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Weighing the stigma of weight: An fMRI study of neural reactivity to the pain of obese individuals

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ABSTRACT

Explicit negative attitudes and blameful beliefs (e.g. poor diet, laziness) towards obese individuals are well documented and are pervasive even among health professionals. Here we sought to determine whether obesity stigma is reflected in a fundamental feature of intersubjectivity namely the automatic neural resonance with others' affective experiences. During fMRI, normal-weight female participants observed short clips depicting normal-weight (NW) and obese (Ob) models experiencing pain. Importantly, participants believed that half of the Ob were overweight due to a hormonal disorder (HormOb) and ignored the cause of obesity of the remaining models (Unknown obese models; UnkOb). Analyses of hemodynamic responses showed reduced activity to the pain of Ob compared to that of NW in areas associated with pain processing and early visual processing. The comparison between the two Ob conditions revealed a further decrease of activity to HormOb's pain compared to UnkOb's (and NW) pain in the right inferior frontal gyrus, an area associated with emotional resonance. Our study demonstrates that stigma for obese individuals can be observed at implicit levels, and that it is modulated by knowledge concerning the etiology of obesity, with the seemingly surprising result that obesity due to disease may result in greater stigmatization. Moreover, the perceived similarity with the models and the ambivalent emotion of pity may index biased brain responses to obese individuals' pain. The study highlights a possibly important neural link between resonance with the pain of others and obesity stigma.

Introduction

Obese individuals are highly stigmatized in contemporary western cultures. Negative attitudes and discriminatory behaviors are well documented and result in unfair and harmful treatments in key domains of life (Puhl and Heuer, 2009). Prevailing stereotypes include the perception of obese individuals as unattractive, lazy, unmotivated and sloppy. Such beliefs are so strong and prevail even among health-care providers, including physicians, dieticians and mental health-professionals (Foster et al., 2003; Puhl and Heuer, 2009). These stigmatizing attitudes among health-care providers should not be neglected as they may compromise the delivery of appropriate clinical treatment (Stone and Werner, 2012). Likewise, the perception by obese patients of such inadequate attitudes can promote poor treatment compliance, avoidance behaviors or pose considerable psychological threats (Dovidio and Fiske, 2012; Puhl and Heuer, 2010).

However, little is known about the nature of negative attitudes towards overweight individuals. One important line of research aims at assessing the role of causal attributions and perception of controllability or uncontrollability of obesity. Typically in these studies the beliefs about the causes of obesity are manipulated, e.g. by providing biological explanations, and subsequently blameful beliefs and negative affects towards obese individuals are measured. As expected, acknowledging uncontrollable causes for obesity successfully diminished reports of blameful attributions (e.g., Anesbury and Tiggemann, 2000; Crandall, 1994; DeJong, 1980). However, mixed results were found regarding the influence of such beliefs on affects, with most studies suggesting, counterintuitively, no reduction in negative affects towards obese individuals (Anesbury and Tiggemann, 2000; Crandall, 1994; Lippa and Sanderson, 2012; O'Brien et al., 2010; Teachman et al., 2003; see Daníelsdóttir et al., 2010 for a review).

One problem of the existing research relates to the frequent use of self-report measures that are extremely vulnerable to self and social desirability concerns (Daníelsdóttir et al., 2010). Also, people may not even be aware of holding negative affects, or their true extent, towards obese individuals. In contrast, implicit measures bypass desirability issues and reflect automatic, or unconscious, attitudes towards specific groups (Bessenoff and Sherman, 2000; Blair, 2002; Greenwald and Banaji, 1995). Implicit measures, such as the Implicit Association Test (IAT; Greenwald et al., 2003), have proven to be useful in the study of

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prejudice towards several social groups (Nosek et al., 2011), including obese individuals (Bessenoff and Sherman, 2000; Gapinski et al., 2006; O'Brien et al., 2010; Schwartz et al., 2003; Teachman et al., 2003).

Another way to study implicit attitudes concerns the use of neuroimaging techniques (Kubota et al., 2012). This line of research emerged with the finding of different patterns of brain activity in response to the mere perception of own-race and other-race faces. In specific, other-race faces elicited increased activity in the amygdala (Phelps et al., 2000), an area related with detection of emotional relevance, and decreased activity in high-order face-related visual areas (e.g. fusiform gyrus), likely due to diminished motivation to process other-race faces (Golby et al., 2001). Thus far the only two studies using neuroimaging to investigate the implicit nature of obesity bias found similar patterns of activity. In these studies, the perception of overweight faces or bodies was associated with activity in brain areas related with affective evaluation of the stimuli, like for example, the amygdala (Krendl et al., 2006) and fronto-central and occipito-temporal regions (Schupp and Renner, 2011). These studies were carefully designed to measure implicit responses and demonstrated that automatic neural markers of biased processing of obese bodies can be observed in the absence of explicit evaluation.

Here we used a more comprehensive approach to study the bias towards obese individuals and explore the underlying psychological mechanisms and neural substrates. According to current neuroscientific models, the mere perception of someone else's emotional state automatically triggers neural and physiological reactions similar to those involved in the first-person experience of similar emotion (Decety, 2011). This mechanism of "neural resonance" allows rapid and automatic state-matching with others' emotional and sensory experiences (de Waal, 2012; Decety, 2011). In the case of pain, shared neural representations include brain structures coding the sensory-somatic features, i.e., somatosensory cortices (Aziz-Zadeh et al., 2012; Betti et al., 2009; Bufalari et al., 2007; Lamm et al., 2010; Osborn and Derbyshire, 2010), and affective-motivational aspects of the painful experience, i.e. insular cortex, medial cingulate cortex, periaqueductal gray and thalamus (e.g., Jackson et al., 2005; Singer et al., 2004). While automatic resonance does not reflect the full complexity of the empathic experience, this mechanism may play a key role in experience sharing, providing the foundations for an empathic response to unfold (Avenanti et al., 2009; de Waal, 2012; Decety, 2011; Zaki and Ochsner, 2012).

Relevant to the present study, activity in pain-processing areas has been found to be reduced for the observation of pain of socially distant or disregarded individuals. For example, reduced sensorimotor resonance (Avenanti et al., 2010) and diminished activity in the left anterior insula (Azevedo et al., 2012) and anterior cingulate cortex (Mathur et al., 2010; Xu et al., 2009), two regions involved in the affective-motivational processing of pain, were found in response to other-race pain compared to that of own-race. Activity in these regions was found to be reduced also for the pain of perceived unfair (Singer et al., 2006), rival (Hein et al., 2010) and stigmatized (Decety et al., 2010) individuals, indicating people are less ready to share the experiences with scarcely significant or disregarded individuals.

The aim of the present study was to investigate if obesity stigma is reflected at such level of empathic resonance. Using fMRI combined with measurements of pupil dilation (an index of autonomic arousal) (Azevedo et al., 2012; Bradley et al., 2008), we compared autonomic and brain responses associated with the perception of obese and normal weight individuals experiencing pain. In line with previous literature, we expected decreased activity in response to the pain of obese individuals in brain regions responsible for the affective responses to pain (e.g. insula) as well as in those processing the sensorimotor (e.g. somatosensory cortices) components of pain. We also predicted decreased activity in face processing areas (e.g. fusiform gyrus, occipital gyrus and superior temporal sulcus) in response to the observation of pain inflicted to obese individuals. The face processing system is responsive both to low-level facial features (e.g. configuration) as well as to emotional and social cues (Haxby et al., 2000). Indeed these areas are modulated by facial expressions of pain (e.g. Simon et al., 2006) and are less responsive to other-race faces (Golby et al., 2001). It is thus important to understand if a bias in processing the facial pain of disregarded individuals is also observed at the face processing level. In order to have a precise estimation of the localization of these regions in our group of participants we used a functional localizer of face processing areas.

