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SURGERY FOR OBESITY AND RELATED DISEASES

Original article

Pain sensitivity and pain scoring in patients with morbid obesity

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Abstract

Background: There are indications that pain perception is altered in patients with obesity, which complicates postoperative pain treatment. An essential part for adequate pain treatment is the capacity of the patient to grade pain.

Objectives: The aim of this study was to identify the differences in pain perception and pain processing in patients with without obesity.

Setting: Dutch Obesity Clinic West; private practice and the Leiden University Medical Center, the Netherlands; university hospital.

Methods: Forty-one patients with severe obesity (body mass index 42.9 ± 4.9 kg/m^2) and 35 control patients (body mass index 23.2 ± 2.8 kg/m^2) received multiple random thermal and electrical stimuli to the skin, in intensity in between pain threshold and tolerance. The consistency of scoring was assessed by a penalty score system and stratified into good, moderate, and poor cohorts.

Results: The penalty scores differed significantly between patients with obesity and controls with higher penalty scores in patients with obesity for both nociceptive assays. Combining the results of the heat and electrical tests indicated that just 28% of the patients with obesity had a penalty score in the good cohort, indicative of consistency in grading incoming stimuli, in contrast to 60% of control patients.

Conclusion: Individuals with severe obesity displayed hypoalgesia to noxious electrical stimuli together with difficulty in grading experimental noxious thermal and electrical stimuli in between pain threshold and tolerance. We argue that the latter may have a significant effect on pain treatment and consequently needs to be taken into account when treating the patients with obesity for acute or chronic pain. (Surg Obes Relat Dis 2017;13:788–795.)

Keywords: pain; nociception; hypoalgesia; visual analogue scale

Approximately 1 in 6 individuals in the Netherlands and 1 in 3 in the United States is a person with obesity, as defined by a body mass index (BMI) ≥ 30 kg/m^2 [1–3]. Although many obese individuals are "healthy" despite their obesity, severe obesity may be associated with a proinflammatory state that affects multiple organ systems. White adipose tissue secretes numerous polypeptides (adipokines), which include proinflammatory cytokines, acute phase peptides, hormones (e.g., leptin), and other reactive substances [1]. The adipokines contribute to a number of metabolic disorders and degenerative diseases such as insulin resistance, metabolic syndrome, cardiovascular

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disease, and neurodegenerative disorders. The number of patients with obesity who present for surgery, bariatric or otherwise, is increasing yearly, and these obesity-induced diseases complicate postoperative treatment—for example, as a result of pulmonary and cardiovascular complications. There are suggestions from experimental pain studies that pain perception in patients with severe obesity differs compared with individuals with lower BMI values, with a tendency for patients with severe obesity to be hypoalgesic—that is, to have reduced numerical pain scores to a variety of painful stimuli [2]. Furthermore, we know from chronic pain states that neuroinflammation plays an important role in the alteration of pain perception [4]. An important issue for the adequate treatment of pain is the capacity of the patient to accurately grade the severity of pain. We and others have recently reported that pain grading using a Numerical Rating Scale (NRS) is a process involving complex central sensory pathways and specific cognitive tasks that are negatively affected by chronic pain and opioid treatment [5,6]. Of importance is the observation from a large number of experimental and clinical studies that severe obesity may be associated with reduced cognitive function, including complex attention, verbal and visual memory, and decision making [1,7–10]. All of these functions play some role in the grading of pain on an imagined 11-point NRS as is often used. Consequently, it may well be that patients with severe obesity may find it more difficult to grade their pain using a NRS.

In this study we determined the ability of patients with severe obesity (BMI $\geq$ 35 kg/m^2) to grade randomly applied noxious stimuli. Multiple random thermal and electrical stimuli with an intensity in between pain threshold and pain tolerance were applied to the skin, and the consistency of scoring (i.e., a higher intensity should be graded with a greater numerical score) was assessed by a penalty score system and by modeling the stimulus–response data. The penalty score was recently introduced and validated in chronic and acute pain patients [5]. We hypothesized that patients with severe obesity would have more difficulty in grading the random stimuli compared with a group of healthy (age-matched) controls. This study was part of a larger project aimed at understanding the process of pain grading in health and disease [5].

