

SCIENTIFIC REPORTS



OPEN

Impulsivity and body fat accumulation are linked to cortical and subcortical brain volumes among adolescents and adults

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Obesity is associated not only with metabolic and physical health conditions, but with individual variations in cognition and brain health. This study examined the association between body fat (an index of excess weight severity), impulsivity (a vulnerability factor for obesity), and brain structure among adolescents and adults across the body mass index (BMI) spectrum. We used 3D T1 weighted anatomic magnetic resonance imaging scans to map the association between body fat and volumes in regions associated with obesity and impulsivity. Participants were 127 individuals (BMI: 18–40 kg/m²; $M = 25.69 \pm 5.15$), aged 14 to 45 years ($M = 24.79 \pm 9.60$; female = 64). Body fat was measured with bioelectric impedance technology, while impulsivity was measured with the UPPS-P Impulsive Behaviour Scale. Results showed that higher body fat was associated with larger cerebellar white matter, medial orbitofrontal cortex (OFC), and nucleus accumbens volume, although the latter finding was specific to adolescents. The relationship between body fat and medial OFC volume was moderated by impulsivity. Elevated impulsivity was also associated with smaller amygdala and larger frontal pole volumes. Our findings link vulnerability and severity markers of obesity with neuroanatomical measures of frontal, limbic and cerebellar structures, and unravel specific links between body fat and striatal volume in adolescence.

The prevalence of overweight and obesity in adolescents and adults has rapidly increased worldwide¹. Excess weight during adolescence predicts higher morbidity and premature mortality in adulthood². Among adults, excessive body fat accumulation increases the risk of developing chronic health conditions including cardiovascular disease, Type 2 diabetes and dementia³. There is increasing awareness about the negative influence of body fat, not only on metabolic and physical health, but also on brain health^{4,5}.

Excess body fat accumulation is likely associated with poorer brain health via several mechanisms such as neuroinflammation and changes in the phospholipid composition of brain lipids^{4,6}. However, the association between excess body fat and the volume of brain regions relevant to the pathophysiology of obesity is still unclear, as previous studies have either focused on single brain regions (e.g., the hippocampus) or broad morphological measures^{6–10}. In addition, most previous studies have been conducted with adolescents⁶ or older adults^{7,8,11}. However, it remains unknown whether the relationship between excess body fat and brain health differs across adolescence and young/middle adulthood. Moreover, past studies using body mass index (BMI) as a proxy for adiposity have yielded mixed findings. For example, increased BMI has been linked to both higher and lower volume of the orbitofrontal cortex (OFC), the insula, hippocampus, striatum, and cerebellum^{12–18}. In addition to BMI, more precise estimates of body fat accumulation are needed given the relevance of such brain regions for neurodevelopment during adolescence and neurodegeneration during mid to late adulthood. Direct measures of actual body fat content obtained through bioelectrical impedance analysis (BIA) may provide a more accurate indicator of body composition than BMI⁷.

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	Total Sample (N = 127)	Adolescents (n = 63)	Adults (n = 64)	
Demographics	Mean ± SD	Mean ± SD	Mean ± SD	<i>p</i>
Age (years)	24.79 ± 9.60	16.37 ± 1.39	33.08 ± 6.53	<0.001
Gender (female/male)	64/63 [†]	31/32	33/31	0.793
Body Composition				
Body Fat (%)	23.46 ± 10.50	21.92 ± 10.93	25.03 ± 9.88	0.098
BMI (kg/m ²)	25.69 ± 5.15	25.12 ± 5.07	26.25 ± 5.21	0.215
UPPS-P Impulsive Behaviour Scale				
Negative Urgency	9.77 ± 2.94	10.38 ± 2.79	9.11 ± 2.97	0.019
Positive Urgency	10.07 ± 2.50	10.33 ± 2.65	9.78 ± 2.32	0.239
Sensation Seeking	10.57 ± 3.15	11.10 ± 2.95	10.00 ± 3.28	0.061
Lack of Premeditation	7.93 ± 2.29	8.33 ± 2.41	7.49 ± 2.08	0.048
Lack of Perseverance	7.28 ± 2.53	7.55 ± 2.66	6.98 ± 2.37	0.231
Total intracranial volume (mm ³)	1,430,703.49	1,474,826.27	1,3831,33.63	0.016
	± 220,186.84	± 204,734.61	± 227,832.94	

Table 1. Characteristics of the study sample by developmental age group. *Note:* SD = standard deviation; [†]denotes frequencies; kg = kilogram, m = metre.