Interestingly, recent research demonstrated that neural resonance may be modulated by cognitive strategies (Sheng and Han, 2012) and perceptions of responsibility regarding the onset of the stigmatized condition (Decety et al., 2010; see also Krendl et al., 2012). Decety et al. (2010), for example, compared brain responses to the perception of pain of stigmatized people (AIDS patients) who were either responsible (infected as a result of intravenous drug use) or not responsible (infected during a blood transfusion) for their condition. The authors observed increased hemodynamic response in pain processing areas (i.e., insula, cingulate cortex, periaqueductal gray) in response to the pain of blood transfusion AIDS patients compared to that of drug use AIDS patients and healthy controls. These findings reveal the malleability of prejudice-related responses and provide the rational to investigate one important issue in obesity stigma, scilicet the role that perceived uncontrollability of obesity may have on stigma-related responses (Daníelsdóttir et al., 2010). To explore this issue, our participants were made to believe that half of the obese targets were obese due to a hormonal disorder and ignored the cause for obesity of the remaining targets. Different neural reactivity (e.g. insula, sensorimotor cortices) to the pain of the two groups of obese targets allowed us to test if acknowledging an external biological cause for obesity, i.e. hormonal disorder, can increase or decrease biased responses.

Finally, having explored the different patterns of brain responses to the emotional experiences of different social targets, we then attempted to identify the psychological processes associated with such bias. Correlations between behavioral measures and biased neural responses have proven to be a very useful tool in this regard. Implicit measures of bias (Avenanti et al., 2010; Azevedo et al., 2012), explicit empathy-related ratings (Cikara and Fiske, 2011; Hein et al., 2010; Singer et al., 2006), or reported willingness to help/harm targets (Cikara and Fiske, 2011; Hein et al., 2010) was found to predict biased neural responses towards the pain of disregarded individuals. Interestingly, a recent study having as reference the Stereotype Content Model (SCM; Fiske et al., 2002), a model that predicts that different social groups elicit different emotions (pity, disgust, envy, pride), found distinct patterns of neural activity in empathy-related regions (e.g. insula) for the misfortunes of members of different out-groups (Cikara and Fiske, 2011). This shows that bias in the degree of automatic resonance with others' experiences is not only dependent on in- and out-group categorization but it is also sensitive to the specific stereotypes and affects associated with the stigmatized target. Here, we collected several behavioral measures – implicit and explicit indices of bias, ratings of each emotion of the SCM and ratings of perceived similarity with the targets – in order to highlight the psychological substrates underlying biased neural responses.

Methods

Participants

The study involved twelve right-handed female healthy volunteers (mean age = 22.2; SD = 2.6) with body mass index (M = 20.68; SD = 1.78) within the normal range (18.5–25), free from any contradiction to fMRI, and no reported history of major psychiatric or medical disorders, including eating disorders and hormonal disorders. All volunteers gave written consent. The study was approved by the local ethics committee.

Visual stimuli

Stimuli consisted of video clips, with 2500 ms of duration, depicting the face of female actors being either penetrated by a syringe (pain conditions) or touched by a Q-tip (touch conditions). The models were two normal weight and four obese women. In keeping with previous studies (e.g. Sheng and Han, 2012; Xu et al., 2009), models displayed painful and neutral expressions in the pain and touch observation conditions respectively. Stimulation sites consisted of six different locations within the cheeks, three on each side, identical for pain and touch conditions and across models. A total of 6 different videos per condition were presented, i.e., 3 pain and 3 touch videos for each model.

Experimental manipulation

Our experimental manipulation consisted in the categorization of the six models into three weight-related categories: 2 normal-weight models (NW); 2 obese models with unknown cause (UnkOb); 2 obese models due to Cushing's Syndrome (HormOb).[1] To refer to obese models irrespective of the cause of obesity (i.e. UnkOb and HormOb) we use the term "Ob". Differentiation between pairs of Ob was achieved with the procedure described below. Participants were given brief descriptions of obesity and Cushing's Syndrome.[2] Subsequently, they carefully read the profiles of each model depicted in the stimuli. Profiles were allegedly assembled by patients of a clinic, and consisted in pseudo information about age, weight, and height, and a brief self-description including profession, hobby and weight reminder (e.g. UnkOb: "I have always been overweight but in the last years I gained extra weight"; HormOb: "unfortunately, I have Cushing's Syndrome which leads me to be overweight"; NW: "I have always had normal weight, never made any diet to keep my figure"). Crucially, obese models associated with HormOb or UnkOb were combined in pairs and counterbalanced between subjects. That is, half of the participants associated one pair of obese models with Cushing's Syndrome while the other half associated the other pair of obese models with Cushing's Syndrome. The causes for obesity in the UnkOb condition were deliberately not specified to provide a representation of obesity stigma close to what happens in daily life, when people typically do not have any information on why a specific person is obese. This approach allowed us to have a better estimation of the role that beliefs of uncontrollability (associated with hormonal disorder) may have in obesity stigma. However, our design does not allow us to explore the influence of beliefs of controllability/responsibility (e.g. poor diet) for obesity. Self-description fragments concerning profession and hobby were fully randomized across models, whereas those fragments regarding physical constitution were randomized within the three model groups (NW, UnkOb, HormOb). These randomizations enabled us to exclude any systematic association between models and profile information. To ensure that the association with Cushing's Syndrome effectively increases the perception of uncontrollability of obesity in these individuals, we administered, online, to a separate group of normal weight female participants ($n = 26$; mean age $= 27.2$, $SD = 3.7$; body mass index: $M = 20.9$; $SD = 1.8$) the online questionnaire Beliefs About Obese Persons (BAOP; Allison et al., 1991). This scale measures beliefs of controllability/uncontrollability of obesity, with higher scores reflecting greater beliefs of uncontrollability. Participants were shown the definitions of Obesity and Cushing's Syndrome and then asked to answer twice (counterbalanced order) to the questionnaire, once regarding obesity in general and another considering individuals who suffer from Cushing's Syndrome. Higher scores were observed for the Cushing's Syndrome version (UnkOb: $M = 4.4$, $SD = 5.5$; HormUb: $M = 18.1$, $SD = 7.7$; $t(25) = -7.72$; $p < 0.001$) confirming that obesity in these individuals is perceived as less controllable.

Behavioral measures

A list of all behavioral measures used can be found in Table 1. Before the fMRI testing, using a computerized visual analog scale (VAS) (min = 0; max = 10), participants were asked to rate each model according to the following dimensions: similarity, "How similar with you is she?"; attractiveness, "How attractive is she?"; dominance, "How dominant does she seem?"; weight, "How much does she weight?" (participants were instructed that mid-range points correspond to normal-weight). To ensure that participants knew which models suffered from Cushing's Syndrome, among the previously described ratings we included a yes/no question: "Does she suffer from Cushing's Syndrome?".