Methods

After approval from the Institutional Review Board, we enrolled 43 morbidly patients with obesity and 38 patients without obesity. The protocol was registered in The Netherlands Trial Register under number 3769. All patients gave written informed consent before enrollment into the study. The study focused on patients with severe obesity (i.e., with a BMI $\geq$ 35 kg/m^2). BMI was calculated by dividing the present weight by body height squared (m^2). BMI classification is done according to the World Health Organization; BMI $<$ 18.5 kg/m^2 is considered underweight; BMI 18.5–25 kg/m^2, normal weight; BMI $\geq$ 25 kg/m^2, overweight; BMI 25–30 kg/m^2, preobese; BMI $\geq$ 30 kg/m^2, obesity; and BMI $\geq$ 35 kg/m^2, morbid obesity. These patients were recruited at the Nederlandse Obesitas Kliniek (Dutch Obesity Clinic) in The Hague, The Netherlands, and were all scheduled to undergo bariatric surgery. The control group consisted of age-matched volunteers with a BMI $\leq$ 30 kg/m^2. Controls were recruited through flyers posted on the university campus and advertisements in local newspapers. Participants were included if they were between 18 and 65 years old and were able to give informed consent. Exclusion criteria were presence of a medical condition (such as cardiac, pulmonary, liver, or renal disease), a psychiatric history, pregnancy or lactation, and history of illicit drug or alcohol abuse. Individuals with obesity with pain symptoms took the validated Dutch version of the PainDetect questionnaire to assess the presence of chronic pain with or without a neuropathic pain component [11,12]. If the PainDetect score was $\geq$19 (a neuropathic pain component is likely), the patients were excluded from the study. Additionally, only individuals with mild nociceptive pain (pain scores $\leq$ 4) were allowed to participate. We previously reported that low nociceptive pain scores do not significantly affect the ability to score pain [5].

Noxious stimulation

Two noxious tests were applied: thermal and electrical stimulation. Heat pain was applied using the 3 $\times$ 3 cm surface probe of the Pathway Neurosensory Analyzer (Medoc Ltd., Ramat Yishai, Israel). The temperature range in this study was 32°C to 52°C. The probe was placed on the volar side of the right forearm on 1 of 3 locations and was placed on the next location for each new stimulation to prevent any sensitization or adaptation. Electrical stimulation was performed using a custom-made current stimulator. The stimulator was attached to 2 electrodes (surface area .8 cm^2) separated by 2 cm placed on the tibial surface of the right leg about 10 cm above the malleolus. The current stimulator produced a constant current of 200 μs pulses at 20 Hz for 5 seconds. The current could vary from 0–128 mA.

Pain tests and scoring

The participants were familiarized with the study design, pain tests, and scoring system before the start of the study. Pain intensity was scored using an 11-point NRS ranging from 0 (no pain) to 10 (worst pain imaginable). Only integers were allowed for scoring. Initially pain threshold and pain tolerance for thermal and electrical noxious stimulation were determined. Pain threshold (PTh) was defined as the lowest stimulus value that caused an NRS of 1; pain tolerance (PTol) was defined as the lowest stimulus value that caused an NRS of 10. Initially, a 5-second

subthreshold stimulus was applied (39°C and 8 mA) and the NRS was scored. Next, in steps of .5°C and .5 mA the stimuli were increased in intensity until PTh was reached. For pain tolerance a similar approach was applied, with the lowest temperature and current causing an NRS of 10 as PTol set point. In each participant this procedure was repeated multiple times until the subsequent values of PTh and PTol values were within ±.5°C and ±.5 mA. After the threshold and tolerance values were obtained, the patients rested for 15–20 minutes.

The magnitude of the random stimuli that were used in the remainder of the study was calculated from the difference between PTh and PTol. This difference was divided by 9, which gives the value of 8 steps above PTh. For example, a PTh and PTol of 37.0 and 50.5°C will lead to a step size of 1.5°C (= [50.5–37] / 9) and consequently the following stimuli will be applied in random order: 38.5°C, 40°C, 41.5°C, 43°C, 44.5°C, 46°C, 47.5°C, 49°C. An identical approach was taken for electrical pain. Resolution of the heat stimuli was .1°C and of the electrical stimuli .5 mA. Electrical and thermal stimuli were alternated with 3–5 minutes between stimuli. If the PTol was not reached at the cutoff temperature of 52°C, the highest pain score was used as the upper limit and a linear distribution of 8 interpolated temperatures was made between the temperature of PTh and 52°C. The participants were blinded to the sequence and intensity of the stimuli.

