Body Mass Index and distribution of body fat can influence sensory detection and pain sensitivity[1]

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Conflict of interest

Funder

What's known?

- Epidemiological evidence suggests that chronic pain and obesity are associated
- Specific mechanisms connected with the association between chronic pain and obesity are not known
- The association between experimental pain and obesity is not conclusive

What does this study add?

- Obese individuals are more sensitive than normal range BMI individuals to pressure pain but less sensitive to thermal pain
- Different body sites may have different pain responses according to their subcutaneous body fat

The influence of Body Mass Index, body fat percentage and its distribution on sensory detection and pain sensitivity responses

ABSTRACT

Background: The aim of this study was to investigate the influence of body fat percentage and its distribution on sensory detection and pain sensitivity responses to experimentally induced noxious stimuli in otherwise pain-free individuals.

Methods: 72 participants were divided into three equal groups according to their Body Mass Index (BMI) (normal, overweight and obese).Thermal sensory detection and heat pain threshold and tolerance were measured using a Medoc Thermal Sensory Analyser II unit, pressure pain threshold (PPT) was measured using a Somedic Algometer and cold pressor pain responses were also measured. Body fat % was estimated using a 4 sites skinfold method.

Results: Mean±SD PPT of the obese group (620.72±423.81 kPa) was significantly lower than normal weight (1154.70±847.18 kPa) and overweight (1285.14±998.89 kPa) groups. RM ANOVA found significant effects for site for cold detection threshold ($F_{(1, 68)}$ =8.3, P=0.005) and warm detection threshold ($F_{(1, 68)}$ =38.69, P=0.001) with waist having lower sensory detection thresholds than thenar eminence. There were significant effects for site for heat pain threshold ($F_{(1, 68)}$ =4.868, p=0.031) which was lower for waist compared with thenar eminence (mean difference=0.89°C).

Conclusion: Obese individuals were more sensitive than non-obese individuals to pressure pain but less sensitive to thermal stimuli, and that body sites may vary in their response to different types and intensities of stimuli. However, the inconsistency of findings within and between existing research studies should catalyse further research in this field.

Significance:

This study provided an evidence that body mass index and distribution of body fat can influence sensory detection and pain sensitivity. Obese individuals were more sensitive than normal range BMI individuals to pressure pain but less sensitive to thermal pain. Different body sites may have different pain responses according to their subcutaneous body fat. This should inform the clinical practice when tailoring pain management for obese patients and strengthen the argument that weight loss for obese pain patients has to be a significant aspect of a pain management programme.

INTRODUCTION

Epidemiological evidence that chronic musculoskeletal pain is more prevalent in obese than non-obese individuals suggests that pain and obesity are associated (Ray, 2011). Mechanical pressure on weight baring joints causing damage to joint tissue has been suggested as a contributing factor, although evidence suggests that chronic pain that does not involve weight bearing structures is also more prevalent in obese individuals, including chronic headaches, and abdominal pain (Kim *et al.*, 2006; Marks, 2007; Abou-Setta *et al.*, 2011). Metabolic changes associated with adiposity may be a contributing factor, including the generation of pro-inflammatory cytokines by adipose tissue resulting in sensitisation of nociceptors and central nociceptive transmission pathways (McVinnie, 2013). This may be reflected in an increased pain sensitivity response to experimental stimuli (Koltzenburg *et al.*, 1992; Watkins *et al.*, 2003; Fain, 2006; 2010; Fain *et al.*, 2010).

Information about an individual's pain sensitivity can be captured by measuring response to mechanical, thermal, chemical and electrical stimuli (Staahl & Drewes, 2004; Olesen *et al.*, 2012). Previously, we conducted a systematic review of studies that compared pain sensitivity response to experimental stimuli between obese and non-obese individuals (Astita et al, 2014). We found seven studies of low methodological quality with inconsistent findings (Pradalier *et al.*, 1981; McKendall & Haier, 1983; Zahorska-Markiewicz *et al.*, 1983; Zahorska-Markiewicz *et al.*, 1988; Raymond *et al.*, 1995; Khimich, 1997; Maffiuletti *et al.*, 2011). Meta-analysis was not possible and we concluded that there was insufficient evidence to determine whether differences in pain sensitivity response between obese and non-obese individuals exist (Astita *et al.*, 2014). (Bohnert *et al.*, 2013) conducted a cross-sectional study that compared pain sensitivity response to contact thermal stimuli at body sites with excess subcutaneous fat (abdomen) and little subcutaneous fat (forehead). They found that obese participants had decreased sensitivity, higher thresholds and lower subjective ratings for painful and non-painful thermal stimuli on the abdomen when compared with non-obese participants. Decreased abdominal sensitivity was associated with measures of adiposity including waist-to-hip ratio and subcutaneous fat thickness. There were no differences between obese and non-obese participants for thermal or pressure measurements on areas with little subcutaneous fat (forehead and hand). They concluded that pain sensitivity response was decreased on areas with excess subcutaneous fat in obese compared with non-obese participants and that this was due in part to decreased fibre density from skin stretching associated with excess fat. In addition they suggested that reduced thermal conductivity associated with excess subcutaneous fat may hinder the transmission of temperature changes to thermal and nociceptive fibres in obese individuals. This finding is inconsistent with the increased pain sensitivity response expected if a low grade pro-

inflammatory state existed in obese individuals (McVinnie, 2013; Paley & Johnson, 2015). (Price *et al.*, 2013) suggested that it was possible that an increased ratio of anti:pro inflammatory molecules in obese adipose tissue could result in locally decreased pain sensitivity. Clearly, there is a need for further studies.