After the fMRI protocol, we confirmed that all participants still associated the right models with Cushing's Syndrome by repeating the physical ratings and Cushing Syndrome question procedure described previously. Participants were also asked to rate (using VAS) how much each model elicited the four prejudice-related emotions proposed by the Stereotype Content Model (Fiske et al., 2002): disgust, pity, envy and pride. In addition, they rated the intensity and unpleasantness of the stimulation depicted on each stimulus, again using a VAS scale (0–10). Then, we measured implicit bias against UnkOb and HormOb with different computerized versions of the IAT (Greenwald et al., 2003) pairing the categories: UnkOb vs NW (IAT-UnkOb); and HormOb vs NW (IAT-HormOb). Black and white drawings of silhouettes of normal-weight and obese persons were used as images to be associated

Table 1
Summary of behavior measures collected and contrasts of interest. § adapted from original. N/A — not applicable. + Comparisons that reached statistical significance.

		Measure (min–max)	Contrast NW > Ob	Contrast UnkOb > HormOb
IAT	Measures automatic (implicit) preferences for one social group over another.	Reaction times (ms)	+	+
IMS §	Measures internal motivation to respond without prejudice.	Likert (1–9)	N/A	
EMS §	Measures external motivation to respond without prejudice.	Likert (1–9)	N/A	+
F-Scale	Self-report measure of negative attitudes and stereotypes against obese.	Likert (1–5)		N/A
Emotion ratings				
Disgust		VAS (0–10)	+	
Pity		VAS (0–10)	+	+
Envy		VAS (0–10)		
Pride		VAS (0–10)		
Physical ratings				
Attractiveness		VAS (0–10)	+	
Similarity		VAS (0–10)	+	
Dominance		VAS (0–10)	+	
Weight		VAS (0–10)	+	
Stimulation ratings				
Intensity		VAS (0–10)		
Unpleasantness		VAS (0–10)		

[1] None of the participants was previously familiar with the Cushing's Syndrome or with cortisol-related disorders, and were convinced that such syndrome caused common obesity, i.e., ignored the fact that Cushing's Syndrome is mostly associated with weight gain in specific body areas. Thus, only in the methods section we refer to Cushing's Syndrome. Throughout the introduction, results and discussion sections we use the expression hormonal disorder to avoid confusion with the specificities of this syndrome.

[2] Obesity is a condition characterised by excessive body weight due to accumulation of adipose tissue, which has an adverse effect on health. Obesity is defined and evaluated in function of the deviation from the considered ideal weight established on the basis of factors such as age, gender and height. Cushing's Syndrome is a hormonal disorder caused by inappropriately high blood levels of the hormone cortisol. The most evident symptom is the excessive accumulation of adipose tissue that leads to obesity. This disorder is considerably rare affecting mostly women between 20 and 40 years of age.

with the target categories. Good (e.g. happiness, peace) and bad (e.g. horrible, evil) words were used as attributes. Positive D scores reflect implicit preference for NW relative to UnkOb and HormOb individuals. To assess explicit negative stereotyped perceptions about obese people we administered the Fat Phobia Scale — short version (F-Scale; Bacon et al., 2001).

Session two

The same participants were asked to return to the laboratory for a second session that took place four to five months after the fMRI session with the aim to collect additional behavioral measures that could help to identify the psychological correlates associated with our finding of larger bias towards HormOb compared to UnkOb. We were especially puzzled with the lack of differences between the two IAT versions collected in the first session (IAT-UnkOb vs IAT-HormOb). Our concern was that the IAT-HormOb could not accurately identify the bias towards this category (i.e. Cushing's Syndrome patients) due to the inappropriateness of stimuli (silhouettes of obese individuals) used to categorize obese with Cushing's Syndrome (see above). With such stimuli it is likely that immediate classification of the visual stimuli is done as obese and only subsequently translated into Cushing's Syndrome. Therefore, in session two we asked participants to carry out another version of the IAT (IAT-UnkOb/HormOb) comparing directly the two categories of Ob, this time using the pictures of the models depicted in the fMRI task as stimuli, and thus allowing stronger association with the syndrome and a more accurate comparison of implicit preferences between these two groups.[3] Positive D scores reflect implicit preference for UnkOb relative to HormOb, while negative D scores indicate the inverse preference. It is worth mentioning that upon arrival participants were again invited to read the definitions of Obesity and Cushing Syndrome and the profiles of the models depicted in the fMRI task. Once more, the ratings/question procedure was repeated to confirm that participants could identify correctly the models associated with the Cushing Syndrome.

Finally, adapted versions of the Internal (IMS) and External (EMS) Motivation to Respond Without Prejudice scales (Plant and Devine, 1998) were used to measure levels of internal and external motivation, respectively, to respond in an unprejudiced way to UnkOb and HormOb individuals. In one version the word “black” was replaced with the word “Obese” and with “Obese with Cushing syndrome” in the other. The order of the two versions (i.e, UnkOb and HormOb) was counterbalanced across the participants. As we were interested in differences between the groups of obese categories, final scores were computed as the difference between both versions, i.e. UnkOb–HormOb.

fMRI protocol

A Siemens Allegra (Siemens Medical Systems, Erlangen, Germany) operating at 3 T and equipped for echo-planar imaging (EPI) acquired functional magnetic resonance (MR) images. A quadrature volume head coil was used for radio frequency transmission and reception. Head movements were minimized by mild restraint and cushioning. Thirty-two slices of functional MR images were acquired using blood oxygenation level-dependent imaging (3.0 × 3.0 × 2.5 mm thick, 50% distance factor, TR = 2.08 s, TE = 30 ms), covering the entire cortex.

Participants were positioned in the scanner in a dimly lit environment. The visual stimuli were presented via a mirror mounted on the MRI headcoil (total display size 19.5° × 14.6° of visual angle). The stimuli were back-projected on a screen behind the magnet with 1024 × 768 resolution and 60 Hz refresh rate. Stimuli presentation was controlled with Cogent2000 (www.vislab.ucl.ac.uk/Cogent/). Six event types were organized in a 2 × 3 factorial design: Stimulation (Pain/Touch) × Model (NW/UnkOb/HormOb). Each subject completed 5 functional runs, each consisting in the fully randomized presentation of 72 stimuli (12 per condition) interleaved with a fixation cross (inter-stimulus interval) of jittered duration (2000–3000 ms) plus 18 nulls events (fixation instead of stimuli). Participants were only instructed to carefully pay attention to the stimuli, and no other instruction or task was provided. After the 5 experimental runs, a functional localizer of brain areas sensitive to face stimuli was carried out. This allowed us to functionally map brain areas that respond to models' faces, rather than processing other features of the visual stimuli, and thus test our hypothesis of decreased involvement of these areas in processing Ob's pain. This session consisted in the passive observation of 8 blocks of photos of static male and female faces and 8 blocks of photos of places. In each block 32 stimuli were presented for 300 ms, with an inter-stimulus interval (fixation cross) of 200 ms. Blocks were presented in a pseudo-randomized way, interleaved with fixation periods of 15 s on average. These stimuli were used in a previous study (Tosoni et al., 2008).

fMRI data analysis

We used the statistical parametric mapping package SPM8 (www.fil.ion.ucl.ac.uk) implemented in MATLAB (v 7.1, The MathWorks, Natick, MA) for data pre-processing and statistical analyses. For each participant a total of 1273 fMRI volumes were acquired, 204 for each of the 5 experimental functional runs, and 253 for the functional localizer run. The first four image volumes of each run were used for stabilizing longitudinal magnetization and were discarded from the analysis. Preprocessing included rigid-body transformation (realignment) and slice timing to correct for head movement and slice acquisition delay. Residual effects of head motion were corrected by including the six estimated motion parameters for each subject as regressors of no interest in the statistical multiple regression model. Slice-acquisition delays were corrected using the middle slice as a reference. All images were normalized to the standard SPM8 EPI template, resampled to 2 mm isotropic voxel size, and spatially smoothed using an isotropic Gaussian kernel of 8 mm FWHM.