Another aspect that remains unclear regarding the link between body fat and brain volumes across adolescence and adulthood is the influence of personality traits implicated in the vulnerability for overweight and obesity. For example, studies have consistently shown that reward sensitivity, namely, a purposeful drive to obtain rewarding stimuli¹⁹ is elevated in individuals with obesity²⁰, particularly among those with binge eating disorder²¹. In contrast, the literature on impulsivity, namely, the tendency to act without forethought²², has been more inconsistent. Specifically, different facets of impulsivity have been linked with BMI and brain volume alterations. BMI was positively associated with the facets of positive and negative urgency²³ and lack of perseverance²⁰, the latter of which was negatively correlated with grey matter volume of the anterior cingulate cortex and the insula in healthy individuals²⁴. Impulsivity has also been positively related to the volume of the striatum²⁵.

Although no structural imaging studies have examined the link between impulsivity, body fat and brain volumes, functional imaging activation studies have shown that impulsivity modulates the response of the striatum during food valuation and food choice tasks among people with overweight and obesity^{26,27}. Therefore, trait impulsivity may moderate the relationship between adiposity and the structure of brain regions implicated in reward processing and value-based decision-making (e.g., OFC, striatum). Since impulsivity encompasses different components, and excess weight has been specifically linked to emotion-related facets such as positive and negative urgency, it is also plausible to expect associations with the structure of limbic regions, such as the hippocampus and the amygdala¹⁸. In addition to the lack of structural imaging studies on facets of impulsivity, additional issues with the “body fat–brain volume literature” to date include the lack of control for confounders, such as age and gender; making it unclear which effects are attributable to adiposity rather than these confounding variables²⁸.

This study aimed to examine the relationship between body composition (i.e., percent body fat), trait impulsivity and regional brain volumes in a large cohort of adolescents and adults with healthy-weight, overweight and obesity. We used a well-validated measure of body fat and a multidimensional measure of impulsivity (the UPPS-P Impulsive Behaviour Scale), and linked them to brain volume measures of regions relevant for overweight and obesity, while controlling for potential confounders (i.e., age, gender, and total intracranial volume). Specifically, based on current neurobiological models of obesity^{5,29–31}, we were interested in the cortical and sub-cortical brain regions ascribed to inhibitory control (i.e., dorsolateral PFC [dlPFC], medial PFC [mPFC]), reward processing (i.e., OFC, ventral striatum, amygdala), habit formation and compulsive eating (i.e., dorsal striatum), and interoception (i.e., the insula). In addition, we were interested in the cerebellum, which is involved in motor and executive functions relevant to obesity^{29–31}.

We hypothesised that (i) in both adolescents and adults, % body fat would be negatively associated with regional volumes of the OFC, dlPFC, mPFC, insula, hippocampus, amygdala, cerebellum, and striatum; (ii) impulsivity would be negatively associated with striatal, limbic, and insula volumes; (iii) impulsivity would moderate the relationship between % body fat and regional brain volumes. In addition, we explored if the associations between % body fat and regional brain volumes differed between adolescents and adults.

Results

Sample Characteristics. Table 1 displays the demographic characteristics, body composition and the UPPS-P scores of the whole sample. Regional brain volumes are summarised for the whole sample (Fig. 1) and separately in adolescents and adults (Table 2).