Data and statistical analyses

We assumed that the applied stimuli were linearly related to the NRS values 2–9. For example, assuming PTh at 37°C (NRS = 1) and PTol at 50.5°C (NRS = 10), the stimulus train 38.5°C, 40°C, 41.5°C, 43°C, 44.5°C, 46°C, 47.5°C, 49°C would correspond with NRS values 2, 3,…8, 9, respectively (Fig. 1 A, yellow symbols). Any deviation from this "ideal" relationship was calculated by subtracting each pain score (j) from the previous one (j – 1). The difference d (= NRS[j] – NRS[j – 1]) was translated into penalty score 0, .5, or |d|. A score of 0 was applied if $d > 0$ (i.e., the stimulus with the higher intensity is rated as more painful than the stimulus of lesser intensity); a score of .5 was applied if $d = 0$ (i.e., the stimulus with the higher intensity is rated as equally painful); and a score of |d| (i.e., the absolute value of the difference in NRS between the 2 stimuli) is given when $d < 0$ (i.e., the stimulus with the higher intensity is rated as less painful). The sum of the penalty score of the individual stimuli was the penalty score used in the statistical analysis. The summed scores range from 0 (perfect score, Fig. 1 A, yellow symbols) to 40 (worst possible score; Fig 1 A, green symbols). The summed penalty scores were divided into 3 cohorts, as discussed previously, representing "good," "mediocre," and "poor" stimulus–response relationships, with respective sum scores ≤ 3.5 (good), 4–7 (mediocre), and ≥ 7.5

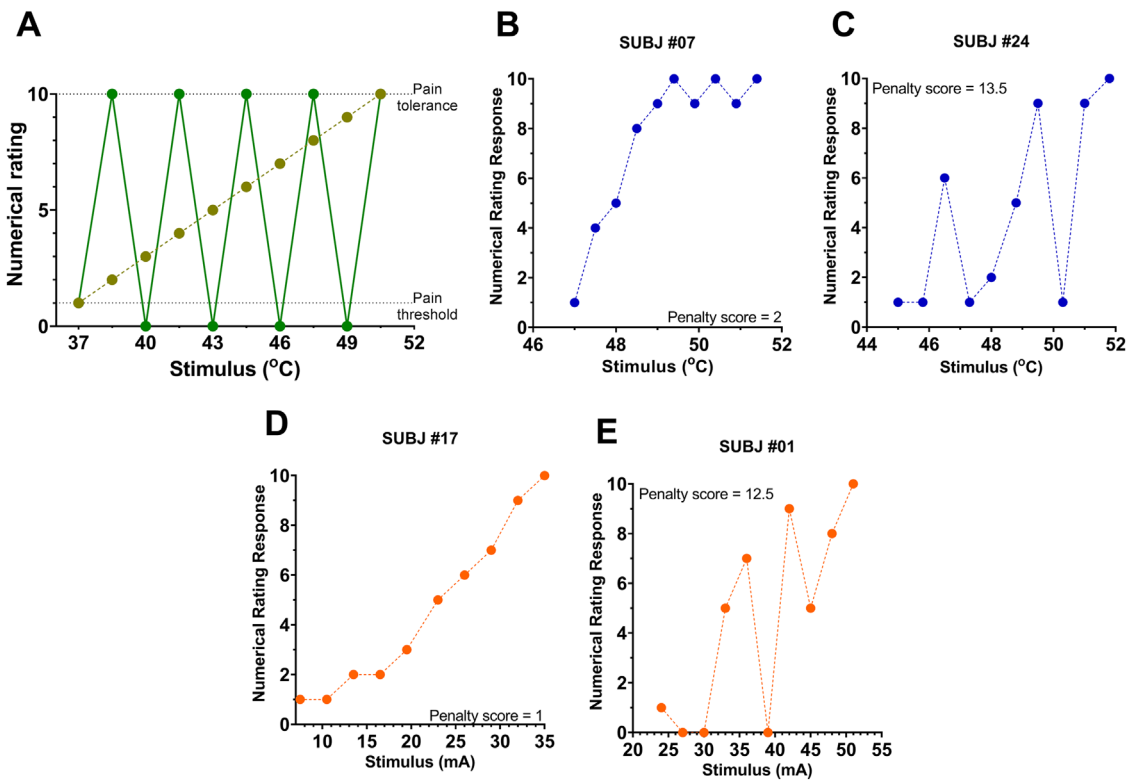

Fig. 1. (A) Best and worst possible scoring yielding penalty scores of 0 (yellow symbols) and 40 (green symbols). (B–E) Examples of the best and worst scoring to the noxious thermal (B and C) and noxious electrical random stimuli (D and E) as observed in the patients with obesity.