Statistical inference was based on a random effects approach (Penny and Holmes, 2004). For each participant, the data was best-fitted at every voxel by convolving each of the 6 events (2 Stimulation × 3 Models) with the SMP8 hemodynamic response function. Hemodynamic analyses were time-locked to the onset of the stimuli (duration = 2500 ms). For each subject, contrast images were estimated according to our effects of interest. At group level, these contrasts were entered in a set of t-test whole-brain analyses. The effects of interest included: (1) brain activity associated with the observation of pain irrespective of model type, (all pain stimuli > all touch stimuli); (2) brain areas reflecting obesity stigma, [(pain > touch)NW > (pain > touch)Ob]; (3) brain activity reflecting the influence of information regarding the causes of obesity on stigma, [(pain > touch)UnkOb > (pain > touch) HormOb], and [(pain > touch)HormOb > (pain > touch)UnkOb]. Note that all analyses are based on the subtraction of touch responses from pain responses. Touch stimuli provide a baseline for each model by minimizing responses related to tactile sensation, action, movement, and responses that although associated with the models are not directly related with the processing of their pain (e.g., visual salience, affective responses to facial features). Hence, throughout the manuscript, when we report effects related to “pain” we are referring to the differential activation of “pain > touch”. Initial voxel-level statistical maps were thresholded at $p < 0.001$ (uncorrected) and corrected for multiple comparisons at cluster level $p < 0.05$ (FWE).

For the functional localizer of face processing areas, data was best-fitted at every voxel by convolving each of the 2 events (Faces × Places) with the SMP8 hemodynamic response function. Hemodynamic analyses were time-locked to the duration of the stimuli, 300 ms. For each

[3] Note that the IAT was carried out after ensuring that participants individuated models with and without Cushing Syndrome. Moreover, IAT practice blocks further strengthened this association. Nevertheless, although we believe this approach allows a better association of models with the two categories, some concerns remain regarding the automaticity of identification. It is possible that participants needed to rely on recall from memory to determine which group each model belonged to.

subject, contrast images were estimated for the comparison (Faces > Places), and entered in individual *t*-test whole-brain analysis at group level. Initial voxel-level statistical maps were thresholded at $p < 0.001$ (uncorrected) and corrected for multiple comparisons at cluster level $p < 0.05$ (FWE), except when specified differently.

Regression analyses

In order to explore the psychological constructs underlying the observed biased neural responses we carried out regression analyses between brain activity and behavioral responses. Average BOLD signals from relevant clusters were extracted and used as dependent measures in separate multiple regression models. Clusters and independent variables were chosen based on the combination of specific theoretical rationale (i.e. predictions outlined in the Introduction) and strong evidence deriving from the results of our categorical comparisons. In specific, to study obesity stigma (contrast: "pain NW > pain Ob") the bilateral insular clusters and bilateral parietal clusters were selected because of their well-recognized involvement in the processing of the affective-motivational and sensory properties of pain, respectively. We also investigated the bilateral posterior temporal clusters based on our hypothesis of diminished responses in high-order visual areas to the pain of Ob. The predictors used were the IAT (average of IAT-UOb and IAT-HdOb scores), a measure of proven predictive value in prejudice-related scenarios, and the differential ratings (NW–Ob) of pity, disgust and similarity. All these measures were found to be significantly different for NW compared to Ob. Pity and disgust are believed to be crucial emotions in prejudice-related cognition (Fiske et al., 2002). Finally, similarity ratings were included based on the idea that perceived similarity is a key moderator of the level of neural resonance with others' actions and emotions (Preston and de Waal, 2002). To explore the psychological underpinnings of the bias related to the perceived uncontrollability of obesity (contrast: Pain UnkOb–Pain HormOb) the IAT-UnkOb/HormOb and the differential ratings (UnkOb–HormOb) of pity, found to be significantly different between these two conditions, were used as predictors of the activity in the right inferior frontal gyrus. Given that we had no theoretical predictions on how to rank regressors by order of importance, we used stepwise selection models (Field, 2005) where the best individual predictor is entered first in the model. Then, variables with the highest partial correlation are sequentially tested for significant improvement of models' predictability. Thus, only variables that help to explain the remaining unexplained variance are to be included in the model. As control, we also performed backward elimination regression models and equivalent results were observed. To correct for multiple comparisons, P values were multiplied by 14 [seven clusters (i.e., regression models) × two independent dimensions of variables (i.e., subjective ratings and measures of bias)], and significance set to $p < 0.05$. This threshold was used both to determine model significance as well as the criteria for variable inclusion in the model.

As confirmatory analyses we also carried out whole-brain correlations using the above mentioned variables separately. Initial voxel-level statistical maps were thresholded at $p < 0.001$ (uncorrected) and corrected for multiple comparisons at cluster level $p < 0.05$ (FWE). Uncorrected activity within brain regions showing brain-behavior correlation in the main regression analyses is also reported.

Pupil dilation

Pupil dilation has been shown to be a measure of autonomic activation and emotional arousal (Bradley et al., 2008). Participants' pupil diameter was monitored at 60 Hz using an ASL eye-tracking system adapted for use in the scanner (Applied Science Laboratories, Bedford, MA; Model 504). Baseline correction was performed by subtracting the first sample (at trial onset) from each of the following pupil samples. Additionally, an eight-point moving un-weighted average was applied to smooth the data. Stimulus luminance was only matched within the model. Therefore, pupil changes to touch stimuli were subtracted from the responses to pain stimuli delivered to the same model. To confirm larger pupil reactivity to pain relative to touch we carried out repetitive paired t-tests between the averaged responses to pain and touch stimuli at each time point. Pupil diameter was significantly larger for pain trials than for touch trials from 1200 ms after onset (ps < 0.05, Bonferroni corrected for number of time points). Data was divided into two different time windows, (Early and Late), according to such time point. Average values of pupil response to the pain (vs touch) of each model, for each time window, were entered in one Time × Model ANOVA design.

Results

Behavioral results

In the emotion ratings we found a significant interaction 4 (Emotion: pity, disgust, envy, pride) × 3 (Model: NW, UnkOb, HormOb) ($F(1,11) = 5.37$, $p < 0.001$), as well as significant main effects of Emotion ($F(1,11) = 8.04$, $p < 0.001$) and Model ($F(1,11) = 4.2$, $p = 0.028$). Newman–Keuls post-hoc analyses revealed that both groups of Ob elicited more pity and disgust feelings than NW (ps < 0.045). In addition, while HormOb were found to elicit more pity feelings than UnkOb ($p = 0.040$), the ratings of disgust were similar between the two groups (ps > 0.05) (Fig. 1A). Regarding the physical ratings, we found significant main effects of Feature ($F(1,11) = 34.4$, $p < 0.001$) and Model ($F(1,11) = 10.8$, $p < 0.001$), and a significant 4 (Feature: similarity, attractiveness, dominance, weight) × 3(Model: NW, UnkOb, HomOb) interaction ($F(1,11) = 24.6$, $p < 0.001$). Newman–Keuls post-hoc analyses revealed that NW models were rated as more attractive, dominant and similar and less fat (ps < 0.002) than the two groups of Ob models. No differences were found between UnkOb and HormOb (ps > 0.05) in any of the features (Fig. 1B).