The aim of this study was to investigate the influence of BMI, body fat percentage and its distribution on sensory detection and pain sensitivity responses to experimentally induced noxious stimuli in otherwise pain-free individuals.

METHODS

Pain sensitivity responses were measured between three study populations categorised according to BMI: normal range (18.50 - 24.99 kg/m^2), overweight (25.00- 29.99 kg/m^2) and obese (≥30.00 kg/m^2)(WHO, 2000). The study was approved by the Research Ethics Committee at the Leeds Beckett University, UK.

Recruitment of participants

The sample size required for each group was calculated using data from a study that found a statistically significant mean difference in cold pressor pain threshold between two groups of pain free-healthy individuals to be 8 seconds (Tashani *et al.*, 2010). G-Power sample size calculation software calculated that 22 participants would be necessary if power (1-β) was 0.95 and α was 0.05, and the analysis of choice was one-way ANOVA. Participants were recruited according to BMI. It was possible that individuals categorised according to BMI were not assigned a similar group as their total body fat so it was decided to recruit 25 participants in each BMI group (25 normal range, 25 overweight and 25 obese) to ensure at least 22 participants in total fat groups and also to account for withdrawals.

Participants were recruited by distributing leaflets advertising the experiment throughout universities in the West Yorkshire region. Interested volunteers received a participant information pack and were contacted again at least 48 hours later. At this point, volunteers still expressing an interest in taking part in the study provided an estimate of their weight and height so BMI could be estimated and used to screen participants into one of three blocks; normal range BMI, overweight and obese. Volunteers were refused entry to the study if the BMI allocation block was full and thanked for their time. If the BMI allocation block had space then volunteers were invited to attend our laboratory on two separate occasions. The participant information explained the nature of the

study but did not communicate our hypothesis or provide any background information related to pain sensitivity and body fat. In addition, participants were not told which BMI group they were allocated to until the end of the experiment. Hence, participants were naive to the effect of fatness on thermal and mechanical sensory testing. The principal investigator was partially blind to group allocation as they measured height and weight but did not calculate BMI group until the end of the experiment after pain sensitivity testing had taken place. Furthermore, the appearance of the participant is likely to have compromised full blinding.

Procedure

The principal investigator (RA, female, Libyan, proficient in English) managed procedures and acquired all measurements during both study visits. No other investigators were present during the study visits.

Visit One – Enrolment and Body Fat Measurements

During the first visit volunteers were briefed about the experiment and screened for eligibility and were given a self-screening questionnaire which contain questions about their health and requested not to participate if they were pregnant, have a chronic pain (e.g. diabetes or high blood pressure) or an existing condition that may affect their sensation or are taking any medication. While subclinical neuropathy was not screened or tested directly the experimental procedures included testing warm and cold sensation which guards against including participants with this condition in the final analysis.

Eligible volunteers were formally invited to take part in the study and provided written consent. They were informed that they could withdraw from the study at any time and without reason. Height and weight were measured. BMI was calculated and cross-checked with the estimated BMI calculated during the initial contact at the end of the experiment. There were no instances of a mismatch between estimated and true BMI categories. Measurements of waist circumference (5 cm above the navel) and hip circumference (at the widest part of the hips) were taken and waist-to-hip ratio (WHR) calculated (Douketis *et al.*, 2005). Skinfold thickness was measured at the bicep, triceps, subscapular and suprailiac to estimate total body fat according to a method described by (Durnin & Womersley, 1974).

Visit Two – Pain Sensitivity Measurements

The second visit took place two to four working days after visit one. Sensory detection and pain measurements were taken in the following sequence; contact thermal stimuli, 15 minute rest, blunt pressure stimuli, 15 minute rest, and cold-pressor pain (Figure 1). During testing participants were instructed to focus on a white board and to concentrate on sensations that they were experiencing from the test stimulus. Instructions were read aloud from a script prior to each test.
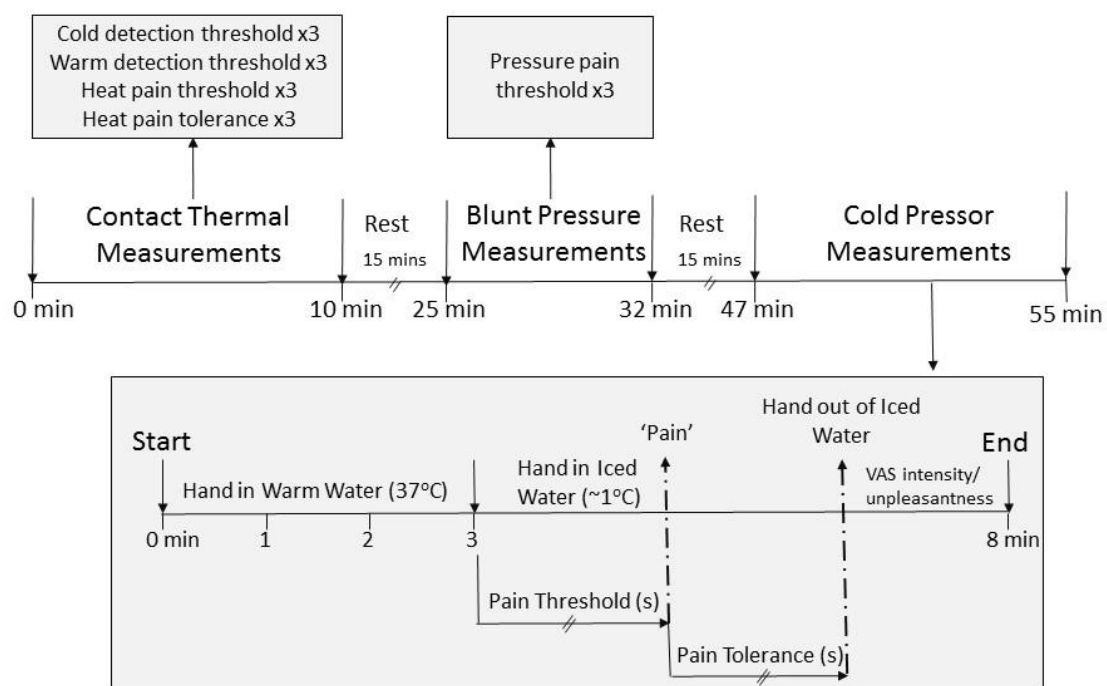
Figure 1