Associations between body fat and brain volumes. *Partial correlation analyses in the regions of interest.* Figure 2 shows the scatterplot graphs of the significant partial correlation results. We found a positive correlation between % body fat and cerebellum white matter volume (left: $r = 0.247$, $p = 0.008$, right: $r = 0.251$, $p = 0.007$) and

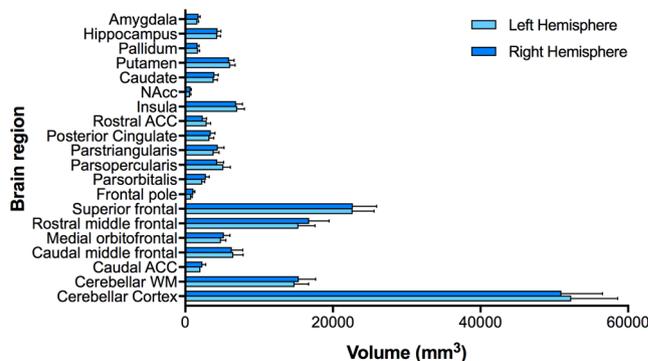


Figure 1. Regional brain volumes (mm^3) depicted separately for the left and right hemispheres (controlling for total intracranial volume).

medial OFC volume (left: $r = 0.238$, $p = 0.008$). No other correlations between % body fat and brain volumes in the regions of interest survived corrections for multiple comparisons.

Analyses by age group (adolescents versus adults): We found a positive correlation between % body fat and left nucleus accumbens (NAcc) volume in adolescents ($r = 0.353$, $p = 0.005$), but not adults ($r = 0.062$, $p = 0.634$). No other correlations survived corrections for multiple comparisons.

Regression analyses controlling for developmental and sociodemographic factors. Regional brain volumes were included in the regression models if the partial correlational analyses showed that these regions of interest were significantly associated with % body fat. Results showed that, after adjusting for ICV and sociodemographic factors, higher percent body fat was the only significant predictor of larger cerebellum white matter volume (left: $\beta = 0.247$, $p = 0.011$; right: $\beta = 0.207$, $p = 0.027$; Table 3) and left medial OFC volume ($\beta = 0.212$, $p = 0.014$).

Analyses by age group (adolescents versus adults): Results showed that, after adjusting for ICV and sociodemographic factors, higher % body fat was the only significant predictor of larger left NAcc volume in adolescents ($\beta = 0.400$, $p = 0.006$), while gender was the only significant predictor in adults ($\beta = -0.458$, $p = 0.007$). The latter finding indicates that being male was associated with a smaller left NAcc volume (Table 4).

Since % body fat may vary between males and females during adolescence, we conducted an additional sensitivity analysis to test if gender influenced the relationship between body fat and NAcc volume in the sub-group of adolescents. We used a hierarchical regression analysis: Age and ICV were entered in the first block of predictors followed by % body fat and gender in the second block. Finally, the interaction (% body fat \times gender) was entered in the third block. Results showed that the interaction between % body fat and gender was not a significant predictor of left NAcc volume, ($\beta = -0.143$, $p = 0.708$, 95% CI = -6.43 , 4.39). Thus, male and female adolescents did not show distinct correlations between % body fat and NAcc volume.

Associations between impulsivity and brain volumes. *Partial correlation analyses in the regions of interest.* Figure 2 shows the scatterplot graphs of the significant partial correlation results. We found a positive correlation between negative urgency and right frontal pole volume ($r = 0.258$, $p = 0.006$). We also found a negative correlation between positive urgency and amygdala volume (left: $r = -0.253$, $p = 0.007$, right: $r = -0.279$, $p = 0.003$). No other correlations between impulsivity and brain volumes in the regions of interest survived corrections for multiple comparisons.

Analyses by age group (adolescents versus adults): Partial correlational analyses between impulsivity and regional brain volumes were conducted separately for adolescents and adults. No correlations survived significance corrections for multiple comparisons.

