjects on a Visual Analogue Scale (VAS) from 0: "No pain" to 10: "Worst imaginable pain". The VAS was rated 2 minutes after immersing the hand in the cold water, at the end of the CPT. If the pain was unbearable, the subjects were allowed to remove the hand from the cold water before time was up and the VAS was rated immediately.

Statistical analysis

Data were presented as arithmetic means \pm standard deviation (SD). Graphs were prepared using Excel 2013 (Microsoft Office Professional Plus 2013, version 15.0.4981.1001, Redmond, Washington, USA) and flowcharts were created using Lucidchart 2018 (Lucid Software Inc., South Jordan, Utah, USA). All statistics were performed using the Statistical Package for Social Sciences software (IBM SPSS, version 25, Armonk, New York, USA).

Shapiro Wilk's test was used to assess if data were normally distributed, where *p*-values ≥ 0.05 were considered significant.

To evaluate if there was a significant difference in the BMI values between the two BMI groups, and to compare additional body composition measures between the groups, a one-way Analysis of Variance (ANOVA) was performed for normal distributed data while a Kruskal-Wallis test was performed for the non-normal distributed data.

A Repeated Measures ANOVA with pairwise comparison was carried out to examine if data of the craniofacial muscles could be pooled for further statistical tests. In addition, Wilcoxon's

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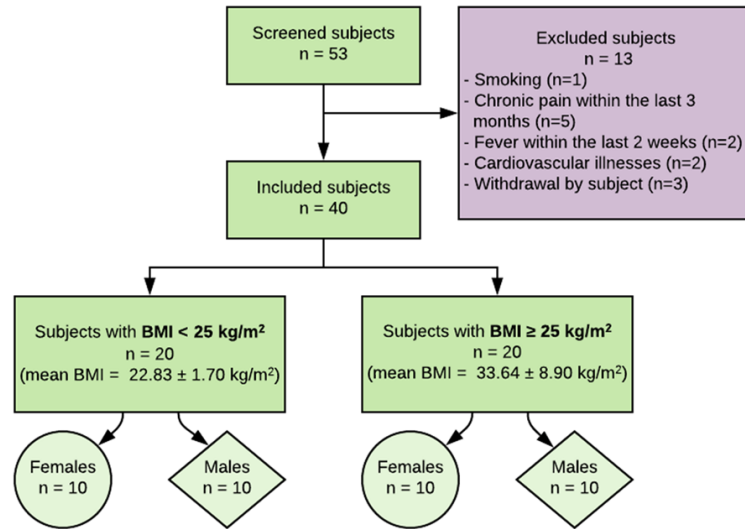


Figure 2. Fifty-three subjects were screened; 13 subjects were excluded and 40 subjects were included in the study and grouped based on Body Mass Index (BMI).

signed rank test was performed to investigate if the data from the left and right deltoid muscle could be pooled. Additionally, paired *t*-tests were run to see if the CPT could provoke the CPM effect in each muscle for all subjects, regardless of BMI and sex.

To examine the effect of BMI and sex on PPT values, a two-way ANOVA was carried out for the temporalis and masseter muscles. Equally, a two-way ANOVA was performed on log-transformed data for the deltoid muscle. To examine the effect of BMI and sex on the CPM effect, a two-way ANOVA was carried out for the data of the percentage change in the PPT (from before the CPT to after the CPT).

Mauchly's test of sphericity and Levene's test for equality of variances were performed to ensure the assumptions of the statistical tests were met. All ANOVAs were considered significant at a *p*-value ≤ 0.05 .

Correlational analyses were carried out to investigate potential correlation between BMI values and PPT before CPT, and between VAS scores and the CPM effect for each muscle. Additionally, correlational analysis was used to test if the obtained body composition parameters were consistent. Pearson's correlation was applied for parametric data, whereas Spearman's rank correlation was used for non-parametric data. Correlation coefficients were eval-

uated according to Evans R classification [38].

