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ORIGINAL ARTICLE

Excessive body fat linked to blunted somatosensory cortex response to general reward in adolescents

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BACKGROUND AND AIMS: The brain reward system is key to understanding adolescent obesity in the current obesogenic environment, rich in highly appetising stimuli, to which adolescents are particularly sensitive. We aimed to examine the association between body fat levels and brain reward system responsivity to general (monetary) rewards in male and female adolescents.
METHODS: Sixty-eight adolescents (34 females; mean age (s.d.) = 16.56 (1.35)) were measured for body fat levels with bioelectric impedance, and underwent a functional magnetic resonance imaging (fMRI) scan during the Monetary Incentive Delay (MID) task. The MID task reliably elicits brain activations associated with two fundamental aspects of reward processing: anticipation and feedback. We conducted regression analyses to examine the association between body fat and brain reward system responsivity during reward anticipation and feedback, while controlling for sex, age and socioeconomic status. We also analysed the moderating impact of sex on the relationship between fat levels and brain responsivity measures. Brain imaging analyses were corrected for multiple comparisons, with a cluster-defining threshold of $P < 0.001$, and minimum cluster size of 38 contiguous voxels.
RESULTS: Higher body fat levels were associated with lower activation of the primary somatosensory cortex (S1) and the supramarginal gyrus during reward feedback after controlling for key sociodemographic variables. Although we did not find significant associations between body fat and brain activations during reward anticipation, S1/supramarginal gyrus activation during feedback was linked to increased negative prediction error, that is, less reward than expected, in illustrative *post hoc* analyses. Sex did not significantly moderate the association between body fat and brain activation in the MID task.
CONCLUSIONS: In adolescents, higher adiposity is linked to hypo-responsivity of somatosensory regions during general (monetary) reward feedback. Findings suggest that adolescents with excess weight have blunted activation in somatosensory regions involved in reward feedback learning.

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INTRODUCTION

The worldwide prevalence of overweight and obesity in adolescents is high (13%), and has been on the rise in the last 30 years.[1] One of the main factors driving the increase of excess weight problems in the adolescent population is the wide availability of high-calorie processed foods with highly rewarding properties.[2,3] In such obesogenic environment, the neurobiological systems that evolved to seek rewards to ensure survival can turn into a health threat by fostering overconsumption of highly rewarding foods, and thus excessive adiposity.[4–6]

The gold standard measure of the neurobiological reward system is the monetary incentive delay task (MID;[7,8]). The MID separates two processes that contribute to individual differences in reward valuation; namely, reward anticipation and feedback.[7] Reward anticipation refers to the motivational processes that are mobilised to obtain rewards as a function of their value or salience. Reward feedback reflects the hedonic impact of reward attainment. This task has shown to be relevant to understand the reward processing underpinnings of obesity. Indeed, MID-evoked hyperactivation of the brain reward system during feedback has been observed in adolescents at high risk of developing obesity by virtue of family history.[9] However, the MID task has never been applied in adolescents with current excess weight problems, and thus we do not know if there is a direct link between excessive adiposity and brain reward system responsivity.

A related question is whether excessive adiposity in adolescents is associated with altered reward anticipation, feedback or both. Existing research on this question has focused on food tasks involving anticipation and consumption of energy rich drinks. Stice *et al.*,[10] using a milkshake paradigm where participants anticipated and received high-calorie milkshakes, found that female adolescents with obesity, compared to those with normal weight, had increased activation of somatosensory regions (mid and anterior insula and frontal, parietal and Rolandic operculum) during both milkshake anticipation and receipt (feedback). In addition, they showed decreased activation of the striatum during feedback. However, it is unclear whether these findings pertain to food stimuli, or reflect a more general alteration of the brain reward system, as measured by the MID task.