Figure 1. A- Measuring responses to thermal stimulation using a Thermal Sensory analyser. B- Timescale of the measurements for cold pressor pain responses.

Contact thermal stimuli

Sensory detection and pain thresholds to cold and heat stimuli were measured using a TSA-II Neuro Sensory Analyzer with a 30 x 30 mm thermode probe applied to the skin (Medoc, Israel). Measurement sites were skin over the thenar eminence followed by skin at the suprailiac above the crest of the ilium. These sites were chosen to compare the effect of thin (thenar eminence) and thick subcutaneous fat sites (Price *et al.*, 2013). The suprailiac was chosen because it is a lateral region of the abdomen. There is a greater distribution of hair in medial region of the abdomen of men and

hair may increase thermal resistance between the contact thermal stimulus and the skin (Setty, 1967).

The delivery of stimuli was controlled using a laptop computer and the order of measurements followed a standard protocol; cold detection threshold, warm detection threshold, heat pain threshold, and heat pain tolerance (Rolke *et al.*, 2006). Each outcome was measured three times and the mean calculated before moving on to the next outcome. The method of descending limits was used for cold stimuli and the method of ascending limits used for heat stimuli with baseline temperature set at 32°C and the rate of temperature change was 1°C/sec (Liem *et al.*, 2005). Participants pressed a hand-held button to stop delivery of the stimulus and signify detection of the sensation under investigation. If the button was not pressed stimuli ceased at predefined limits (0 or 50.5°C). Cold detection threshold was taken as the point at which the participant experienced "… the slightest change of temperature to cold"; warm detection threshold was taken as the point at which the participant experienced "…the slightest change of temperature to warm"; heat pain threshold was taken as the point at which the participant experienced "…the first painful sensation…. [When the stimuli] will change in quality from cold to, for example, ´aching´, ´stinging´, or ´burning´"; and heat pain tolerance was taken as the point at which the participant experienced "… burning painful sensation…. [When the stimuli] will change in quality from ´hot painful sensation´ to, for example, ´burning´ or ´stinging hot´".

Blunt pressure stimuli

Blunt pressure pain threshold (PPT) was measured using a hand held Algometer with a 1 cm diameter circular probe (range = 0-2000 kPa, Somedic, Sweden) applied on the skin over the first dorsal interosseous muscle of the non-dominant hand. The participant was seated with their hand supported by the hand of the investigator which was resting on a side table. The probe of the Algometer was placed over the skin of the first dorsal interosseous muscle and pressure exerted until the participant said "….´Now´, as soon as the pressure starts to be painful". The rate of force applied was held constant at a rate of 10 kPa/s and monitored using the in-device force application rate monitor. Three measurements were taken and the mean calculated (Chesterton *et al.*, 2007).

Cold pressor stimuli

Participants immersed their non-dominant hand in a warm water bath at 37°C for 3 minutes to standardise skin temperature. Then they immersed their hand in a bucket containing a slurry of ice-

water and identified pain threshold as the point at which they experienced "…. the first sensation of pain in the hand or fingers " by saying the word 'Pain' out loud (von Baeyer *et al.*, 2005; Tashani *et al.*, 2010). After this the hand remained immersed until the participant "…. [could] no longer tolerate the pain in your hand". Then the hand was withdrawn from the ice-water slurry and the time to pain tolerance calculated from the time of pain threshold to the time of hand withdrawal. Investigators asked participants to take their hand out of the ice-water slurry three minutes after pain threshold. Then participants completed two 100 mm visual analogue scales (VAS) to measure pain intensity immediately before removing the hand from the slurry of iced water ('How painful was the stimulus just before withdrawing your hand from the iced water?'' 0 mm = 'no pain, 100 mm = 'worst possible pain imaginable') and pain unpleasantness immediately before removing the hand from the slurry of iced water (''How unpleasant was the stimulus just before withdrawing your hand from the iced water?'' 0 mm = 'not unpleasant at all' and 100 mm = most unpleasant that I could imagine).

Data Analysis

Descriptive data were expressed as mean and standard deviation where appropriate. Normal distribution was tested using the Kolmogorov–Smirnov test. If data was normally distributed an unpaired t-test was used to compare two groups and a one-way ANOVA to compare more than two groups with Tukey's test used as a post-hoc test for multiple comparisons. If a non-normal distribution was found data was log transformed and tested again for normality. If normality was not obtained after log transformation the data was tested using a Median test which is a non-parametric statistics used to examine if the data of two groups or more have the same median.