Regression analyses controlling for developmental and sociodemographic factors. Regional brain volumes were included in the regression models if the partial correlational analyses showed that these regions of interest were significantly associated with impulsivity. Results showed that after adjusting for ICV and sociodemographic factors, higher positive urgency was the only significant predictor of smaller amygdala volume (Left: $\beta = -0.255$, $p = 0.011$; Right: $\beta = -0.267$, $p = 0.010$; Table 3). No other predictors of brain volumes were significant.

Impulsivity as a moderator of the relationship between body fat and brain volumes. The interaction term between % body fat and impulsivity (UPPS-P total score) accounted for a marginally significant proportion of the variance in left mOFC volume (adjusted for ICV), $b = -0.95$, $t(110) = -1.97$, $p = 0.051$. Visual inspection of the interaction plot showed that as % body fat increased, and impulsivity reduced, left mOFC volume increased (Fig. 3). Specifically, at low impulsivity, individuals with higher % body fat had larger left mOFC volumes than those with lower % body fat, $b = 20.54$, $p = 0.002$, CI [7.947, 33.136]. Similarly, at average impulsivity, individuals with higher % body fat had larger left mOFC volumes than those with lower % body fat, $b = 12.09$, $p = 0.024$, CI [1.634, 22.556]. In contrast, at high impulsivity, left mOFC volume did not significantly differ depending on % body fat, $b = 3.65$, $p = 0.614$, CI [-10.661 , 17.957]. There were no other significant interactions between % body fat and impulsivity (all p values > 0.30).

		Adolescents (n = 63)	Adults (n = 64)	p
		Mean ± SD	Mean ± SD	
Subcortical Brain Region				
Nucleus Accumbens	L	677.98 ± 100.87	617.42 ± 135.83	0.004
	R	760.27 ± 98.19	647.56 ± 112.30	<0.001
Thalamus	L	8277.14 ± 908.13	8009.12 ± 1009.43	0.109
	R	7253.26 ± 836.64	7153.55 ± 821.50	0.490
Caudate	L	3923.02 ± 478.16	3752.77 ± 508.06	0.049
	R	4070.50 ± 481.82	3835.88 ± 514.21	0.007
Putamen	L	6204.69 ± 599.75	5954.88 ± 717.78	0.031
	R	6200.62 ± 556.86	5616.06 ± 688.87	<0.001
Pallidum	L	1794.73 ± 196.53	1614.34 ± 236.84	<0.001
	R	1721.29 ± 217.48	1597.98 ± 186.01	0.001
Hippocampus	L	4380.08 ± 411.82	4286.80 ± 452.98	0.216
	R	4355.05 ± 470.60	4392.73 ± 450.70	0.639
Amygdala	L	1645.95 ± 204.70	1632.78 ± 163.16	0.684
	R	1810.15 ± 246.20	1786.57 ± 215.00	0.559
Cerebellum White Matter	L	14622.49 ± 1821.66	14996.89 ± 1988.22	0.259
	R	15473.59 ± 2350.27	15272.18 ± 2226.57	0.613
Cerebellar Cortex	L	54738.91 ± 5929.91	49640.83 ± 5596.17	<0.001
	R	52063.52 ± 5568.18	49783.18 ± 5333.28	0.017
Cortical Brain Region				
Insula	L	7269.70 ± 1033.67	6766.89 ± 862.09	0.003
	R	7018.74 ± 897.97	6730.08 ± 778.67	0.051
Rostral Middle Frontal	L	16231.07 ± 2291.25	14348.84 ± 1748.06	<0.001
	R	17825.99 ± 2512.15	15672.94 ± 2454.31	<0.001
Pars Opercularis	L	5346.42 ± 968.867	4958.05 ± 901.81	0.018
	R	4534.83 ± 895.24	4079.03 ± 795.96	0.002
Pars Triangularis	L	4083.46 ± 786.012	3577.48 ± 547.64	<0.001
	R	4647.72 ± 915.88	4130.06 ± 676.16	<0.001
Superior Frontal	L	23552.59 ± 3106.86	21715.92 ± 2345.78	<0.001
	R	24174.45 ± 3197.76	21099.92 ± 2426.01	<0.001
Rostral Anterior Cingulate	L	2971.87 ± 535.74	2787.86 ± 521.99	0.047
	R	2466.52 ± 482.18	2258.95 ± 481.53	0.014
Caudal Anterior Cingulate	L	2120.03 ± 434.86	1945.75 ± 543.26	0.042
	R	2438.57 ± 438.84	2205.83 ± 415.09	0.002
Lateral OFC	L	8269.04 ± 929.672	7666.42 ± 875.58	<0.001
	R	8285.90 ± 1070.23	7565.97 ± 945.28	<0.001
Medial OFC	L	4887.42 ± 655.82	4747.45 ± 679.16	0.264
	R	5463.80 ± 869.29	4947.30 ± 707.23	<0.001
Pars Orbitalis	L	2391.65 ± 344.449	2174.92 ± 296.07	<0.001
	R	2997.61 ± 454.91	2588.89 ± 351.73	<0.001
Frontal pole	L	833.13 ± 155.536	737.58 ± 145.48	<0.001
	R	1166.13 ± 213.39	983.67 ± 176.00	<0.001