To establish the link between the responsivity of the brain reward system and excess weight problems, specific measures of adiposity are needed. The most typically used index, body mass index, reflects several types of tissue, including lean muscle, and thus it is not sufficiently specific.[11,12] This is particularly true during adolescence, due to continuing growth of tissues other than fat

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(for example, Loomba-Albrecht *et al*.[13]). In a recent study, Rapuano *et al*.,[14] measured total body fat using bioelectric impedance, and found a positive association between body fat levels and activation of the somatosensory cortex, which is functionally connected with the brain reward system through dopaminergic pathways.[15,16] The somatosensory cortex has also been linked to reward feedback processing in the context of tactile and monetary-based decision-making, and its activity is modulated by dopaminergic function.[17,18] A related question concerning the link between brain reward function and adiposity is if the responsivity of the brain reward system differs between males and females, which naturally have different levels of body fat. In this vein, recent research has shown that males compared to females have higher responsivity of the brain reward system during adolescence.[19]

This study has two primary aims: (1) to examine the association between the activation of the brain reward system measured with functional magnetic resonance imaging (fMRI) during the MID task and total body fat measured with bioelectric impedance among adolescents; (2) to examine whether sex moderates the association between the responsivity of the brain reward system and adiposity. We hypothesised that body fat would be positively associated with activation of the brain reward system, particularly during reward feedback,[9,10] and that this relationship would be stronger in males relative to females.[19]

MATERIALS AND METHODS

Participants and procedure

Sample size was determined by a multivariate power analyses that indicated that 68 participants were required to detect a medium sized effect of $d = 0.5$, with 80% power and $P < 0.05$. The final sample comprised 68 adolescents (34 females) who met the study selection criteria and successfully completed all assessments (see Supplementary Figure S1 for a flowchart of the recruitment and selection process). Descriptive information about sociodemographic variables and body composition characteristics of the sample is shown in Table 1.

The selection criteria for participants were as follows: (I) aged between 14 and 18 years or middle adolescence; (II) age- and sex-adjusted body mass index (BMI) within the normal weight, overweight and obese ranges according to the International Obesity TaskForce;[20] (III) absence of current or past medical illness (for example, metabolic diseases) or psychiatric disorders (for example, eating disorders; mood disorders), and (IV) MRI contraindications (for example, claustrophobia, ferromagnetic implants). Participants were recruited via advertisements in the University campus and newsletters, and local newspapers and radio stations. People interested in participating were contacted by phone to screen their potential eligibility. Participants who *a priori* met the selection criteria were invited to a face to face session together with their parents. In this session, they were briefed about the study and provided parental or personal consent. They were also assessed for weight, height and body fat, and medical and psychiatric history.

The study was approved by the Ethics Committee for Research in Humans of the University of Granada (Spain) and was conducted in accordance with the Declaration of Helsinki.

Measures

Body fat. Total body fat was measured with bioelectric impedance using a body composition analyser (TANITA BC-420 (GP Supplies Ltd., London, UK)), following a similar approach in previous research in adolescents with excess weight.[14] Bioelectric impedance analysis constitutes a reliable method to estimate body fat[21,14] (see also Vicente-Rodríguez *et al*.[22]). The measure of body fat used in this study was recorded previously to enter to the MRI scanner.

fMRI measure of reward sensitivity. The Monetary Incentive Delay task (MID; based on Knutson *et al*.[8] and adapted by our group, see Verdejo-Román *et al*.[23]) is an fMRI measure of reward processing consisting of reward anticipation and feedback. Figure 1 displays a schematic representation of the task design. At the beginning of each trial, participants were shown one of two cues (green or blue square) indicating potential winnings or no financial outcome at the end of the trial. The incentive value of each trial was signalled by means of the number of horizontal lines crossing the square (one line for 0.2 €, two for 1 € and three for 5 €). Each cue was presented for a fixed duration of 750 ms. Subsequently, a cross-fixation was shown during a variable period of 3 to 5 s, and after this interval participants had to perform a reaction-time task: respond to a white target star appearing for a variable length of time (150–450 ms) with a button press. Then participants received feedback (hit/miss) about the accuracy of their response for 1500 ms, together with the information about the amount of money won in that trial (when adequate, that is, correct responses in reward cued trials) and their cumulative total at that point of the experiment. Finally, another fixation period (1500 ms) was included before the next trial. Therefore, total trial duration ranged between 6900 and 9200 ms. Participants performed 24 trials of each type of cue yielding a total of 96 trials.