In addition, responses to thermal stimulation were analysed using a repeated measure ANOVA (RM ANOVA) to analyse within-subject variables across sites (2 levels: thenar eminence, waist) and between-subjects variables group (3 levels: normal range, overweight, obese) and sex (2 levels: men, women). In the Multivariate test the Pillai's Trace was reported and to determine within-subjects effects sphericity was assumed in all tests. A sequence of linear regression analysis using a Forward approach was applied. Equations were calculated by regressing dependent variables (i.e. measurements from contact thermal, blunt pressure, and cold pressor stimuli) with independent variables (i.e. site, sex, BMI, waist-hip ratio) using the Forward Analysis function in SPSS. In this function, SPSS will only produce an output for independent variables that are significant predictors of a dependent variable with a positive β indicating that an increased predictor value leads to an increase in the value of the dependent variable. In addition, *t* indicate how significantly an independent variable predicts the dependent variable. R^2 indicates the proportion of variance in the

dependent factor that was explained by the independent variable, with F and its p value indicating the significance level of the linear model at $p<0.05$.

Body fat percentage was not incorporated into the independent factors list because of its high co-linearity with BMI in this data set. Statistical analysis was performed using SPSS version 21 (IBM).

RESULTS

Characteristics of the sample population

Seventy five participants were recruited but one participant did not return for their second study visit within the time period allowed for the study to remain open. Thus, 74 participants completed all procedures and their data was used in subsequent analyses (25 normal range, 24 overweight and 25 obese, 37 females). One-way ANOVA found significant differences across the groups for age (F (2, 73) 5.4, p=0.007; weight (F (2, 73) 67.20, p<0.001; BMI (F (2, 73) 133.6, p<0.001; percentage body fat (F (2, 73) 18.04, p<0.001; and WHR (F (2, 73) 9.63, p=0.017, Table 1). There were no significant differences in height between groups. Post-hoc tests found that the age of the obese group (36.30±7.5 years) was higher than the normal range (28.30±9.3 years, p=0.005), but there were no statistically significant differences in age between normal range or obese groups and the overweight group (32.7±9.1 years, p>0.05). Post-hoc tests found that weight was significantly higher for the obese group (96.9±14.60 kg) compared with the normal range (61.3 ±7.6 kg, p<0.001) and overweight groups (77.0±8.4 kg, p<0.001). Post-hoc tests found higher percentage body fat in the obese group (33.4±7.30%) compared with the normal range group (21.0±7.40%, p<0.001). The obese group had higher values for waist-hip ratio (0.85±0.1) than the normal range group (0.8±0.1, p<0.001) and overweight groups (0.8±0.1, p=0.032).

Unpaired t-tests on the whole sample (n=74) found no differences between men and women in age, height, or women and men in normal range, overweight or obese groups (Table 1). Women had significantly higher percentage body fat in the normal range group (women=26.0±6.3%, men=15.5+3.8%, p<0.001), overweight group (women=32.8±2.9%, men=22.9+6.8%, p<0.001) and obese group (women=39.3±2.7%, men=28.04±5.8%, p<0.001). Women had higher WHR in the overweight group (women=0.81±0.08, men=0.87±0.04, p=0.02) but not in the normal range or obese groups.

Table 1
Mean ± standard deviation of characteristics of participants according to BMI group (n=74). All data were normally distributed. #One-way ANOVA with Tukey's test. *statistically significant at p<0.05

Characteristic	Normal range BMI (n=25)	Overweight BMI (n=24)	Obese BMI (n=25)	F value	p value#
Age (years)	28.3±9.30	32.7±9.10	36.3±7.50	5.4	0.007*
Weight (kg)	61.3±7.60	77.0±8.40	96.9±14.60	67.1	0.000*
Height (cm)	166.4±10.75	166.5±10.60	169.4±11.30	0.619	0.542
BMI (kg/m^2)	22.1±2.04	26.87±1.30	34.4±3.90	133.6	0.000*
Percentage body fat	21.0±7.40	27.9±7.20	33.4±7.30	18.0	0.000*
Waist-to-Hip Ratio	0.8±0.1	0.8±0.1	0.85±0.1	4.29	0.017*

Contact thermal measurements

Repeated measure ANOVA

Repeated measure ANOVA on cold detection threshold found a significant main effect for site ($F_{(1, 68)}$=8.3, p=0.005) with cold detection threshold higher at suprailiac than thenar eminence (mean$\pm$SD difference=0.64$\pm$1.9°C). There were no significant interactions between site x sex ($F_{(1, 68)}$=1.26, p=0.266) or between site x group ($F_{(2, 68)}$=2.95, p=0.059) or between site x sex x group ($F_{(2, 68)}$=0.131, p=0.878). For warm detection threshold there was a significant main effect for site ($F_{(1, 68)}$=38.69, p=0.001) with warm detection threshold higher at suprailiac than thenar eminence (mean$\pm$SD difference=1.5$\pm$2.5°C). There were significant interactions between site x sex ($F_{(1, 68)}$=7.282, p=0.009) with men having a lower warm detection threshold at the suprailiac (mean$\pm$SD difference=1.068$\pm$0.49 °C). There were no significant interactions between site x group ($F_{(1, 68)}$=1.07, p=0.35) or site x sex x group ($F_{(2, 68)}$=2.64, p=0.079). For heat pain threshold there was a significant main effect for site ($F_{(2, 68)}$=4.87, p=0.031), with heat pain threshold higher at the thenar eminence than the suprailiac (mean$\pm$SD difference=0.89$\pm$3.6 °C). There were no significant interactions between site x sex and site x sex x group. For heat pain tolerance there were no significant main effects for site or any interactions between site, sex and group.