Results

Subjects

Fifty-three subjects were screened, and 40 subjects were included in the study after exclusion of 13 (Figure 2). Recruited participants finished the experimental session and no safety issue was reported or recorded. Included subjects were divided into groups according to their BMI.

The distribution of BMIs, WHtR, waist circumference, hip circumference, weight, and body fat percentage did not follow normal distribution ($P < 0.001$, $P < 0.001$, $P = 0.002$, $P = 0.015$, $P = 0.008$, $P < 0.001$, respectively); hence, the non-parametric Kruskal-Wallis test was applied to test the difference between the BMI groups. Equally, a one-way ANOVA was applied for the normally distributed data of height and WHR ($P = 0.838$, $P = 0.504$, respectively). The tests revealed significant differences between the two BMI groups for weight ($P < 0.001$), waist circumference ($P < 0.001$), hip circumference ($P < 0.001$), body fat percentage ($P < 0.001$), BMI ($P < 0.001$), WHtR ($P < 0.001$), and WHR ($P = 0.001$). There were no significant differences between groups for age ($P = 0.099$) and height ($P = 0.865$) (Table 1).

The normal BMI group included 10 males and 10 females, with a mean BMI of 22.83 ± 1.70 kg/m² and a mean age of 23.30 ± 1.81 years within a range of 20-27 years. The other group included subjects with a high BMI and consisted of 10 females and 10 males. In the high BMI group, the mean BMI was 33.65 ± 8.91 kg/m², and the mean age was 27.05 ± 8.53 years within a range of 20-51 years. The scale was not able to measure the weight for one subject in the high BMI group due to subject's weight exceeding the scale capacity; therefore, the subject's self-reported weight was used to calculate the BMI. For this subject the body fat percentage could not be obtained and therefore the subject was excluded from analysis of

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Table 1. Characteristics of participants according to BMI groups

| Body composition parameter | Normal BMI group (mean ± SD) | High BMI group (mean ± SD) | p-value |
|----------------------------------|---------------------------------|-------------------------------|---------|
| Height (cm) | 174.43±11.17 | 174.97±8.85 | 0.865 |
| Weight (kg) | 69.94±11.37 | 103.63±31.97 | <0.001* |
| Waist circumference (cm) | 77.03±8.27 | 102.55±20.49 | <0.001* |
| Hip circumference (cm) | 98.25±8.98 | 118.26±17.55 | <0.001* |
| Body fat percentage ¹ | 22.38±2.41 | 35.02±11.43 | <0.001* |
| BMI (kg/m ²) | 22.83±1.70 | 33.65±8.91 | <0.001* |
| WHR | 0.46±0.84 | 0.59±0.11 | <0.001* |
| WHR | 0.78±0.06 | 0.86±0.08 | 0.001* |

1: Body fat percentage was calculated for 19 subjects in the high BMI group. *: significant at a 0.05 significance level. BMI: body mass index, WHTR: waist-to-height ratio, WHR: waist-to-hip ratio, SD: standard deviation.

parameters in which body fat percentage was required.

Craniofacial muscle sensitivity

All mean PPT values in the craniofacial region were normally distributed (masseter $P=0.791$, temporalis $P=0.112$). Data for craniofacial muscles could not be pooled, as the mean PPT of the left masseter muscle was significantly different from both the left and right temporalis muscles ($P=0.001$ and $P=0.000$, respectively). Repeated measures ANOVA showed no difference between left and right masseter muscles ($P=0.910$) or the left and right temporalis muscles ($P=1.000$). This finding allowed pooling of data from right and left side of each muscle.

In subjects with a high BMI, the mean PPT values of masseter and temporalis muscles were 158.69 ± 57.15 kPa and 188.29 ± 75.44 kPa, respectively. In subjects with a normal BMI, the mean PPT value for the masseter muscle was 153.17 ± 59.30 kPa and 169.03 ± 75.69 kPa for the temporalis muscle. The two-way ANOVA for the masseter and temporalis muscles yielded no significant differences in muscle sensitivity between the BMI groups (masseter $P=0.763$, temporalis $P=0.425$). Similarly, no significant differences in the muscle sensitivity were found between males and females, irrespective of BMI (masseter $P=0.169$, temporalis $P=0.182$).