Participants rated pain videos as more intense ($F(1,11) = 259$, $p < 0.001$) and unpleasant ($F(1,11) = 188.6$, $p < 0.001$) than touch videos. However, neither the interactions 2 (Stimulation: pain, touch) × 3 (Model: NW, UnkOb, HormOb) (intensity: $F(1,11) = 1.15$, $p = 0.33$; unpleasantness: $F(1,11) = 0.88$, $p = 0.43$) nor the main effects of model (intensity: $F(1,11) = 2.08$, $p = 0.15$; unpleasantness: $F(1,11) = 0.71$, $p = 0.50$) were found to be significant (Figs. 1C, D). These findings reveal that the observed painful stimulation was judged to be similar across model type.

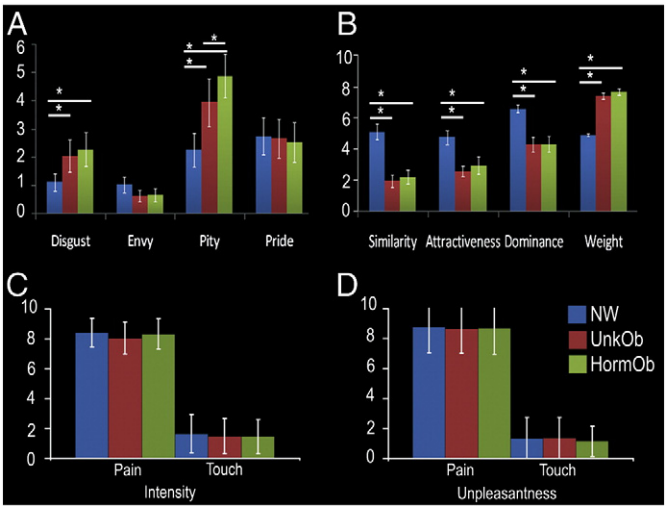

Fig. 1. Mean subjective ratings (and SD) of: A) how much each group of models elicited the emotions proposed by the Stereotype Content Model (i.e. disgust, envy, pity, pride; Fiske et al., 2002); B) perceived physical characteristics (i.e. similarity, attractiveness, dominance, weight); C) Intensity and Unpleasantness of the stimulation. *p < 0.05.

Table 2
Brain responses to the observation of pain irrespective of model type. i.e all pain stimuli vs all touch stimuli. SI — primary somatosensory cortex; SII — secondary somatosensory cortex. $p < 0.05$ (FWE, cluster level). Reported coordinates of local maxima defined in Montreal Neurologic Institute (MNI) stereotactic space.

Area	Number of voxels	Coordinates			t-Value
		x	y	z	
Pre-frontal cortex and insular cortex					
Right precentral gyrus/inferior frontal gyrus (pars opercularis/pars triangularis)	1029	56	10	30	15.94
Right insular cortex	–	40	−2	−10	4.95
Left precentral gyrus/inferior frontal gyrus (pars opercularis)	432	−58	10	28	8.13
Left insular cortex	–	−42	−4	7	5.25
Parietal cortex					
Left inferior parietal cortex (SII)	1409	−58	−22	22	7.60
Left supramarginal gyrus (SII)	–	−60	−36	46	7.00
Right postcentral gyrus (SI)	2043	34	−36	54	8.76
Right supramarginal gyrus (SII)	–	68	−22	32	8.38
Temporal, occipital cortex					
Right Inferior temporal gyrus	4229	44	−62	−10	19.81
Right occipital cortex	–	52	−68	−14	11.63
Left fusiform gyrus	2737	−42	−52	−20	23.06
Left occipital cortex	–	−44	−68	−8	14.29

Concerning the measures of bias, IAT scores revealed significant implicit bias both for the IAT-Ob ($M = 0.35$, $SD = 0.35$; $t(11) = 3.42$, $p = 0.006$) and the IAT-HormOb ($M = 0.44$, $SD = 0.30$; $t(11) = 5.0$, $p < 0.001$) versions. No difference was observed between these two ($t(11) = 0.94$, $p = 0.36$). The IAT-UnkOb/HormOb,[4] i.e. the version comparing directly UnkOb and HormOb, was found to be non-significant ($M = 0.14$, $SD = 0.42$; $t(11) = 1.13$, $p = 0.28$). However, when excluding an outlier ($SD > 2.5$) the difference became significant ($M = 0.23$; $SD = 0.27$; $t(10) = 2.83$, $p = 0.017$), meaning greater preference for UnkOb compared to HormOb. At an explicit level, F-Scale scores ($M = 2.76$; $SD = 0.50$) were not significantly different from the mean score of 2.5 that reflects neutral attitudes towards obese individuals ($t(11) = 1.8$; $p = 0.098$). IMS scores to the two Ob categories (UnkOb: $M = 34.92$, $SD = 8.3$; HormOb: $M = 38.33$, $SD = 4.8$) did not differ significantly ($t(11) = 1.69$, $p = 0.12$). However, EMS (UnkOb: $M = 17.33$, $SD = 7.86$; HormOb: $M = 19.58$, $SD = 9.75$) was found to be higher for HormOb ($t(11) = 2.2$, $p = 0.050$) suggesting that participants felt that external (societal, cultural) pressures to act in a non-prejudiced fashion are stronger if obese individuals are known to suffer from a hormonal disorder.

Pupil dilation

Only the main effect of Time was significant ($F(1,11) = 46.80$, $p < 001$). Neither, the 3 (Model: NW, UnkOb, HormOb) × 2 (Time: early, late) interaction ($F(1,11) = 1.27$, $p = 0.30$) nor the main effect of Model ($F(1,11) = 0.92$, $p = 0.41$) reached statistical significance, revealing that pain stimuli elicited similar levels of autonomic activity across model types. These results, together with the comparable subjective ratings of intensity and unpleasantness of the stimulation applied to the different models, suggest that the differences found in brain responses to the pain of Ob (vs NW) cannot be merely associated with reduced general arousal and/or aversiveness of the stimuli but relate to specific aspects of the neural processing of vicarious pain.

fMRI results

The observation of pain irrespective of model type, i.e. all pain stimuli vs all touch stimuli, revealed activation of brain regions involved in the processing of affective, sensory and motor qualities of the stimuli (Table 2). We found two bilateral clusters in the parietal cortex that included primary and secondary somatosensory cortices. Additionally, two bilateral clusters were found with peaks in pre-frontal regions and extending to the insula. The clusters in the posterior regions included the fusiform gyrus, occipital cortex and posterior temporal cortex, areas associated with visual processing.

Interaction between pain and model type

To test the hypothesis that stigma against obese people is reflected in the degree of neural resonance with others' emotional experiences we first contrasted the pain observation (vs. touch) of NW with that of Ob (i.e., irrespective of the cause of obesity). We found reduced activity in response to Ob's pain in the bilateral insular cortex, thalamus and anterior parietal regions (including the somatosensory cortices). A similar bias was also observed in the posterior brain areas, such as the occipital cortex, fusiform gyrus and posterior temporal cortex (Table 3; Fig. 2). The signal plots in Fig. 2 confirm that the reduced activity associated with Ob's pain was found irrespective of the cause of obesity, i.e. both for UnkOb and HormOb. The statistics of the individual contrasts (pain NW > pain UnkOb) and (pain NW > pain HormOb) are reported in Table 3. No significant activity was found for the inverse contrast (pain > touch)Ob > (pain > touch)NW.

Next, we directly compared brain responses to pain observation (vs. touch) of UnkOb and HormOb. This revealed diminished activity in the right inferior frontal gyrus pars triangularis (rIFG) for the pain of HormOb (Table 3; Fig. 3). No significant activity was found for the inverse contrast (pain > touch)HormOb > (pain > touch)UnkOb.