Imaging analyses interrogated brain activity changes during two periods, the reward-anticipatory period, which included the cue presentation, the variable waiting delay and the actual response period, and the reward-feedback period, involving the presentation of visual feedback (hit/miss). For the anticipatory period we defined four events of interest: high reward (5 €), medium reward (1 €), low reward (0.2 €), no outcome (0 €). Specifically, a linear contrast (high reward > medium reward > low reward > neutral (no outcome) trials) was defined at the first level

Table 1. Sociodemographic characteristics and body composition data

	Total Mean (s.d.)	*Males Mean (s.d.)*	*Females Mean (s.d.)*	*Test statistics*	P-*value*
Age	16.56 (1.35)	16.44 (1.42)	16.68 (1.30)	$t(1,66) = 0.714$	0.478
Education (years)[a]	10.56 (1.35)	10.44 (1.42)	10.68 (1.30)	$t(1,66) = 0.714$	0.478
Monthly Income	*n* (%)	*n* (%)	*n* (%)		
< 600 €	3 (4.4)	1 (2.9)	2 (5.9)		
601–1000 €	9 (13.2)	3 (8.8)	6 (17.6)		
1001–1500 €	26 (38.2)	13 (38.2)	13 (38.2)	$\chi^2 = 3.697$	0.594
1501–2000 €	11 (16.2)	5 (14.7)	6 (17.6)		
2001–2500 €	8 (11.8)	4 (11.8)	4 (11.8)		
> 2500 €	11 (16.2)	8 (14.7)	3 (8.8)		
BMI-for-age[b]	69.33 (28.83)	70.18 (28.00)	68.49 (30.03)	$t(1,66) = -0.240$	0.811
Fat%	21.77 (10.85)	16.36 (9.26)	27.18 (9.63)	$t(1,66) = 4.725$	< 0.001
Participants with Excess weight[c]	*n* (%) = 22 (34.4)	*n* (%) = 9 (32.4)	*n* (%) = 13 (38.24)	$\chi^2 = 1.075$	0.437

Abbreviation: BMI, body mass index. [a]All participants were enrolled in formal education. Education years were calculated from 6 years old. [b]Based on international criteria.[20] [c]Participants showing excess weight based on their fat percentage.[24]

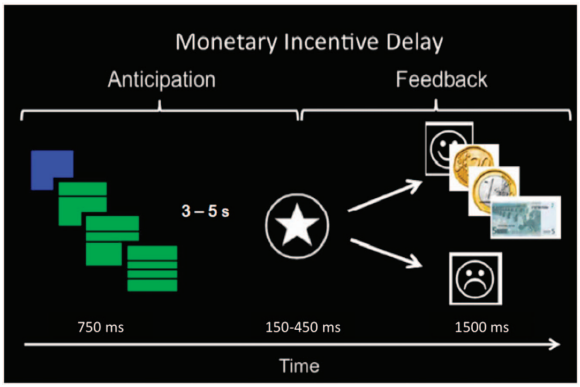

Figure 1. Schematic representation of the monetary incentive delay task.

(within-subject) to explore brain activation during reward anticipation. A win vs miss contrast was used for the reward-feedback period.