Table 2
Mean ± standard deviation contact thermal, blunt pressure and cold pressor stimuli according to BMI group (n=74). ✖ Not normally distributed. Median test was applied. ✓ Normally distributed. *statistically significant at p<0.05. ᵃDifference between obese and overweight groups were significant (p=0.009); ᵇDifference between overweight and normal weight groups were significant (p=0.017).

Dependent Variable	Normal range BMI (n=25)	Overweight BMI (n=24)	Obese BMI (n=25)	Normality	p value#
Contact Thermal Stimuli - Thenar Eminence					
• Cold detection threshold (˚C)	30.19±1.16	29.52±2.5ᵃ	30.7±0.73ᵃ	✖	0.023*
• Warm detection threshold (˚C)	33.45±0.71ᵇ	34.16±1.17ᵇ	33.85±1.2	✖	0.035*
• Heat pain threshold (˚C)	42.75±3.5	43.88±3.2	42.29±3.4	✓	0.257
• Heat pain tolerance (˚C)	48.23±2.1	48.71±2.40	48.33±2.61	✖	0.587
Contact Thermal Stimuli - Suprailiac					
• Cold detection threshold (˚C)	29.69±1.2	29.47±2.44	29.38±1.70	✖	0.246
• Warm detection threshold (˚C)	34.72±1.13	35.34±2.44	35.7±2.5	✖	0.961
• Heat pain threshold (˚C)	41.39±3.066	43.46±3.97	41.38±3.07	✓	0.050*
• Heat pain tolerance (˚C)	47.35±1.6	48.7±8.042	46.71±1.77	✖	0.097
Blunt Pressure Stimuli - Thenar Eminence					
• Pain threshold (kPa)	1154.70±847.18	1285.14±998.89	620.72±423.81	✖	0.005*
Cold Pressor Stimuli - Hand					
• Pain threshold (s)	17.64±15.90	12.40±12.92	12.72±14.66	✖	0.209
• Pain tolerance (s)	43.47±37.90	33.65±24.90	35.02±38.17	✖	0.368
• Pain Intensity (VAS, 100mm)	66.56±15.16	62.70±14.75	68.32±16.11	✓	0.431
• Pain unpleasantness rating (VAS, 100mm)	57.56±23.56	62.166±17.50	65.96±24.57	✓	0.411

Blunt pressure pain

A Median test found significant differences across the groups for pressure pain threshold (p=0.005) and post-hoc tests found that there pressure pain threshold was lower for the obese group compared with both the overweight group (p=0.005) and with the normal range group (p=0.001, Table 2). There were no significant differences between the overweight and normal groups (P>0.05). Data for females and males was normally distributed and analysed separately using one-way ANOVA with Tukey's post-hoc test. Pressure pain threshold was lower in obese females (626.4±415.2 kPa) and normal BMI females(911.03±479.2 kPa) compared with the overweight females (1440.17±645.5 kPa, p=0.002). There were no differences in pressure pain threshold between the male groups.

Cold pressor pain

One-way ANOVAs or non-parametric equivalents found no significant differences across the groups for cold pressor pain threshold, tolerance, intensity or unpleasantness (Table 2).

Regression analysis

Higher BMI predicted lower pressure pain threshold, (β=-0.272, t=-0.240, R^2=0.074, F=5.763, p=0.019)
(Figure 2). In addition to the regression analysis, a boxplot graph (Figure 3) showed that males have lower heat pain threshold than females.
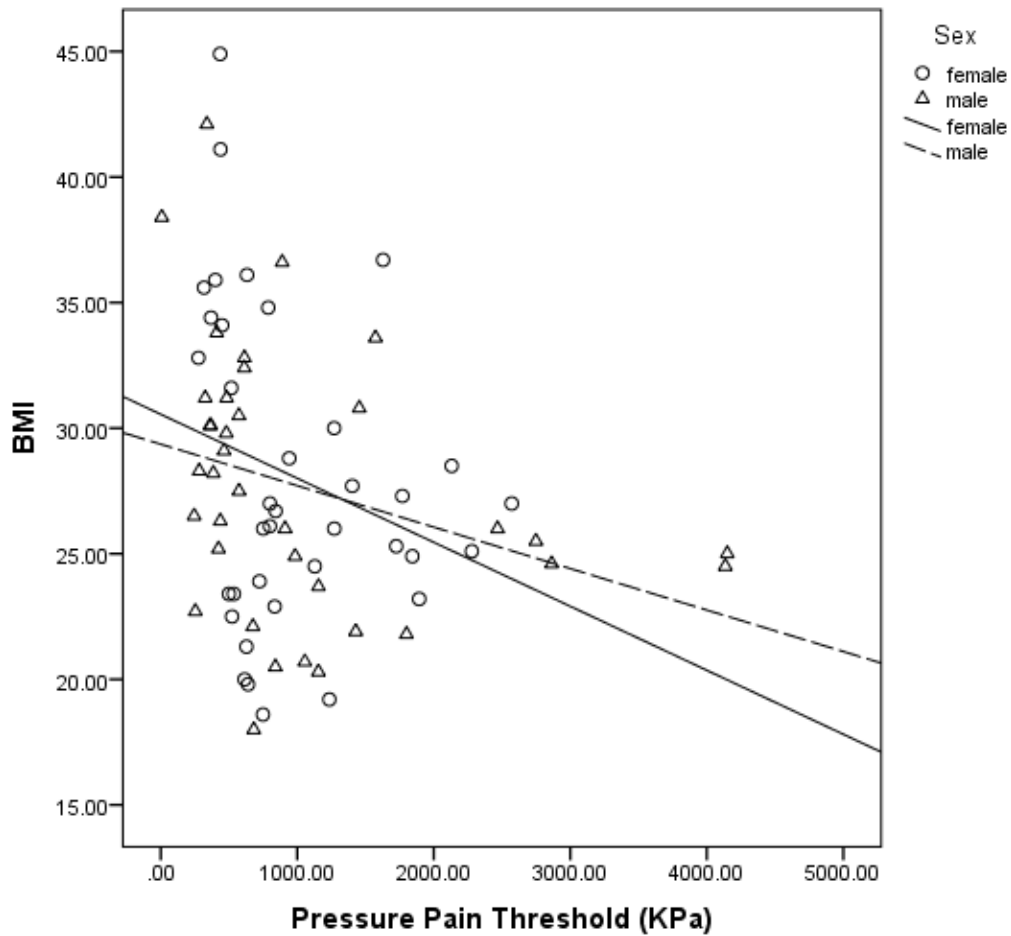
Figure 2. Scatter graph of the correlation between BMI (as the independent variable) and pressure pain threshold (as the dependent variable) of both males and females