(poor). The penalty scoring system was recently validated in chronic and acute pain patients [5].

The sample size of the study was based on observations from our previous study in patients with moderate to severe pain [5]. Assuming a difference in prevalence of score "good" between population of 24% with a standard deviation (SD) of 30%, with $\alpha = .05$ and $\beta = .1$, a group size of 33 is calculated. To take into account any margin of uncertainty around the effect size and SD, the size of the obesity and control group was somewhat expanded. Data analysis was performed using SPSS Statistical software (Version 23.0, IBM Corp., Armonk, NY). Pain threshold and tolerance were compared between patients with obesity and patients without obesity using Student's *t* tests. Penalty scores were analyzed by nonparametric tests. Mann-Whitney U tests were used to determine whether the penalty scores differed between patients with obesity and control patients. Fisher's exact tests were used to assess whether the distribution of penalty scores across the 3 cohorts (good, mediocre, poor) differed between study groups. The relationships among age and BMI and penalty scores were evaluated by Spearman's ρ. *P* values $< .05$ were considered significant. Data are presented as mean ± SD or median (range) unless otherwise stated.

The stimulus–response data were analyzed with a sigmoid function to get an indication of the within-subject variability. The sigmoid function has parameters MIN, the stimulus corresponding with PTh; MAX, the stimulus corresponding with PTol; N5, the stimulus intensity that corresponds with an NRS value of 5; and shape parameter G [5]:

$$NRS(STIM) = MIN + (MAX - MIN) \cdot [(STIM/N5)^G / (1 + (STIM/N5)^G],$$

where STIM is the intensity of the applied random stimulus.

The data were analyzed in NONMEM, a statistical package for nonlinear mixed-effects analysis using a population approach (ICON Development Solutions, Hanover, MD). *P* values $< .05$ were considered significant. Data are presented as median ± standard error (SE).

Results

Participants

Forty-three patients with severe obesity and 38 controls were enrolled in the study of which 41 and 35 participated in the testing (see Consort flow chart, Supplemental Fig. 1). One patient with obesity was excluded because of the presence of a chronic pain syndrome with a neuropathic component, another because testing occurred after bariatric surgery had been performed. Of the 38 controls, 3 patients did not participate because of logistic reasons. The participants' characteristics are given in Table 1.

Table 1
Participants' characteristics

	Severely obese participants	Control participants
Number of participants	41	35
Sex distribution (M/F)	3/38	16/19
Age (yr)	43.4 ± 10.7	31.6 ± 12.9
Age range	23–61	18–57
BMI (kg/m^2)	42.9 ± 4.9	23.2 ± 2.8
BMI range	37.4–58.5	19.2–29.7
Education level N (%)		
Low-level education	29 (70.7)	2 (5.7)
Mid-level education	10 (24.3)	13 (37.1)
Higher-level education	2 (5.0)	20 (57.2)
Electrical pain threshold (mA)	16.2 ± 9.2[*]	11.4 ± 3.9
Electrical pain tolerance (mA)	38.0 ± 17.7[†]	25.0 ± 8.7
Heat pain threshold (°C)	42.9 ± 2.8	42.8 ± 2.4
Heat pain tolerance (°C)	49.3 ± 1.6[‡]	49.7 ± 1.7[§]

BMI = body mass index; F = female; M = male.

Values are mean ± SD. Because some patients reached the 52°C cutoff value, heat PTol values were calculated from 35 patients ([‡]) and 29 patients ([§]).

[*] $P = .02$.

[†] $P < .001$ versus control patients.