Image acquisition and preprocessing. A 3.0 T clinical MRI scanner, equipped with an eight-channel phased-array head coil, was used (Intera Achieva, Philips Medical Systems, Eindhoven, The Netherlands). During task performance, two T2*-weighted echo-planar imaging (EPI) sequences were acquired according to the following parameters: Repetition time (TR) = 2000 ms, Echo time (TE) = 35 ms, Field of view (FOV) = 230 × 230 mm, 96 × 96 matrix, flip angle = 90º, and a total of 21 axial slices of 4 mm with a 1 mm gap). Slices were collected in sequential ascending order, paralleled with the anterior and posterior commissure. Specifically, we collected 432 scans for the MID task. A sagittal three-dimensional T1-weighted turbo-gradient-echo sequence (3D-TFE) (160 slices, TR = 8.3 ms, TE = 3.8 ms, flip angle = 8°, FOV = 240 × 240, 1 mm^3 voxels) was also obtained in the same experimental session to discard gross anatomical abnormalities. Stimuli were presented through magnetic resonance-compatible liquid crystal display goggles (Resonance Technology Inc., Northridge, CA, USA), and responses were recorded through Evoke Response Pad System (Resonance Technology Inc., Northridge, CA, USA). The functional images were analysed using Statistical Parametric Mapping (SPM8) software (Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London, UK), running under Matlab R2009 (MathWorks, Natick, MA, USA). Images were aligned with the anterior commissure-posterior commissure (AC-PC) plane. Preprocessing of the functional scans included slice-timing correction, realignment to correct for motion-related artifacts, spatial normalisation into the standard Montreal Neurological Institute space using SPM8's EPI template and smoothing with full width at a half maximum of the Gaussian kernel (8 mm). We also visually checked the spatial normalisation of the mean EPI image to the SPM's EPI template. Two independent raters performed the inspection of the realignment parameters and the spatial normalisation. Five participants showed more than two degrees or millimetres of movement in any of the six directions, during the MID task, and thus they were excluded due to excessive within-run motion (Supplementary Figure S1).

Statistical analysis

Behavioural analyses. We conducted all behavioural analyses in SPSS v. 19 (SPSS; Chicago, IL, USA). We examined the data distribution to ensure that variables met the required assumption for the analyses. Reaction time in the MID task was log-transformed to fit normal distribution.

Sociodemographic and body composition characteristics

We conducted *t*-tests to examine sex differences on age, years of education, BMI-for-age centile and body fat percentage, and χ^2-tests to examine sex differences on socioeconomic status (SES) and excess weight status.[24] We also examined the associations between sex, BMI and body fat using correlation analyses.

MID behavioural measures

To test the main effect of the MID's reward manipulation, we analysed reaction times and hit rates (proportion of wins) across the four reward conditions (high, medium and low rewards and neutral/no outcome) using repeated measures analysis of variances (ANOVAs). To examine sex differences in task performance, we conducted (I) two mixed-design ANOVAs including the four reward conditions and sex as within and between-group factors, respectively, and reaction times and hit rates as dependent variables; and (II) correlation analyses between sex and reaction times and hit rates. The association between body fat and task performance (reaction times and hit rates) was examined with correlation analysis.

Neuroimaging analysis. Image processing was carried out with Statistical Parametric Mapping 8 (SPM8; The Wellcome Department of Cognitive Neurology, London, UK). Task regressors were convolved with the SPM8 canonical hemodynamic response function, and were modelled as the time elapsed between the presentation of each cue and the participants' response (reward anticipation), and the time in which the visual feedback was presented on the screen (reward feedback). A parametric contrast was numerically defined as (2 1 −1 −2) reflecting a high reward > medium reward > low reward > neutral (no outcome) anticipation effect. Reward feedback contrast of interest were defined as win > miss trials. To prevent motion artifacts, six head motion parameters were entered as regressors of no interest in all first-level analyses.

On the basis of on our main hypothesis, we restricted the analyses to regions of the mesolimbic and corticolimbic reward systems (for example, refs 25,26), including somatosensory regions (primary somatosensory cortex and Rolandic operculum) given their well-established role on reward processing in obesity (for example, refs 4,6,14,16). We used the WFU Pickatlas v.2.4[ref. 27] to create a single mask that comprised the midbrain, striatum, thalamus, hippocampus, amygdala, anterior and posterior cingulate cortices, insula, Rolandic operculum, supplementary motor area, postcentral gyrus and prefrontal and parietal cortices, based on the Automatic Atlas Labelling (AAL) anatomical parcelation included in the application.

One-sample *t*-tests were conducted on the resulting first-level contrast images to assess activation during task conditions. To examine the association between body fat and brain activation during reward anticipation and feedback, we conducted a voxel-wise correlation analyses in SPM, controlling for sex, age and SES. To examine sex differences in the association between body fat and brain activation in the MID task, we conducted a voxel-wise correlation analyses with body fat, in a two-sample *t*-test with sex as a between-group factor, controlling for age and SES.