Figure 1. A- Measuring responses to thermal stimulation using a Thermal Sensory analyser. B- Timescale of the measurements for cold pressor pain responses.

Figure 2. Scatter graph of the correlation between BMI (as the independent variable) and pressure pain threshold (as the dependent variable) of both males and females

Figure 3. Box and whisker plot, showing the 25th, 50th and 75th percentile and upper and lower values of the heat pain threshold of both males and females. No outliers were found.
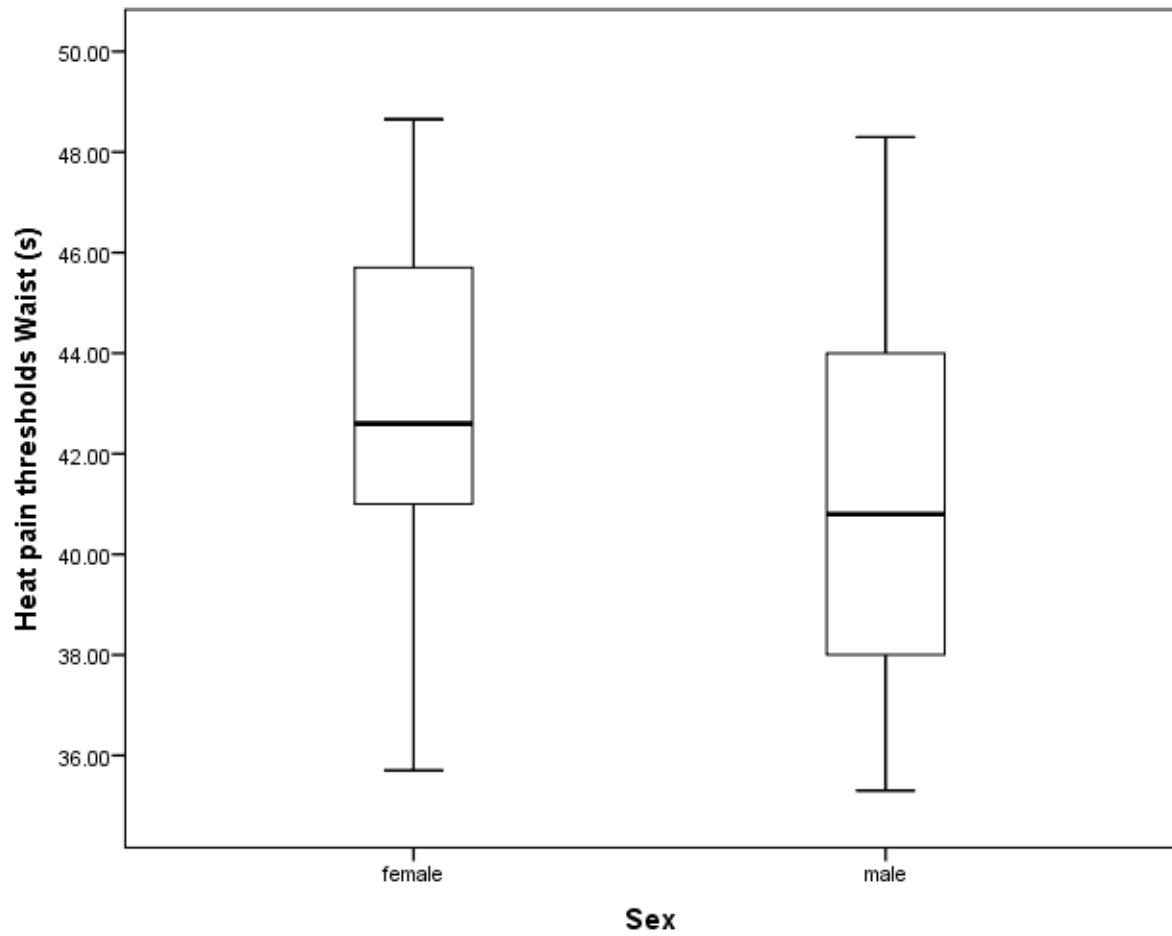
Figure 3. Box and whisker plot, showing the 25th, 50th and 75th percentile and upper and lower values of the heat pain threshold of both males and females. No outliers were found.