Table 2. Regional brain volumes in mm³ (controlling for total intracranial volume) by developmental age group.

Discussion

We aimed to map the association between body fat, impulsivity and subcortical regional brain volumes in a cohort of adolescents and adults across the BMI spectrum. Our study led to several key findings. Specifically, higher percent body fat was associated with larger bilateral cerebellum white matter (WM) and left medial orbitofrontal cortex (OFC) volume in the whole sample comprising adults and adolescents, and with larger left NAcc volume among adolescents only. In addition, negative urgency was correlated with larger frontal pole volume, while positive urgency was correlated with smaller amygdala volume. Finally, we found that impulsivity moderated the relationship between percent body fat and left medial OFC volume in the whole sample.

First, we found a correlation between percent body fat and larger cerebellar WM across the whole sample comprising adults and adolescents. Our finding mirrors results from previous research that used BMI as a measure of obesity¹³ and is in line with past studies showing positive relationships in the temporal and parietal lobes^{6,32}. However, our finding is not consistent with previous studies that found a negative relationship between BMI and WM volume in the basal ganglia and corona radiata^{33,34}. Although the cerebellum has traditionally been ascribed

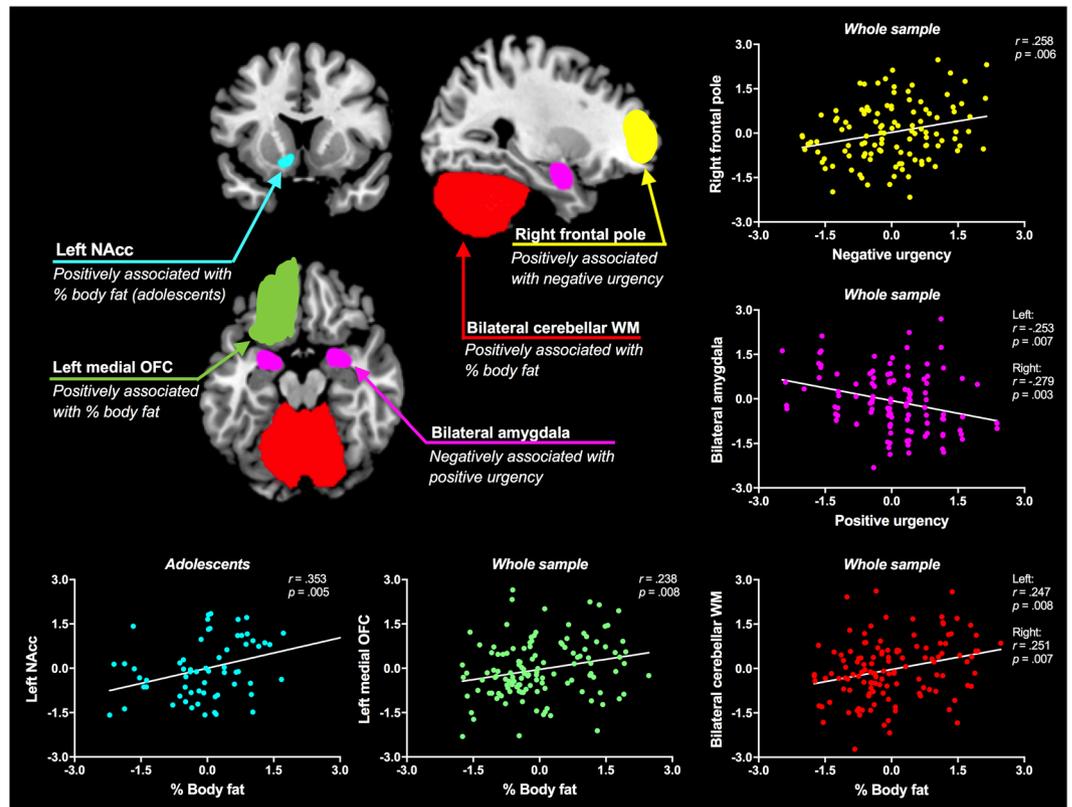


Figure 2. Scatterplot graphs illustrating the partial correlations between regional brain volumes (mm^3) and % body fat, positive urgency or negative urgency (controlling for total intracranial volume). The x-axis of each scatterplot graph represents the standardised residuals of % body fat, positive urgency or negative urgency and the y-axis represents the standardised residuals of regional brain volumes. Note: NAcc = nucleus accumbens, OFC = orbitofrontal cortex and WM = white matter.

to motor function, emerging evidence suggests that this brain region plays a key role in reward-based learning and executive control, which are compromised in obesity^{35,36}. The discrepant results across previous studies may be due to differences in sample composition. Studies that found negative correlations typically included participants from an older age group or with a wider age range than those studies that found positive correlations, including the current study.