Thresholding criteria. The analysis of sociodemographic characteristics and behavioural measures of the MID task used a standard threshold of significance ($P < 0.05$). A multiple comparisons correction was applied on two-tailed *P*-values in the correlation analyses of the MID task ($P < 0.01$).

Neuroimaging analyses were corrected for multiple comparisons using a combination of voxel intensity and cluster-defining thresholds. The significance threshold was determined by 1000 Monte Carlo simulations using AlphaSim, as implemented in the SPM REST toolbox (Resting-State fMRI Data Analysis Toolkit).[28] The input parameters to AlphaSim included an individual voxel threshold probability of $P < 0.001$, a cluster connection radius of 5 mm, and the actual smoothness of imaging data after model estimation. At 16.5 mm FWHM smoothness for the task contrasts, a minimum cluster-defining threshold of 38 voxels was obtained, corresponded to a corrected *P*-value < 0.05.

RESULTS

Sociodemographic and body composition characteristics

Descriptive data for age, SES, BMI-for-age centile, body fat percentage and the number of participants with excess weight are displayed in Table 1. There were no sex differences in sociodemographic characteristics or BMI-for-age centile. Although males showed less body fat than females, there were no differences in the number of participants with excess weight as a function of sex. BMI-for-age significantly correlated with body fat percentage in both males and females ($r = 0.746$ and 0.719, respectively; $P < 0.001$).

Table 2. Descriptive data of the performance in the monetary incentive delay task

	Total		*Males*		*Females*	
	RT[a] *mean (s.d.)*	*Hit rate*[b] *mean (s.d.)*	*RT*[a] *mean (s.d.)*	*Hit rate*[b] *mean (s.d.)*	*RT*[a] *mean (s.d.)*	*Hit rate*[b] *mean (s.d.)*
No reward	257 (41)	0.55 (0.15)	253 (47)	0.57 (0.18)	260 (35)	0.53 (0.13)
Low reward	237 (32)	0.52 (0.11)	230 (36)	0.54 (0.11)	244 (27)	0.50 (0.11)
Mid reward	241 (36)	0.56 (0.12)	235 (40)	0.58 (0.12)	246 (31)	0.54 (0.11)
High reward	227 (33)	0.58 (0.12)	222 (40)	0.60 (0.14)	232 (25)	0.56 (0.08)

Abbreviation: RT, reaction time. [a]Reaction times are shown in milliseconds. [b]Proportion of wins.[42]

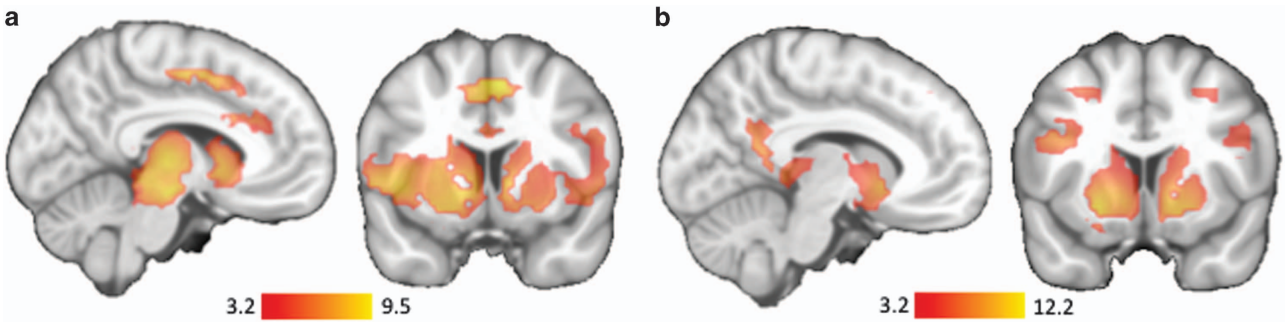

Figure 2. Pattern of activations in the monetary incentive delay task. Note. (**a**) Reward anticipation (high > medium > low > neutral). (**b**) Reward feedback (win > miss). The color bar indicates *t*-value.