DISCUSSION

Blunt pressure pain

This study found that pressure pain threshold measured at a site with small accumulations of subcutaneous fat (thenar eminence) was lower for the obese group compared with overweight and normal range. In addition, higher BMI predicted lower pressure pain threshold. These findings suggest that obesity increases sensitivity to noxious pressure stimuli. To date, there have been very few studies investigating pressure pain sensitivity response and body fat. In 1982 (McKendall & Haier, 1983) conducted a study compared pressure pain threshold and tolerance at the index finger of 26 participants whose weight was >130% of their ideal body weight (i.e. obese) with 34 participants whose weight was less <130% Ideal Body Weight (i.e. non-obese). They found that obese participants were significantly more sensitive to the noxious pressure stimuli and hypothesised that weight differences between participants may be related to differences in ingestive behaviours controlled by endogenous opioids. In contrast, other studies have found that sensitivity to pressure pain threshold increases with increasing body fat. (Raymond et al., 1995) found no significant differences in blunt pressure pain threshold or pain tolerance at the finger between 104 individuals categorised according to BMI as obese without binge eating disorder, obese with a binge eating disorder and non-obese. (Khimich, 1997) measured pressure pain threshold by applying a needle to the skin of the forearm in 206 individuals and found higher sharp pressure pain thresholds in participants with higher body weight and greater fatness. More recently, (Price et al., 2013) found no significant differences in blunt pressure pain threshold measured at the thenar eminence or thumbnail between 20 participants categorised as obese on BMI and 20 age- and gender-matched non-obese controls. Likewise, (Icagasioglu et al., 2015) measured pressure pain threshold in the deltoid, tibialis anterior, and first interosseus dorsalis muscle of the hand and found no difference between 80 adult obese and non obese people admitted to an obesity and metabolic syndrome outpatient clinic. They concluded that there was no significant correlation between obesity and pain threshold.

We found that sex differences were more evident between groups with females being more sensitive than males to pressure pain threshold. This is consistent with research on sex and gender and pain where females have lower thresholds to experimentally induced pain (Fillingim et al., 2009), although some authors dispute the magnitude of these differences in experimental pain (Racine et al., 2012a; b). Sex and gender differences in pain sensitivity result from a mixture of biological (e.g. hormones) and psycho-social (gender role expectation and anxiety toward pain)

(Greenspan *et al.*, 2007; Alabas *et al.*, 2012; Alabas *et al.*, 2013). Interestingly, however, males had lower warm detection thresholds at the suprailiac than females. This may be related to suprailliac thickness which was greater in females (22.01±8mm) compared with males (18.7±11mm, p=0.047).

Differences in study methodologies may account for some of the inconsistencies in the findings for blunt pressure pain, although in general study methodologies are similar. All studies measured pressure pain threshold at sites with small accumulations of subcutaneous fat (e.g. finger, thenar eminence, forehead) and none, including ours compared with measurements from a site with larger accumulations of subcutaneous fat (e.g. abdomen). This between site comparisons should be included in the design of follow-up studies. The highest quality study to date is by (Price *et al.*, 2013). They delivered pressure stimuli to the skin over the thenar eminence but unlike ourselves found no significant differences in blunt pressure pain threshold between obese and non-obese groups. Our findings are strengthened by our regression model analysis that found that a decrease in pressure pain threshold was predicted by increasing BMI and increasing percentage body fat, which is consistent with the direction of change of our between group analysis. Furthermore, we used a slightly larger sample size (≥24 participants/group vs. 20/group), and a pressure algometer manufactured by a different company. Nevertheless, it is important to resolve the discrepancy in findings in previous studies of similar design by conducting a future study with a much larger sample size.

In our study we found evidence of a linear correlation between PPT and BMI. However, when mean PPT values were calculated for each group we found that the mean PPT of the overweight group was higher than that of the normal weight and obese groups suggesting the relationship between PPT and BMI was not linear. There may be two reasons for this anomaly in the data:

1. Data were not normally distributed and mean and SD values, presented because of convention, were not the best way to represent the data. The median data of normal and overweight groups were similar to each other (839KPa and 875KPa respectively) and significantly higher than that of the obese group (610KPa). Thus, median PPT followed a linear relationship which diminishes when BMI increased above the overweight cut point.

2. The ethnocultural composition of groups was not balanced with more non-white British participants in the overweight group, than the normal BMI group. There is strong evidence that ethno-cultural background affects pain sensitivity response (Rahim-Williams *et al.*, 2012). In the male group the linear relationship of PPT with BMI was clear (mean PPT=1418.8KPa for normal BMI, 1130 KPa for overweight and 615.4 kPa for obese).