Several mechanisms have been proposed to explain the positive relationship between adiposity and cerebellar WM volume. One possible explanation is that adiposity leads to chronic inflammation, which directly links changes in peripheral health to poorer white matter integrity, and in particular, a higher density of glial cells in the lipid-based myelin sheath^{37,38}. It may also be that increased body fat results in damage to WM, including higher WM hyperintensities as shown on hippocampal volume in clinical populations with obesity³⁹. Future studies should aim to examine the specific mechanism underlying the relationship between larger cerebellar WM volume and adiposity using advanced MRI techniques such as diffusion tensor imaging (DTI) to assess obesity-related changes in the microstructure of WM.

Second, percent body fat was positively correlated with the volume of the medial OFC; a brain region implicated in reward processing of food cues. Our finding is consistent with some previous research that has found a positive relationship with BMI as a proxy for obesity^{10,14}, but not with other studies that have shown a negative relationship^{32,40}. Furthermore, we also found that the positive association between body fat and left medial OFC volume was moderated by impulsivity. Specifically, among individuals with lower impulsivity, those with higher body fat had larger medial OFC volumes than those with lower body fat. In contrast, among individuals with higher impulsivity, body fat did not significantly predict left medial OFC volume. The finding that impulsivity moderates the association between body fat and medial OFC volume may contribute to explaining the discrepant findings reported in previous studies (i.e., positive versus negative associations between adiposity and medial OFC volume). Previous findings support the idea that the medial OFC plays a key role in the pathophysiology of obesity, particularly in the preference and anticipation of reward⁴¹. Importantly, we extend upon previous findings by showing that the association between excess body fat and brain regions implicated in obesity differs depending on personality traits (i.e., impulsivity). Thus, future studies examining the association between adiposity and brain volumes should consider the role of trait impulsivity.