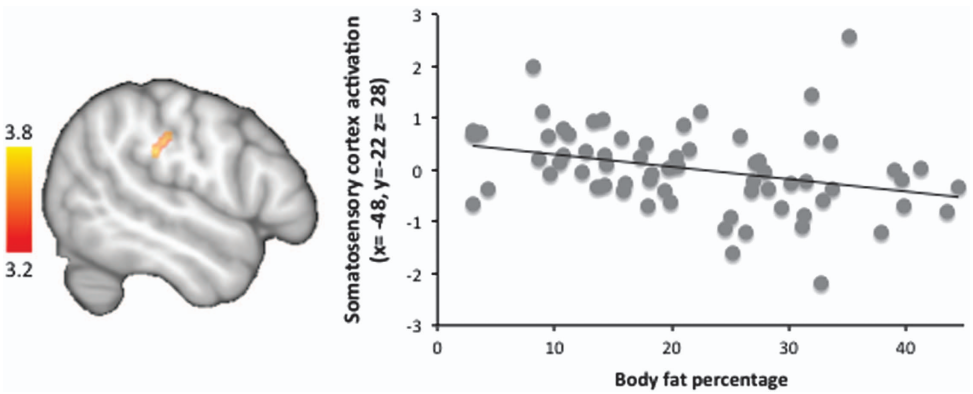

Figure 3. Brain associations with body fat percentage during reward feedback in the monetary incentive delay task. Note. The color bar indicates *t*-value. The brain image reflects the association between body fat and reward feedback (win > miss). The *X* axis represents body fat percentage. The *Y* axis represents the beta eigenvalues extracted from the peak activation of the somatosensory cortex.

MID behavioural measures

Results are displayed in Table 2. There was a significant effect of reward magnitude on reaction times (F (1, 65) = 29.106; $P < 0.001$; $\eta^2_p = 0.573$) and hit rates (F (1, 65) = 6.659; $P = 0.001$; $\eta^2_p = 0.235$). Participants were faster in the high reward condition compared to the other conditions (high > medium, $t = -7.032$; $P < 0.001$; high > low, $t = -3.525$; $P = 0.001$; high > neutral, $t = -8.565$; $P < 0.001$). With regard to hit rates, participants showed greater wins in the high reward relative to the low reward condition, although no other differences were significant (high > low, $t = 4.529$; $P > 0.001$; *P*minimum (min.) = 0.088 for the remaining contrasts). There were no sex differences or sex by reward condition interactions on reaction time or hit rates ($F = 3.345$; *P*min. = 0.072; $\eta^2_p = 0.048$ for sex differences in hit rates).

Body fat was not significantly correlated with reaction times or hit rates in the total sample (*P*minimum corrected = 0.029 and 0.055, respectively), males (*P*min. corrected = 0.110 and 0.267, respectively) or females (*P*min. corrected = 0.405 and 0.134, respectively).

Neuroimaging

Brain activation during reward anticipation and feedback. Figure 2 (left panel) and Supplementary Table S1 show the pattern of brain activations associated with reward anticipation. The parametric increase in reward magnitude was associated with activations in the dorsolateral and medial prefrontal cortices, motor cortex, supplementary motor area, somatosensory cortex, intraparietal cortex, anterior cingulate cortex, the insula extending to the frontal operculum, the ventral and dorsal striatum, the thalamus, the amygdala and the hippocampus and regions within the midbrain. We did not find any regions associated with a parametric decrease in reward magnitude.

Figure 2 (right panel) and Supplementary Table S2 show the pattern of brain activations associated with reward feedback. The processing of win > miss feedback was associated with activations in the dorsolateral and ventrolateral prefrontal cortex, motor and parietal cortex, posterior cingulate cortex, striatum, the amygdala-hippocampus complex, the thalamus and regions within the midbrain. In addition, this contrast was associated with a pattern

of deactivations involving regions of the dorsolateral and ventrolateral prefrontal cortices (different portions than the previous one), and the frontal operculum, the somatosensory cortex, the supramarginal gyrus and the anterior cingulate cortex (Supplementary Table S2).