The mean BMI of patients with obesity was 42.9 ± 4.9 kg/m^2 with a range of 37.4–58.8 kg/m^2. The BMI of controls was 23.2 ± 2.8 (range 19.2–29.7) kg/m^2. Eleven control patients had a BMI > 25 kg/m^2 (but < 30 kg/m^2) and were therefore considered overweight. The age range was similar between study groups. In contrast to controls, most patients with obesity were female (38/41). None of the control participants but 13 of the patients with obesity reported chronic pain symptoms with pain scores < 4. All symptoms were joint-related with pain in lower back, hips, knee, and/or feet. None of these patients had a PainDetect score > 19 (mean score 7.7 ± 3.3 with range 1–13). Four patients used analgesic medication (tramadol, pregabalin, ibuprofen, etoricoxib). Two patients had type 2 diabetes treated with oral medication. Electrical but not heat pain threshold ($P = .05$) and tolerance ($P = .001$) were higher in patients with obesity than in control participants (Table 1).

Penalty scores

The pain threshold and tolerance values (Table 1) formed the basis of the linear distribution used to determine the random stimuli. In Fig. 1 examples of NRS profiles with best and worst penalty scores are given for thermal stimuli (panels B and C) and electrical stimuli (panels D and E). In patients with obesity the penalty scores ranged from 1.5–13.5 (heat pain) and from 1.0–12.5 (electrical pain). The penalty score distributions are given in Table 2 and Fig. 2. The penalty scores differed significantly between patients with obesity and controls, with higher penalty scores in patients with obesity for both nociceptive assays (heat pain: $P = .01$, electrical pain: $P = .03$). The penalty

Table 2
Penalty scores and distribution into cohorts good (0–3.5), mediocre (4–7), and poor (>7)

	Morbidly obese participants		Healthy controls	
	Heat pain	Electrical pain	Heat pain	Electrical pain
Mean ± SD	5.7 ± 3.6	4.4 ± 2.8	3.6 ± 1.8	2.9 ± 1.6
Median (range)	3.5 (1.5–13.5)*	3.5 (1.0–12.5)†	3.0 (1.5–9.0)	2.5 (1.0–8.5)
Distribution (% of patients)				
Cohort good (95% CI)	53.8 (38.9–68.7)	52.6 (37.7–67.5)	71.4 (56.2–86.3)	77.1 (63.2–91.0)
Cohort mediocre (95% CI)	23.1 (10.5–35.7)	36.8 (22.4–51.2)	22.9 (9.0–36.8)	20.0 (6.8–33.3)
Cohort poor (95% CI)	23.1 (10.5–35.7)	10.5 (1.4–19.6)	5.7 (.0–13.4)	2.9 (.0–8.5)

CI = confidence interval; SD = standard deviation.
*$P = .01$ versus healthy controls.
†$P = .03$ *versus* healthy controls.

score distribution differed significantly between study groups for electrical pain, with 47.3% (patients with obesity) versus 22.9% (controls) of scores > 3.5 (χ^2–Fisher's exact test $P = .049$), but not for heat pain (scores > 3.5 in 46.2% of patients with obesity versus 28.6% of control participants, $P = .15$). The contingency table (Table 3) shows that patients with obesity were less consistent than healthy controls in their scoring of heat and electrical pain. Patients with obesity and control patients had 42% (27.8% in good cohort) and 66% (57.1% in good cohort) overlap, respectively.

The combined patients with obesity and control data sets indicated a significant correlation between BMI and penalty scores with higher scores at higher BMIs for electrical pain ($\rho = .29$, $P = .01$) but not heat pain ($\rho = -0.04$, $P = .7$; Fig. 3 A). A correlation between age and penalty scores was observed for electrical pain ($\rho = .29$, $P = .01$) but not heat pain ($\rho = -.05$, $P = .7$; Fig. 3 B).

Chronic pain did not affect penalty scores or its distribution in patients with obesity (Mann-Whitney U test penalty scores in patients with pain [n = 13] versus scores in patients without pain [n = 28] $P = .49$ for heat and $P = .48$ for electrical pain tests).

Stimulus–response relationship

The parameters estimates are given in Supplemental Table 1. Examples of data fits are given in Supplemental Fig. 2. In patients with obesity the response curves for electrical pain were shifted to the right by 5.4 mA compared with controls (N5 patients with obesity 22.9 ± 1.7 mA versus N5 control 17.8 ± 1.3 mA, $P < .05$). For heat pain the N5 did not differ between patients with obesity and control patients (N5 = 46.4 ± .2°C in both groups). This indicates hypoalgesia to electrical pain but not heat pain in the patients with obesity. An important difference between the 2 populations was the 30%–60% larger within-subject variability observed in the patients with obesity for both pain tests (heat pain SD 1.8 ± .1 [patients with obesity] versus 1.5 ± .1 [controls], $P < .05$; electrical pain SD 1.6 ± .1 [patients with obesity] versus 1.0 ± .05 [control], $P < .01$), indicative of their lesser ability to consistently score the random stimuli.