Thermal Pain

We found significant effects for BMI for innocuous thermal sensations with obese participants having higher cold detection thresholds than overweight and overweight participants having higher warm detection thresholds than normal range on the thenar eminence. (Price *et al.*, 2013) found no differences in cold and warm detection threshold on areas of skin likely to have less subcutaneous fat (i.e. forehead and hand). However, (Price *et al.*, 2013) found that obese participants had significantly higher cold and warm detection thresholds than normal range participants on the abdomen whereas we did not find any differences between obese and other groups for cold and warm detection thresholds at the suprailliac. We also found that the suprailiac (likely to have thick subcutaneous fat) had higher thermal detection thresholds than the thenar eminence (likely to have less subcutaneous fat). Our ANOVA found significant main effects across groups for heat pain threshold but pairwise comparisons did not identify any significant between group differences. There were no main effects across groups for any other painful thermal stimuli (i.e. contact heat pain tolerance, and cold pressor pain threshold, tolerance and intensity). (Price *et al.*, 2013) found that obese participants had higher heat pain threshold and heat pain tolerance at the abdomen but not at the forehead or hand. Our ANOVA found a significant main effect for site with heat pain threshold higher at the thenar eminence than the suprailiac. However, the magnitude of the mean difference was very small (0.89°C) and the standard deviation nearly 4 times as large (+3.6°C). There were no other within or between group differences for thermal pain outcomes. It is tempting to speculate that increased sensitivity at the suprailiac, but not at the thenar eminence may be due to increased levels of pro-inflammatory cyctokines in the local tissue environment resulting in localised peripheral sensitisation of nociceptors. This may also explain why we did not observe any changes in pain sensitivity in the hand resulting from cold pressor stimuli. However, the finding that there were lower blunt pressure pain thresholds at the thenar eminence compared with the suprailiac does not appear to be consistent. Moreover, if there was only an accumulation of pro-inflammatory mediates in local tissue that only affected heat sensitive receptors we might have expected to observe a reduction in heat detection threshold at the suprailiac, which we did not.

Limitations

One limitation of our study was that we did not screen for signs of subclinical neuropathy due to an impaired glucose tolerance, as might be suspected in obese individuals. Furthermore, psychophysical measurement of pain processing is dependent on an individual's ability to make a decision about their pain experience. Sensory decision making associated with techniques used to measure pain

threshold in our study have been shown to be reliable but are still prone to procedural errors. One problem with the methods of limits is that measurement errors can be introduced based on reaction time and that reaction times may differ between test sites. However, it is the method of limits is often used to compare thresholds to sensory stimuli at different body sites. Our findings are consistent with previous studies that have found differences in somatosensory thresholds at different body sites. For example, an investigation of 36 participants, divided in two groups (low and high body fat content), tested vibratory threshold at 24 body sites and found that this threshold depends significantly on the sites stimulated (p = 0.001) (Bikah *et al.*, 2008). They concluded that body fat significantly affected ability to perceive vibratory stimuli (p =0.048) with the high body fat group exhibiting higher vibratory threshold. Nevertheless, variations in operational procedures used whilst executing studies are likely to have introduced measurement errors in studies in the field and this may explain the inconsistency in the findings between investigators investigating the influence of obesity on pain sensitivity responses to experimentally induced noxious stimuli.

Sensory perception is also influenced by physiological (e.g. thermosensory pathways), psychological (e.g. attention) and social (e.g. context of experiment). There is a tendency in psychophysiological studies to focus on physiological explanations for observations although psychological and social factors are likely to have had a greater influence on measurements, and the introduction of measurement error, between studies. Recently for example, (Kucyi *et al.*, 2015) using similar psychophysical techniques to ourselves demonstrated that feigned pain reports have higher variability and inferior repeatability than sincere reports. Physiological factors that influence the perception of temperature change include the depth, density and sensitivity of cold and warm receptors in the skin and the sensitivity of central nervous system transmission and modulation pathways and cerebral processing structures (Burke & Mekjavic, 1991). Studies generating magnitude estimation maps of thermosensation suggest that cold sensation is greatest at the head then the torso and decline towards the extremities, with females manifesting greater regional differences to cold stimulation across the body than men (Gerrett *et al.*, 2014; Gerrett *et al.*, 2015). Regional variations to hot stimulation across the body were less apparent than for cold and females reported greater magnitude sensations than males at all locations. Furthermore, there are variations within body segments. (Ouzzahra *et al.*, 2012) found that lateral regions of the abdomen and mid-back were more sensitive than the medial areas and suggested that variations correspond to more hair in medial regions increasing thermal resistance between the contact thermal stimulus and the skin thus reducing warm sensitivity (Setty, 1967). Clearly, thermo-physiological modelling of regions of the body is far from complete and the numerous factors that may influence sensory report means

that it is not possible from our study to attribute differences in thresholds to innocuous temperature changes to the amount of subcutaneous fat at respective sites.

The categorization of obesity in this study was based on BMI values references adopted by the WHO. While this is a widely accepted method it is not very accurate as some individuals with a greater muscle mass could fall into overweight groups. However, recruitment in our study was from the general population and not from athletic groups and BMI in the general population is correlated with total body fat content, although older individuals tend to have more percentage body fat than younger individuals and this is why the maximum age in our study was 45 years. Fat body percentage was calculated using an equation that combined 4 sites measurements. While this gives an indication of a body fat percentage it is not a very accurate method. Therefore, we recommend that future studies should measure body fat content and distribution using body composition scanners such as dual-energy X-ray absorptiometry.

Conclusion

In conclusion, our study provided tentative evidence that obese individuals were more sensitive than non-obese individuals to pressure pain but less sensitive to thermal stimuli, and that body sites may vary in their response to different types and intensities of stimuli according to underlying levels of subcutaneous fat. However, the inconsistency of findings within and between existing research studies should catalyse further research in this field.

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