Functional localizer of face processing areas

Two clusters in the right posterior regions of the brain were found more active in response to faces than places stimuli (Fig. 4). One cluster comprised the posterior regions of the temporal cortex, including the fusiform gyrus, and a portion of the cerebellum (peak: 46, −56, −22; $t = 13.92$; 482 voxels). The other cluster was found in the occipital gyrus (peak: 48, −84, −2; $t = 7.12$; 212 voxels). Knowing that activity in these areas is usually found bilaterally we looked at uncorrected activations in the posterior regions of the left hemisphere.[5] Indeed we found one cluster in the left fusiform gyrus (peak: −44, −80, −16; $t = 6.58$; 61 voxels).

In order to understand if the activity found to be differentially active in response to the pain of NW compared to that of Ob (i.e. [(pain >

[4] Administered in the second session.

[5] Please note that with these analyses we are not interested in making any population-level statistical inference about the regions of the brain that respond to faces, but we just seek to obtain an estimate of the localization of face processing areas in our group of participants.

Table 3
Brain activity reflecting differential processing of the pain (vs touch) of the different models. p < 0.05 (FWE, cluster level). SI — primary somatosensory cortex; SII — secondary somatosensory cortex; IFG — inferior frontal gyrus; *Partial overlap with activity found in the functional localizer of face processing areas. Reported coordinates of local maxima defined in Montreal Neurologic Institute (MNI) stereotactic space.

	Pain NW > pain Ob					Pain NW > pain UnkOb					Pain NW > PAIN HormOb					Pain UnkOb > pain HormOb				
	Coordinates					Coordinates					Coordinates					Coordinates				
Area	x	y	z	t	k	x	y	z	t	k	x	y	z	t	k	x	y	z	t	k
Right postcentral gyrus (SI)	54	−20	34	10.90	576						56	−20	32	6.90	304					
Right inferior parietal cortex (SII)	56	−22	20	5.65	–															
Left inferior parietal cortex (SII)	−62	−14	14	7.59	160	−60	−24	22	4.77	311										
Left insular cortex	−38	−2	4	4.05	119															
Right insular cortex	40	4	−2	8.41	266															
Left fusiform/occipital cortices *	−44	−56	−22	8.44	419						−44	−56	−22	6.47	163					
Right posterial temporal cortex (fusiform)*	50	−68	−12	7.94	620	54	−62	−8	4.10	177	50	−70	−10	5.56	173					
Left occipital cortex	−6	−92	−12	7.51	270	−20	−88	−14	7.72	262										
Thalamus	−4	−10	−4	5.93	152						−8	−4	−2	6.95	350					
Right IFG (pars triangularis)											46	20	8	6.44	176	48	24	6	9.05	160

touch)NW > (pain > touch)Ob]) could be related to biased processing of models' face rather than to the processing of other visual features, we re-tested this contrast but now using the regions activated during the localizer [p < 0.001 (uncorrected)] as the search volume (using SPM's small volume correction). We found significant activation in three localizer-defined regions (p < 0.05, FWE cluster level): left fusiform area (peak: −44; −50; −20; t = 7.73; 32 voxels), right occipital cortex (peak: 50, −78, −2; t = 7.54; 81 voxels) and posterior right temporal cortex (peak: 54; −62, 12; t = 3.84; 14 voxels) (Fig. 4). Thus, these additional analyses confirmed biased pain processing in face sensitive brain areas.

Regression analyses

We carried out multiple regression analyses in order to investigate how specific psychological constructs modulate neural activity reflecting obesity stigma, i.e., pain NW > pain Ob (Fig. 5). We found that decreased activity in the right posterior temporal cortex to the pain of Ob vs NW could be predicted ($R^2 = 0.603$; $F = 15.19$; $p = 0.042$) uniquely by stronger feelings of pity towards Ob ($\beta = -0.777$, $t = -0.390$, $p = 0.042$). Conversely, in the model predicting activity in the right postcentral gyrus we found a trend ($R^2 = 0.588$; $F = 14.29$; $p = 0.056$) with judgments of similarity as a single predictor ($\beta = 0.767$, $t = 0.380$, $p = 0.056$). No other model was found to be significant (all ps > 0.05). We found no behavioral measure predicting the observed increased activity in the rIFG for the pain of UnkOb vs HormOb (p > 0.05).

To confirm these findings we carried out whole-brain correlation analyses. We found a correlation between similarity ratings and activity in the right postcentral gyrus (peak: 60, −18, 22; t = 7,24; 104 voxels) confirming that decreased perceived similarity with Ob is associated with diminished sensorimotor resonance with Ob's pain. No brain region was found to significantly correlate with ratings of pity at the selected threshold. However, data inspection at an uncorrected level revealed that ratings of pity correlate with activity in the right posterior temporal cortex (peak: 54, −62, −12; t = 6.99; 50 voxels) in agreement with the results of the main multiple regression analyses. No other significant correlation was found for any contrast/behavior measure. The inverse contrasts, i.e. pain NW > pain Ob and pain UnkOb > pain HormOb, were also tested but no significant correlation was observed.

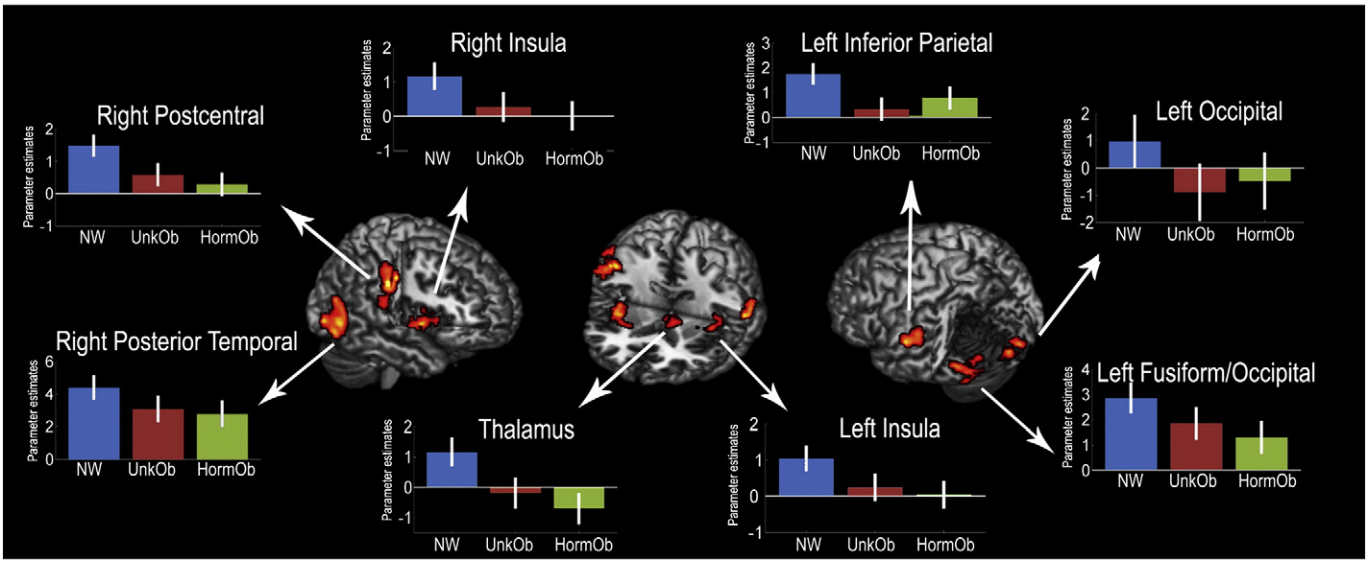

Fig. 2. Decreased brain responses to the observation of pain (vs touch) of Ob (i.e. UnkOb and HormOb) compared to that of NW models (p < 0.05, FWE, cluster level). Reduced activity was found in areas involved in processing the motivational-affective (i.e., bilateral insular cortices and thalamus) and sensory-discriminative (i.e., parietal regions) aspects of pain, as well as visual processing regions (i.e., posterior temporal and occipital cortex). Activation profiles in parameter estimates are plotted for each area.