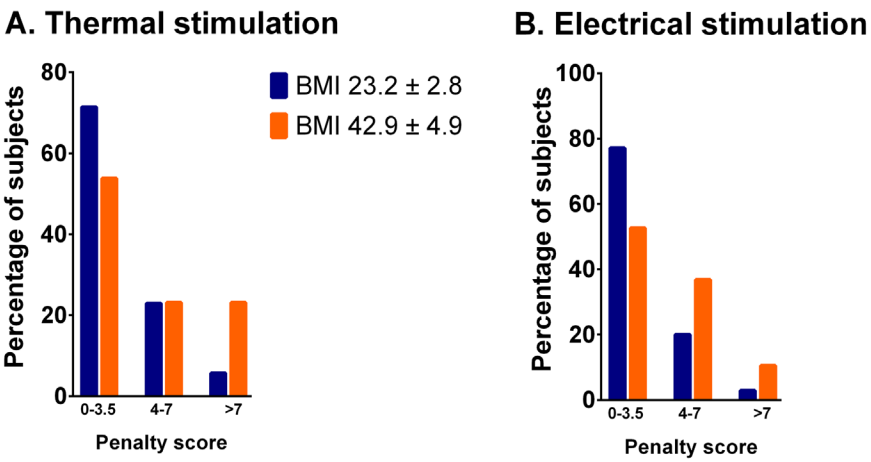

Fig. 2. Distribution of penalty scores for heat and electrical noxious stimulation in participants with a BMI of 23.2 ± 2.8 kg/m^2 (n = 35) and a BMI of 42.9 ± 4.9 kg/m^2 (n = 43). The BMI data are mean ± SD. BMI = body mass index; SD = standard deviation.

Table 3
Contingency table of good (0–3.5), mediocre (4–7), and poor (>7) penalty scores in obese and control patients

Morbidly obese participants				
		Penalty scores heat pain		
		0–3.5	**4–7**	**>7**
Penalty scores electrical pain	**0–3.5**	27.8%	13.9%	8.3%
	4–7	19.4%	8.3%	11.1%
	>7	2.8%	2.8%	5.6%
Control participants				
		Penalty scores heat pain		
		0–3.5	**4–7**	**> 7**
Penalty scores electrical pain	**0–3.5**	57.1%	14.3%	5.7%
	4–7	11.4%	8.6%	—
	>7	2.9%	—	—

Discussion

Our analyses indicate that otherwise healthy patients with severe obesity, with an average BMI of 43 kg/m^2, have a reduced capacity to grade random noxious stimuli compared with age-matched controls with an average BMI of 23 kg/m^2. Penalty scores to electrical and thermal noxious stimuli were in the same range compared with those of chronic pain patients, another population that has difficulty grading painful stimuli [5]. Additionally and in contrast to chronic pain patients, the patients with severe obesity were hypoalgesic to electrical stimuli and required a greater intensity to reach pain threshold and tolerance, causing a shift in parameter N5 (the stimulus intensity that corresponds with an NRS of 5).

There is increasing evidence for an association between severe obesity and an increased prevalence of chronic pain [1,13,14]. Part of the pain in obesity is related to increased pressure on the load-bearing segments of the body, such as neck, back, and joints of the lower extremities [14]. Additional evidence suggests that pain in obesity is associated with a genetic predisposition, metabolic factors, low-grade inflammation (related to the release of proinflammatory cytokines from the white adipose tissue), and psychological status (e.g., high pain catastrophizing) [3,13,14]. In our relatively small cohort, 13 (32%) patients with obesity suffered from chronic nociceptive pain, in all cases related to the joints of the lower extremities. Irrespective of the presence of mild pain, we observed that participants with severe obesity had higher electrical pain threshold and tolerance values compared with control patients, an indication of lower sensitivity to electrical pain stimulation. We recently performed a systematic review of studies that compared pain threshold and tolerance values between patients with obesity and patients without obesity [2]. Four of 7 studies reported higher stimulus intensities required to reach pain threshold and tolerance, in agreement with our observation on electrical pain [15–18]. Three of these 4 studies used electrical stimulation to measure threshold values. We have no clear explanation why, in contrast to heat stimulation, the electrical stimulation is linked to higher thresholds in obesity. As discussed elsewhere, electrical stimulation surpasses the nociceptive nerve endings in the dermis and directly stimulates the sensory and nonsensory nerves in an unnatural fashion [19]. In contrast, heat pain stimulates the nociceptors through activation of heat-sensitive receptors on the dermal nerve endings. Additionally, the fat tissue surrounding the nerve fibers of the skin may serve as an insulator, causing a reduced transfer of the electrical current to the sensory nerves in the hypodermis. We hypothesize that the (prediabetic) metabolic or inflammatory changes of obesity cause a reduced sensitivity of small peripheral nerves to electrical stimulation. There is additional proof for this