Deltoid muscle sensitivity

The mean PPT value of the deltoid muscle was 276.69 ± 134.63 kPa in subjects with a high BMI and 254.19 ± 113.87 kPa in subjects with a normal BMI. The mean PPT values for the left ($P=0.014$) and right ($P=0.028$) deltoid muscles

did not follow a normal distribution. Wilcoxon's signed rank test showed no significant difference between left and right deltoid muscles ($P=0.727$) and therefore data were pooled.

Data for the deltoid muscle were not normally distributed and equal variances could not be assumed. Therefore, data for the deltoid muscle were log transformed. The log-transformed data were normally distributed ($P=0.207$) and equal vari-

ances could be assumed ($P=0.414$). A two-way ANOVA revealed no significant difference in the PPT before CPT between the BMI groups ($P=0.595$). Furthermore, there was no significant difference in the PPT before CPT between males and females ($P=0.086$).

The CPM effect

The mean temperature of the water bath for CPT was monitored and was registered as $5.50\pm 1.12^\circ\text{C}$ before the CPT and $5.99\pm 1.28^\circ\text{C}$ after the CPT. All participants felt cold pain and rated pain on the VAS (mean score: 6.18 ± 2.03).

CPT was used to test the CPM effect. The CPM effect was calculated as the percentage change in PPT values obtained before CPT to those obtained after the CPT. This was done to examine the functioning or alterations in descending inhibitory pain pathways (**Figure 3**). Shapiro Wilk's test of normality showed that PPT values before the CPT (masseter $P=0.791$, temporalis $P=0.112$) and after the CPT (masseter $P=0.138$, temporalis $P=0.158$) for masseter and temporalis muscles followed normal distribution, while PPT values before the CPT ($P=0.014$) and after the CPT ($P=0.12$) for the deltoid muscle were not normally distributed. The percentage change in PPT before CPT to after the CPT followed normal distribution for all muscles (masseter $P=1.000$, temporalis $P=0.221$, deltoid $P=0.854$).

The mean PPT value was higher after the CPT than those obtained before CPT for all examined muscles, and paired *t*-tests and the Wilcoxon's signed rank test showed that the difference in mean PPT was significant (masseter $P=0.006$, temporalis $P<0.001$, deltoid $P<0.001$).

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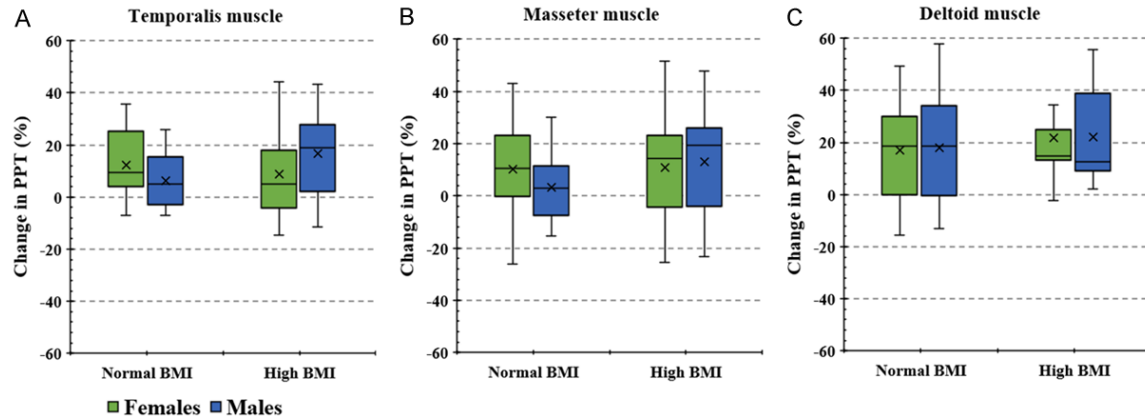


Figure 3. The percentage change in pressure pain threshold (PPT) from before the cold pressor test (CPT) to after CPT for A: temporalis, B: masseter, and C: deltoid muscles for subjects with a normal Body Mass Index (BMI) and a high BMI.