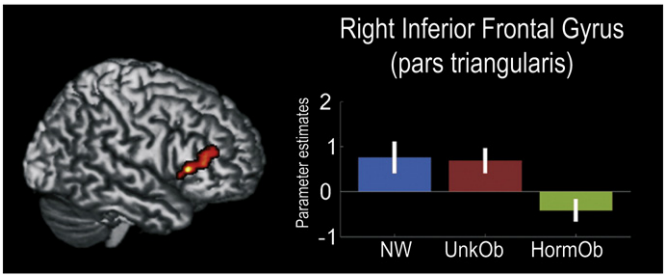

Fig. 3. Decreased brain activity in the right inferior frontal gyrus (pars triangularis) in response to the observation of pain (vs touch) of HormOb compared to that of UnkOb models. $p < 0.05$ (FWE, cluster level). Activation profiles in parameter estimates are shown for each condition.

Discussion

In the present study we used fMRI to investigate the stigma of obesity. In particular, we examined whether weight-stigma is reflected in the neural resonance with affective experiences (pain in our case) of obese individuals. In addition, we assessed how information about the causes and uncontrollability (Decety et al., 2010; Krendl et al., 2012) of obesity might modulate stigma. We found decreased neural reactivity to Ob's pain in areas associated with the representation of sensory and affective-motivational aspects of pain. Furthermore, we show that assuming an uncontrollable medical explanation for obesity, such as a hormonal disorder, can lead to a further inhibition of resonance with these individuals.

Obesity stigma

Here we demonstrate that neural correlates of weight bias extend beyond automatic evaluation of bodies and faces (Krendl et al., 2006; Schupp and Renner, 2011) and include a fundamental feature of intersubjectivity that is the automatic resonance with others' affective experiences. This ability to neurally represent others' states constitutes an important bridge between first- and third-person experiences, providing the foundations for the empathic experience to build on. Our results reveal decreased activity to the observation of pain of Ob compared to that of NW in areas associated with pain processing, i.e. bilateral insula, somatosensory cortices and thalamus, revealing diminished resonance with Ob's pain.

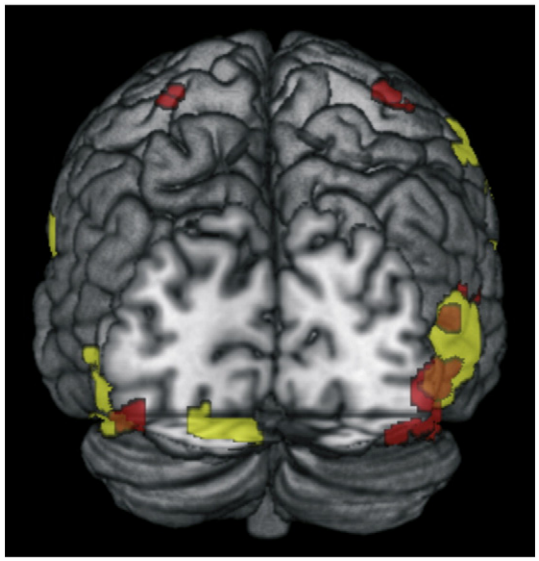

Fig. 4. Overlap (in orange) between the activity map of the functional localizer of face processing areas (in red; $p < 0.001$ uncorrected) and clusters in the posterior regions of the brain reflecting decreased resonance with Ob models pain compared to that of NW (in yellow; $p < 0.05$ FWE at cluster level).

In line with our predictions, the observed reduced activity in the somatosensory cortices suggests decreased mapping of the sensory properties (e.g. intensity and location, Brooks and Tracey, 2005; Keysers et al., 2010), of Ob's pain. Conversely, the insula is an important structure in the representation of affective-motivational responses to others' pain (Lamm et al., 2011). The insula integrates information from various regions of the brain and is involved in complex body and emotion related functions such as the matching of internal bodily states with motivational and social conditions that provides a unified meta-representation of the global emotional moment (Craig, 2009; Critchley, 2005). Importantly, this structure plays a crucial role in understanding others' affective experiences as well as in anticipating the emotional impact of such events on one's own body. Indeed, activity in the insula has been consistently observed to be impaired in response to the pain of disregarded others (e.g. Azevedo et al., 2012; Hein et al., 2010; Singer et al., 2006). Here we extend previous studies by showing diminished affective resonance with the pain of obese individuals.

Decreased hemodynamic responses were also found in visual processing areas including the right posterior temporal cortex and bilateral fusiform/occipital cortices, two regions involved in the perception of faces as confirmed by the overlap with activity from the functional localizer of face sensitive areas. These results suggest that biased responses to Ob's pain are not restricted to pain processing areas and include high-order visual regions. Interestingly, higher-order visual areas are less active during the perception of static faces of disregarded individuals, a phenomenon usually interpreted as diminished individuation or decreased motivation to process the faces of such individuals (Golby et al., 2001; Kaul et al., 2012; Kubota et al., 2012). We now provide evidence that these areas are modulated also by the affective facial expressions of disregarded individuals.

Understanding the origins of obesity stigma is not a simple matter. The many attempts to explain the phenomenon have identified numerous factors ranging from cognitive explanations, such as attributions of responsibility for the condition, to aversive emotional reactions to the sight of obese bodies. Adopting a comprehensive approach, we have been able to find further support to some of these factors and identify others. In line with previous literature, participants perceived Ob models as less attractive, weaker and less similar than NW models (Foster et al., 2003; Staffieri, 1967). Additionally, obese models were associated with higher disgust feelings (Krendl et al., 2006; Lieberman et al., 2011; Vartanian, 2010). While all these variables are very likely to contribute or reflect the complexity of obesity stigma, we provide direct evidence for the important role played by subjective feelings of pity and perceived similarity with the targets. In specific, increased pity feelings predicted decreased neural responses to Ob's pain in early visual areas (see further discussion below on the role of pity on stigma). Interestingly, the level into which participants judged themselves as less similar to Ob predicted impaired activity in brain regions responsible for mapping the sensory properties of pain. These findings are in line with the idea that similarity and familiarity play a central role in empathy-related responses (Cialdini et al., 1997; Oveis et al., 2010; Preston and de Waal, 2002; Valentini et al., 2011) and intergroup biased processing (Azevedo et al., 2012; Liew et al., 2011). It is not clear to what extent this measure is a mere consequence of other processes determining the bias or it represents a fundamental factor by itself. Nevertheless, mounting evidence suggests that such differentiation between oneself and less meaningful or disregarded others has a considerable predictive value. It is very likely that automatic judgments of similarity play a crucial role in evaluating the relevance and setting the psychological distance with others. Perceiving someone (e.g. an obese person) as very dissimilar to oneself may inhibit self-other merging and the sharing of other's experiences.