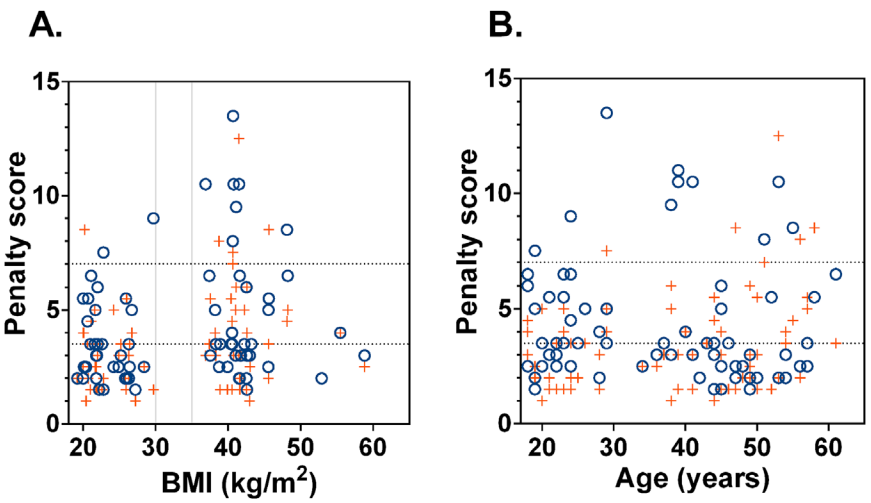

Fig. 3. (A) Penalty score versus body mass index (BMI). Heat pain: ρ = –.04, P = .7. Electrical pain: ρ = .29, P = .01. (B) Penalty score versus age. Heat pain: ρ = –.05, P = .7. Electrical pain ρ = .29, P = .01. The vertical gray lines depict the BMI cutoff of 30 and 35 kg/m^2 between non–morbidly obese participants and patients with morbid obesity. Blue ′ odenote heat pain data, orange + electrical pain data.

hypothesis. Fifty percent of our patients with severe obesity displayed signs of small-fiber neuropathy as measured by cornea confocal microscopy (unpublished observation). Miscio et al. [17] performed a sensory conduction study in 20 nondiabetic morbidly obesity patients (mean BMI 41 kg/m^2) and observed decreased action potential of median, ulnar, and sural nerves. The picture that emerges from these data is that in obesity the sensory nerve fibers undergo functional changes causing hypoalgesia to some experimental stimuli. A reduced sensitivity to pain seems in disagreement with the observation of an increased prevalence of chronic pain in obesity. However, our data seem reminiscent of other forms of small fiber neuropathy in which loss of function of several sensory tests corresponds with chronic pain behavior [20].

Our 2 analyses (penalty scores and data fitting) indicated that patients with obesity were less able to grade random noxious thermal and electrical stimuli. Combining the results of the heat and electrical tests (Table 3) indicates that just 28% of the patients with severe obesity had a penalty score between 0 and 3.5 (good cohort), in contrast to 66% of control participants. This is an important observation and in agreement with our experience in clinical practice that patients with obesity have difficulty grading their pain in a consistent manner. This reduced ability to properly communicate their pain to clinicians together with a much greater variability in drug pharmacokinetics makes the pharmacologic treatment of pain in the patients with obesity a challenging task [13,21].