Our results also showed a correlation between percent body fat and NAcc volume in adolescents, but not adults. This finding is in line with the role of the NAcc in reward processing, specifically, the experience of reward⁴². Previous research has shown that NAcc volumes are positively correlated with another measure of

Predictor	Cerebellum WM (left)				Cerebellum WM (right)				Amygdala (left)			
	β	<i>p</i>	95% CI		β	<i>p</i>	95% CI		β	<i>p</i>	95% CI	
			LB	UB			LB	UB			LB	UB
Age	0.060	0.741	-59.091	82.782	0.039	0.821	-72.460	91.185	-0.056	0.760	-8.049	5.898
Age Group	0.104	0.559	-942.422	1734.605	0.009	0.957	-1501.720	1586.138	0.067	0.712	-106.982	156.184
Gender	-0.155	0.077	-1239.546	64.943	-0.137	0.104	-1374.218	130.465	0.060	0.494	-41.937	86.301
Body Fat (%)	0.247	0.011	10.388	79.336	0.207	0.027	5.294	84.823	0.100	0.303	-1.620	5.158
UPPS-P NU	0.067	0.502	-84.012	170.499	0.091	0.344	-76.381	217.188	0.085	0.396	-7.131	17.889
UPPS-P PU	-0.130	0.182	-246.190	47.378	-0.133	0.157	-291.063	47.557	-0.255	0.011	-33.353	-4.494
	Amygdala (right)				Medial OFC (left)				Frontal Pole (right)			
Age	-0.024	0.899	-9.643	8.485	0.080	0.621	-16.606	27.673	-0.165	0.333	-11.263	3.853
Age Group	-0.024	0.897	-182.262	159.799	-0.073	0.647	-514.563	320.936	-0.190	0.257	-224.605	60.634
Gender	-0.048	0.598	-105.560	61.123	0.026	0.738	-169.144	237.986	-0.125	0.129	-123.107	15.887
Body Fat (%)	0.109	0.281	-1.997	6.813	0.212	0.014	2.743	24.262	0.067	0.456	-2.285	5.061
UPPS-P NU	0.002	0.988	-16.136	16.384	-0.105	0.236	-63.594	15.839	0.145	0.123	-2.939	24.179
UPPS-P PU	-0.267	0.010	-43.435	-5.924	0.057	0.514	-30.683	60.940	0.055	0.546	-10.860	20.420

Table 3. Summary of multiple regression analyses including sociodemographic variables, % body fat, impulsivity and brain volumes (mm^3). Note: β -values reflect ICV-adjusted predictions of regional brain volumes; bold values denote significance $p < 0.05$; WM = white matter; LB = lower bound of 95% confidence interval (CI), UB = upper bound of 95% CI; UPPS-P NU = negative urgency subscale of the UPPS-P Impulsive Behaviour Scale; UPPS-P PU = positive urgency subscale of the UPPS-P Impulsive Behaviour Scale.

Predictor	Adolescents				Adults			
	β	<i>p</i>	95% CI		β	<i>p</i>	95% CI	
			LB	UB			LB	UB
Age	0.157	0.208	-6.486	29.170	-0.224	0.074	-9.765	0.459
Gender	0.013	0.937	-62.477	-67.626	-0.458	0.007	-211.464	-35.648
Body Fat (%)	0.400	0.006	1.090	6.293	0.210	0.144	-1.016	60.779

Table 4. Multiple regression analyses including sociodemographic variables, % body fat and left NAcc volume (mm^3) by developmental age group.

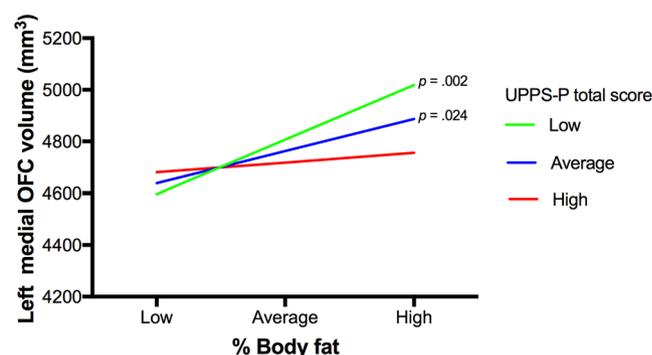


Figure 3. Line graph showing the moderating effect of impulsivity (total UPPS-P score) on the relationship between % body fat and left medial orbitofrontal (OFC) volume (mm^3) controlling for total intracranial volume. Values for % body fat and total UPPS-P scores are depicted at low (-1SD), average, and high ($+1\text{SD}$) levels of the predictor variables.