Associations with body fat

There were no associations between body fat and brain activation during reward anticipation. In the reward feedback contrast (win > miss) body fat was significantly associated with lower activation in a cluster of 42 voxels comprising the primary somatosensory cortex (S1) ($x = -48$, $y = -22$, $z = 28$; $t = 3.45$) and the supramarginal gyrus ($x = -51$, $y = -31$, $z = 28$; $t = 3.76$), after controlling for sex, age and SES (Figure 3).

For illustrative purposes, we plotted the correlation between body fat and the BOLD signal in S1 and the supramarginal gyrus during 'win vs baseline' and 'miss vs baseline' (excluding neutral trials), by extracting the eigenvalues from the voxels of the S1/supramarginal gyrus cluster. These *post hoc* analyses were conducted to examine if positive or negative prediction errors (that is, more or less reward than expected) drove the correlation between body fat and BOLD activation during feedback. The correlations suggest that the effect was driven by negative prediction error (Supplementary Figure S2). However, this should not be considered for statistical inference. They are biased estimates of the effects given that the eigenvalues were extracted from simple effects from non-independent regions extracted from the main analysis which associated body fat with a contrast including both separate variables, win and misses.

Differences related to sex in body fat-brain activation association

We did not find significant sex differences in the association between body fat and brain activation during the anticipation or the feedback contrasts at the selected threshold. Using a more liberal correction threshold ($P < 0.005$; CS = 217), there was a positive association during reward anticipation in males between body fat and the activation of a cluster of 250 voxels. The cluster comprised the right hippocampus-amygdala complex ($x = 24$, $y = -13$, $z = -14$; $t = 2.79$), the posterior insula extending to the putamen ($x = 36$, $y = -7$, $z = 4$; $t = 3.42$), the anterior insula extending to the frontal operculum ($x = 45$, $y = 11$, $z = 4$; $t = 3.39$), and the ventrolateral prefrontal cortex ($x = 51$, $y = 29$, $z = 4$; $t = 3.49$) (Supplementary Figure S3). No significant associations were found in females in this contrast.

DISCUSSION

This study aimed to test the association between levels of body fat and the responsivity of the brain reward system in adolescents, and whether sex moderated this relationship. We found that higher levels of adiposity are associated with lower activation of the primary somatosensory cortex (S1) and the supramarginal gyrus during reward feedback. Adiposity was not associated with brain activation during reward anticipation, although *post hoc* analyses suggested that reduced S1 activation during feedback was linked to an increased negative prediction error (that is, less reward than expected). Sex does not moderate the association between body fat and reward-evoked brain activation. However, adolescent males showed a trend towards positive correlations between body fat and activation of fronto-limbic regions during reward anticipation, which was not evident in females.

Our finding of a negative association between body fat and S1/supramarginal activation suggests that adolescent obesity is linked to alterations in somatosensory processing of reward feedback.[17,18,29,30] Previous research had shown that adults with obesity have abnormally increased baseline S1 metabolism.[31] In addition, adolescents with obesity show greater activation of S1 while watching food commercials.[14] Our findings extend the relationship to monetary rewards, suggesting a more general role of this region on reward processing in the context of adolescent obesity. This notion resonates with previous research showing that dispositional differences in dopamine availability (linked to general reward responsivity) modulate somatosensory cortex activity in the MID task.[18] In addition, PET studies have shown that higher baseline metabolism in S1 is associated with decreased availability of dopamine D2-type receptors in the striatum in obesity.[16]