In contrast to our previous studies on race-bias and pain resonance (Avenanti et al., 2010; Azevedo et al., 2012), we did not find any specific

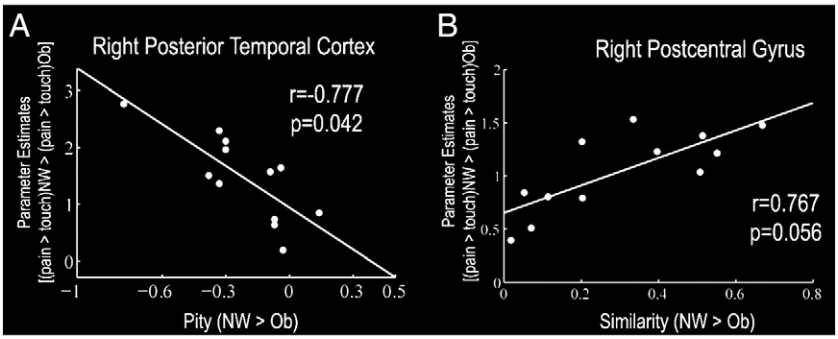

Fig. 5. Behavioral predictors of reduced brain activity for the observation of pain (vs touch) of Ob compared to that of NW. A) Increased pity feelings for Ob (vs NW) predicted reduced activity in the right posterior temporal region in response to Ob' pain; B) Decreased perceived similarity with Ob (vs NW) predicted reduced responses in the right postcentral gyrus.

association between neural responses and implicit obesity bias, as indexed by the IAT, which measures general social preferences (i.e., associations between social groups and "good" and "bad" concepts) and it is a good predictor of neural responses related to predominantly implicit forms of prejudice, such as racial bias. The lack of any association between implicit bias and neural activity in the regions of interest may suggest that obesity stigma occurs at a more conscious level with respect to other biases, as it remains a socially acceptable form of bias (Puhl and Heuer, 2010). It may also be the case that neural responses to the pain of obese individuals are influenced by cognitions and beliefs about such individuals more than by implicit vs explicit variables.

Stigma and the perceived cause of obesity

Our paradigm also allowed us to demonstrate that obesity stigma can be influenced by the available information about its etiology. We found relatively larger resonance with UnkOb's pain relative to that of HormOb in the rIFG, an area activated by empathy-related scenarios (Beeney et al., 2011; Carr et al., 2003; Shamay-Tsoory et al., 2009; Simon-Thomas et al., 2012). This area has been consistently implicated in the evaluation and imitation of facial emotional expressions (Carr et al., 2003; Jabbi and Keysers, 2008; Saarela et al., 2007). In particular, the rIFG is thought to be important for understanding and integrating the meaning of an expression (Budell et al., 2010; Vachon-Presseau et al., 2012) and for downregulating emotional responses so that overarousal and personal distress are avoided (Decety et al., 2010; Goldin et al., 2008; Rameson et al., 2012). Although we cannot be sure whether such differential activity reflects diminished processing/evaluation of facial expressions or decreased regulation of emotional reactions to the perception of pain, the results suggest that the bias implies relatively high-order levels of vicarious processing (de Greck et al., 2013). Unlike general stigma against Ob which was found at various levels of stimuli processing (including early visual processing and emotional affective processing), HormOb specific bias was only evident at later stages of the neural response to others' pain, likely due to the additional cognitive properties of this form of bias. That participants presented greater bias towards HormOb compared with UnkOb was also supported by higher IAT scores. Interestingly, participants reported a greater external, but not internal, motivation to behave without prejudice with HormOb compared to UnkOb. Thus, although there is an explicit component in the weight stigma per se, the more subtle etiology-related bias may be mostly underpinned by implicit attitudes.

At the subjective level, HormOb models were associated with increased pity feelings relative to UnkOb and NW models. Although we found no direct relationship between these ratings, or any other behavioral measure, and diminished neural resonance with HormOb in the rIFG, these results further suggest that this emotion plays a role on the exacerbation of stigma-like responses against obese individuals. Pity is a complex, mixed emotion usually elicited by negative outcomes that cannot be controlled. Moreover, it conveys both positive and negative affects. Indeed, it promotes sympathetic feelings but also assumes the lower-status of the target (Fiske et al., 2002; Smith, 2000). Such paternalistic feelings, although well intended, may disrespect the targets by legitimizing their subordinate status and diminishing their social worth. In keeping, a recent fMRI study (Cikara and Fiske, 2011) found that despite high self-reported sympathetic feelings for pity targets, brain activity reflected a stigma-like response pattern. Stigma starts with the identification and labeling of human differences associated with undesirable characteristics. It follows that these targets are set apart, separated in a "us" versus "them" fashion, resulting in loss of status and discrimination (Link and Phelan, 2001, 2006). We argue that the association with an undesirable characteristic, such as a disease, might promote further segregation and stigmatization (Phelan, 2002). Although HormOb are not to blame for their condition, they were not only "marked" as ill but were also deprived of the power to control their weight. Disease-related labels may strengthen perceptions of defectiveness and hopelessness. Excessive emphasis on biological-deterministic causes of illness induces the notion of irreversibility and accentuates the difference between those who are affected and those who are not (Phelan, 2002; Wahl, 2012).

Our result that lack of responsibility decreases empathic reactivity and increases stigma may seem at odds with respect to the finding of increased resonance with the pain of AIDS patients not responsible for their condition (infected during a blood transfusion) compared to that of those judged responsible (due to intravenous drug use) or healthy controls (Decety et al., 2010). However, several differences between these two studies may help to explain this apparent discrepancy. The first is the remarkably diverse nature and severity of the diseases presented (AIDS vs hormonal disorder). The second is that in the case of AIDS patients disease was a common feature of both stigmatized groups. The third is the block design and primes used in the AIDS patients study where participants were informed on each trial to what group the target belonged. As discussed by the authors this procedure may have increased the cognitive control and top-down sympathetic feelings when processing blood transfusion AIDS target's pain. Interestingly, this was likely reflected in the increased rIFG activity which is the same area found less responsive in the present study to HormOb's pain. The fourth is that, unlike our study, the research on AIDS patients focused on exploring the differences between responses to responsible vs not responsible stigmatized targets. The fifth is that intravenous drug use besides providing a cue of responsibility is a stigmatizing factor per se.

Finally, we should also specify that the pain observation approach does not allow to study the entire empathic experience or the ultimate empathy-related behavioral responses (Batson, 2009; see also Valentini and Koch, 2012). Additional processes such as perspective-taking, i.e. explicit reasoning about others' states (Decety, 2011; Zaki and Ochsner, 2012), or the regulation of one's own biased attitudes (Bartholow and Henry, 2010; Bessenoff and Sherman, 2000; Eres and Molenberghs, 2013) are likely determinants of the final empathic response. Indeed,

cognitive representation of others' feelings and motivational drives are essential to empathic concern and sympathetic responding (as discussed previously regarding the AIDS stigma study). Nevertheless, we provide evidence that obesity stigma can be manifested in an elementary form of human bonding that is the ability to automatically resonate with others' sensory and affective experiences (de Waal, 2012). We also show that ambivalent feelings states such as pity, usually associated with compassionate behavior, can dampen neural resonance with the pain of others. Despite their egalitarian goals and pro-social motivations people may be affected by stigma at implicit levels. Thus, increasing the awareness of one's own negative affects is extremely important, especially among health-professionals. Indeed, unconscious biased attitudes may result in discriminatory behavior such as passive harm (e.g. neglect or avoidance) and compromise an appropriate treatment delivery (Dovidio and Fiske, 2012; Penner et al., 2010).

Acknowledgments

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