Table 2. Correlational analysis between various factors

| Correlated factors | Correlation coefficient (r) | p-value |
|---------------------------------------|-----------------------------|---------|
| BMI and body fat percentage | 0.778 | <0.001* |
| BMI and WHtR | 0.836 | <0.001* |
| BMI and WHR | 0.621 | <0.001* |
| BMI and PPT before CPT (masseter) | 0.064 | 0.693 |
| BMI and PPT before CPT (temporalis) | 0.134 | 0.979 |
| BMI and PPT before CPT (deltoid) | 0.089 | 0.584 |
| VAS score and CPM effect (masseter) | 0.204 | 0.206 |
| VAS score and CPM effect (temporalis) | 0.250 | 0.120 |
| VAS score and CPM effect (deltoid) | -0.051 | 0.753 |

*: significant at a 0.05 significance level. r: correlation coefficient, BMI: body mass index, VAS: visual analogue scale, WHtR: waist-to-height ratio, WHR: waist-to-hip ratio, PPT: pressure pain threshold, CPM: conditioned pain modulation.

The two-way ANOVA revealed no significant differences in the CPM effect between the two BMI groups for both the craniofacial and deltoid muscles (masseter $P=0.396$, temporalis $P=0.463$, deltoid $P=0.484$). Similarly, there were no significant differences in the CPM effect between males and females for the craniofacial and deltoid muscles (masseter $P=0.706$, temporalis $P=0.831$, deltoid $P=0.901$) (**Figure 3A-C**).

Correlation analysis

Correlational analysis was conducted in order to detect potential correlation between craniofacial muscle sensitivity, WHtR, WHR, body fat percentage and BMI, and between the CPM effect and VAS score (**Table 2**). Correlational

analysis revealed strong, positive correlations between BMI and WHR ($r=0.621$, $P<0.001$), between BMI and WHtR ($r=0.836$, $P<0.001$), and between BMI and body fat percentage ($r=0.778$, $P<0.001$) for all subjects. Weak correlations were found between other factors (**Table 2**).

Discussion

This study investigated craniofacial muscle sensitivity in high and normal BMI pain-free individuals. Although findings provided more knowledge about BMI effect on pain sensitivity, variations in mechanical thresholds were large enough to block indicating a clear association if it was existed and this

might be a consequence of a relatively small sample size of this study. Based on current obtained data, only tendencies could be revealed. More experiments are required to find whether a true statistically significant difference exists between the subgroups. This is in particular relevant for the high BMI group, in which the BMI variation was greater. Considering the explorative nature of this pilot study, findings are discussed in the following to highlight the value and novelty of this study and also to provide further insights for next investigation.

Association between BMI and craniofacial mechanical muscle sensitivity

The relation between BMI and mechanical muscle sensitivity of the temporalis and mas-

seter muscles was investigated and no significant association was found. This finding is consistent with previous findings from *Price et al.*, who found no significant difference between individuals with obesity and normal weight participants, when measuring PPT on the forehead [22]. It seems that this outcome is body-site dependent, since *Tashani et al.* found that individuals with obesity had a lower PPT compared to normal weight individuals when investigated on the hand [21]. Similarly, other studies have demonstrated an association between pain and obesity, in places with increased mechanical loading [12, 17]. Results from the current study indicate that a similar association is not present when muscle sensitivity is assessed in places without mechanical loading, such as the masseter and temporalis muscles. The deltoid muscle was also assessed in this study as a reference point outside the craniofacial region. No significant association between deltoid muscle sensitivity and BMI was found either. These results indicate that the sensory threshold might not generally be decreased in overweight and obese individuals, but that other mechanisms potentially impact the pain mechanisms if any association exists.