The aforementioned study on brain reactivity to food commercials found a significant association between body fat and higher activation of S1 during passive observation of ads containing highly palatable food.[14] Although our result was in the opposite direction (that is, more body fat, less activation of S1), both findings might be seen as complementary according to the reward prediction error theory (for example, Schultz[32]). We showed that the relationship between body fat and S1 activation during feedback seems to be linked to increased negative prediction error (less reward than expected). The finding by Rapuano *et al.*,[14] suggests that adolescents with higher levels of body fat hyper-activate S1 during reward anticipation (food advertising). Thus, both findings suggest that body fat may be related to abnormal activation of S1 in the context of increased negative reward prediction error. Alternatively, our results could also be explained in the framework of the incentive sensitisation theory.[33,34] This model, which was originally proposed in the context of addiction, articulates how sensitization of the brain reward system can lead to an enhanced valuation of preferred rewards (that is, food in the context of obesity, or drugs in the context of addiction) and diminished valuation of alternative reinforcers (for example, money). Recent theories have proposed that this phenomenon can contribute to explain the brain alterations associated with excess weight and obesity, where food reward experiences can sensitise brain responses to food and de-sensitize brain responses to other forms of reward.[35,36] However, we acknowledge that our results cannot directly speak to this notion, as we did not include food rewards in our task, and we did not find significant associations between body fat and behavioural measures of motivation towards general (monetary) rewards.

Although we did not find a significant interaction of sex by adiposity, the trend correlation between body fat and amygdala, insula and VLPFC in males deserves further investigation in samples that are better powered to detect sex differences. The trend correlation involves core regions of the brain reward system, and previous evidence has suggested that this system is more sensitive in males versus females during adolescence.[19,37] Specifically, amygdala activations during reward processing have been associated with reward-related arousal, and insula activations have been linked to conscious awareness of positive feelings elicited by rewards in meta-analytic research.[25] In addition, the VLPFC is importantly implicated in goal-directed behavior in the context of reinforcement learning.[38,39]

Altogether, we show that higher adiposity is linked to lower activation of the primary somatosensory cortex and the supramarginal gyrus during reward feedback among adolescents; probably reflecting an increased negative prediction error in these regions, which are importantly involved in reward learning. The finding is strong in the sense that it is adequately powered, and based on an extensively validated probe of the function of the brain reward system. It also has important theoretical and practical implications. Theoretically, it suggests that elevated adiposity is linked to abnormal activation of feedback-related brain regions in response to general rewards, indicating that adolescent obesity may be linked to broad alterations in the brain reward system, beyond those specifically associated with food reward.[14] In practice, our findings suggest that weight loss interventions

focused on increasing the hedonic value of non-food rewards, to counter food-related reward biases, can be worth testing. Nonetheless, the study also needs to be appraised in the context of its limitations. For instance, the cross-sectional nature of the design precludes us from drawing any causal link from the relationship between body fat and brain activation. In addition, given the lack of body fat by sex interactions on the association between adiposity and brain activation, the role of sex differences remains elusive. Although our study was well powered to detect main effects of body fat on reward-evoked brain activation, we acknowledge that it was not specifically powered to detect sex differences, and hence this question needs to be addressed by future studies that are powered to detect such differences. Besides, AlphaSim can produce subtle inflations of Type I error,[40] but we chose it to counter the risk of Type II error,[41] as Type I error was less problematic given the theoretically-constrained imaging analysis approach. An additional limitation refers to the timing parameters between events of interest in the version of the MID task used in this study. We applied a fixed inter-trial interval (ITI) of 1500 ms between the feedback and the presentation of the reward cue in the next trial. As a result, the time course of the hemodynamic response is in the order of seconds, and thus correlation between the two events is likely. Although we did not contrast for differences between anticipation and feedback periods directly, this fixed ITI may result in feedback processes loading on the regressor for the anticipatory periods, making activation during the feedback period more difficult to detect. The jittering of this ITI could provide a better resolution of analyses of the BOLD response of the two interrelated processes studied. Nonetheless, we observed robust responses for both the anticipation and feedback periods. Finally, our results regarding reward feedback processing and its interpretation could have been complemented with a more sophisticated version of the MID task that allows testing the parametric increase or decrease in wins and misses magnitude.

Altogether, we found that elevated fat levels are linked to abnormally decreased activation in reward-related somatosensory region in response to general reward feedback among a well-powered, representative sample of adolescents.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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