Our study does not provide any insight in the mechanisms of the lesser ability of the participants with severe obesity to consistently score random stimuli. We cannot exclude that because we performed a small cross-sectional study that non–obesity-related biopsychosocial factors that are not know to us or were not controlled for in the study played some role in the study outcome. Such factors include the socioeconomic status of the participants or their educational level (Table 1). Additionally, hormonal or nutritional factors may have had some influence. A possible biological cause for our observations is that because of (subclinical) peripheral nerve damage, sensory perception is modified, with alterations in central processing and consequently a lesser ability to discriminate between stimuli of different intensities. Another possibility is that the proinflammatory state caused by the adipokines induces neuroinflammation similar to the inflammatory state seen in chronic pain patients, with alterations in pain perception and pain modulation. Another attractive hypothesis is that sensory grading in obesity is affected as a result of diminished cognitive function. The adipokine-induced neuroinflammation is associated with cognitive decline, with deterioration of specific brain functions including complex attention, verbal and visual memory, and decision making [1,7–10]. As we and others discussed previously [5,6], grading of sensory stimuli is the translation of incoming sensory stimuli into a quantitative verbal response. To that end one has to imagine an abstract quantitative scale of sensory stimuli from no pain to most severe pain imaginable, place incoming stimuli in the correct position, and communicate the result. This is a complex task that relies on various cognitive functions (attention, imagination, scaling, numeric memory, number coding, decision making) [22]. Even a slight cognitive impairment may affect any of these cognitive functions. One important caveat of our study is that we did not assess cognition of our study population. Further studies are therefore needed to determine a possible link among obesity, cognition, and pain behavior. Our findings in the patients with obesity are in agreement with observations in chronic pain patients (mean BMI 25 kg/m^2) showing similar patterns in penalty scores.[5] Correspondingly, in chronic pain patients there is evidence for structural and functional changes in the brain that correlate with impaired cognition and possibly with impaired grading of sensory stimuli [6,23,24]. Hence, we argue that our data in patients with obesity may be explained by cognitive changes related to obesity-induced neuroinflammation. A role for peripheral nerve damage or previously mentioned biopsychosocial influences cannot be excluded, however.

Study limitations

Our patients with obesity were predominantly female. Although obesity prevalence is generally higher in women [25], this may have affected the outcome of our study. However, we previously were unable to detect any sex effect on penalty scores in healthy controls and chronic pain patients [5]. We therefore assume that female gender is not an additional risk factor for the inadequacy of pain scoring in obesity, but further studies are needed to elucidate this matter. Assuming some cognitive changes in the patients with obesity, it may well be that they had a lesser ability to understand the various components of the study. Although we carefully and repetitively instructed all participants, some cognitive limitations may have had a negative effect on the study outcome. Still, we anticipated such an effect and consider it an inherent part of the study and its outcome.

Thirteen patients with obesity suffered from mild chronic pain. As discusses earlier, we previously observed that chronic moderate to severe pain worsens the adequacy of pain scoring, which we related to pain-induced neuroplastic changes in the central nervous system rather than to the presence of pain itself [5]. Because the pain scores of our current groups of participants with obesity were mild (<4) and there were no neuropathic symptoms, we argue that the effect of pain in our population of individuals with severe obesity was of minor influence on the study outcome [5]. However, it is important to realize that some effect of the presence of mild pain might have worsened the study outcome.

We applied experimental noxious stimuli that differ significantly from clinical pain. For example, clinical pain is not random and has distinct biopsychophysical characteristics. Extrapolation of our findings to the clinical setting should therefore be done with care. Yet, our current findings give proof for our clinical experience that patients with severe obesity have difficulty with the consistent scoring of acute pain. Our current findings are therefore important and should be carefully considered when treating a patient with obesity with opioid analgesics, keeping in mind that both over- and underdosing should be prevented. Our findings are also relevant for the treatment of acute pain after surgery. Possibly, taking into account more objective measures of pain, such as composite scores derived from hemodynamic parameters such as the nociception level, may be helpful in treating postoperative pain in patients with severe obesity [26].

Finally, we studied a small cross-sectional population of individuals with severe obesity. Hence our study is best considered preliminary and must form the basis of further studies.

Conclusion

Compared with patients without obesity, patients with obesity displayed hypoalgesia to noxious electrical stimuli together with difficulty in grading experimental noxious thermal and electrical stimuli in between pain threshold and tolerance. We argue that the latter may have a significant effect on pain treatment and consequently needs to be taken into account when treating patients with obesity for acute or chronic pain.

Disclosure

The authors have no commercial associations that might be a conflict of interest in relation to this article.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.soard.2017.01.015.

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