Although no significant differences in pain sensitivity were found between the groups, a Mann-Whitney U test showed a significant difference between mean BMIs in the groups. This indicates that the two groups were recognizable. Therefore, BMI-associated muscle sensitivity might be body-region dependent. Further investigation to measure pain sensitivity at different body regions would substantiate the findings.

The study by *Price et al.* found a difference in pain sensitivity between individuals with obesity and normal weight participants in places with excessive fat accumulation, indicating that the association possibly exists in places with non-mechanical loading and excess of fat [22]. The direction of the possible association remains uncertain, as *Price et al.* found a decreased pain sensitivity in individuals with obesity, when investigating PPT on the abdomen [22]. This is contrary to the hypothesis of the current study and other previous findings of an association between pain and obesity in general [12, 17, 21]. Therefore, future studies that assess body fat distribution at test regions would be highly

beneficial. In addition, identification of circulating biomarkers of pain and inflammation, e.g., cytokines levels in biological fluids, would facilitate understanding of mechanisms underlying obesity-pain association. This would show whether a systemic generalized condition exists, or body sites and fat layers can play a major role in regional pain sensitivity as it has been found in some studies.

Pain sensitivity is affected by CPM, a mechanism which is found to be impaired in some chronic pain conditions (e.g., headaches) leading to increased pain sensitivity [26, 34].

In addition to testing ascending pain pathways and sensitivity to mechanical stimuli, the current study investigated responsiveness of descending inhibitory pain pathways by application of CPT and measurement of CPM effect. No difference in the CPM effect was identified between individuals with normal and high BMI. *Skovbjerg et al.* [35] who assessed PPT (over tibialis anterior muscle and the upper trapezius muscle) and CPM effect in a large sample of Danish population, however identified decreased CPM effect and increased pain sensitivity in females. Results from our study are not comparable with this study mainly due to the difference in body region selected for the assessments. Our findings revealed that high BMI might not affect the efficiency of the mechanisms underlying the CPM effect since an efficient CPM effect was evident in all healthy participants regardless of BMI.

Sex- and age-related responses

The current study did not reveal any sex-related responses in any of the outcomes. This is similar to previous findings from *Rolke et al.*, who also carried out thermal and mechanical QST in the facial region of healthy subjects, and found no differences between sexes [39]. However, other investigators are pointing towards a higher pain sensitivity to experimentally induced pain in females. Sex-related responses might be due to several factors such as biological, social, and psychological factors [40]. The difference in the CPM effect between males and females was also investigated in this study, where no significant differences were found. This is inconsistent with the findings from *Skovbjerg et al.*, who found a lower CPM effect in females than in males, indicating the exis-

tence of a difference in the CPM effect between sexes [35]. The efficacy of the CPM effect is suggested to be age-related in women, as higher pain sensitivity was found in relation to lower estrogen levels in the normal menstrual cycle [40, 41]. During menopause, estrogen levels decrease, suggesting that pain sensitivity might increase with age in females [42]. The subjects included by *Skovbjerg et al.* [35] had a mean age of 50.7 years, which is markedly higher than the mean age of subjects in the present study. In addition, *Skovbjerg et al.* [35] found that subjects above 40 years had a higher PPT than those under 40 years. Since the age range in the present study was wider in the high BMI group compared to the normal BMI group, this might explain why no significant difference in PPT was found between the groups.

Likewise, the sample size was larger in the previous study, emphasizing that a bigger sample size in the current study could possibly have shown that responses can be sex-dependent.

In the present study, the age range was wider in the high BMI group compared to the normal BMI group. This might explain why no significant difference in PPT was found between the groups, since *Skovbjerg et al.* [35] found that subjects above 40 years had a higher PPT than those under 40 years. Therefore, further research is needed to clarify if BMI, age and sex interact with craniofacial mechanical muscle sensitivity.

Conclusion

Findings revealed no significant difference in craniofacial mechanical muscle sensitivity between normal and high BMI pain-free individuals regardless of sex.

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Disclosure of conflict of interest

None.

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