obesity, namely, BMI in adults^{12,14,17}, but here we provide the first evidence of this association among adolescents using body fat as an indicator of obesity. A potential explanation for the discrepancy between current and previous findings may be differences in developmental stages, as neuroscience evidence suggests that the adolescent developmental period is linked to rapid maturation of the reward system⁴³. Recent research in children demonstrates that responsivity to food advertisements and higher NAcc volume are associated with genetic risk for obesity and higher percent body fat, which suggests that larger NAcc volume is a vulnerability factor in obesity⁴⁴. The NAcc also supports the early formation of unhealthy eating behaviours due to a combination of enhanced

reward-related sensitivity in the striatum and delayed development of the prefrontal cortex⁴⁵. The positive link between adiposity and volume in the NAcc may be explained by increased signalling of adipose tissue to the brain^{12,14}. Taken together, the findings suggest that larger NAcc volume in adolescents with increased body fat may contribute to altered reward-related cue processing. Although not the main focus of our paper, our finding that gender predicted striatal volume in adults, in particular, that women have larger left NAcc volume, supports existing research showing that women have larger dorsal striatum (putamen) and dorsolateral prefrontal cortex volumes¹⁴. Overall, these findings provide evidence for age and gender-related differences in the structure of brain regions involved in habit learning, executive control, and reward processing.

Positive urgency was negatively associated with amygdala volume, and negative urgency was positively associated with frontal pole volume independent of adiposity and developmental stage. The inverse association between positive urgency and amygdala volume has also been shown in individuals with addiction (e.g., cocaine dependence and pathological gambling)⁴⁶. The amygdala plays an important role in reward and emotion processing and is a key component of the corticostriatal circuit, comprising the OFC, anterior cingulate cortex, insula and striatum, which is altered in obesity^{5,41,47,48}. Thus, smaller amygdala volumes might predate higher trait impulsivity and reward sensitivity, and confer vulnerability to obesity, but longitudinal studies are needed to test this notion⁴⁶. The direct association between negative urgency and frontal pole volume - a region implicated in the integration of cognitive and affective information⁴⁹, is consistent with previous research that found a positive association between frontal pole volume and delay discounting⁵⁰. Importantly, our finding provides evidence that the frontal pole is involved not only in behavioural impulsivity (i.e., delay discounting), but also trait impulsivity (i.e., negative urgency). Nevertheless, in other studies, higher trait impulsivity has been linked to smaller PFC brain regions (i.e., the frontal gyrus and orbitofrontal cortex)⁵¹. However, the latter study included only healthy adolescents, while we included both adults and adolescents with a wide range of adiposity. The discrepant finding could also be explained by the use of different measures of impulsivity, namely, the UPPS-P or the Barratt Impulsiveness Scale.

Interestingly, percent body fat and trait impulsivity were associated with volumes of distinct and overlapping regional brain areas, which indicates that several brain regions are implicated in obesity independent of impulsivity. Similarly, recent neuroimaging research has shown that BMI and impulsivity are differentially associated with regional brain volumes, namely, the amygdala and hippocampus versus the frontal gyrus, respectively⁵². Alternatively, it has been proposed that eating-specific impulsivity constructs, such as uncontrolled eating, may show overlapping alterations with obesity and impulsivity, but more markedly so with obesity. This idea is supported by consistent findings that BMI is moderately, positively correlated with eating-specific impulsivity as measured by self-reported uncontrolled eating^{53,54}, but weakly associated with general impulsivity^{52,55}. In addition, eating-specific impulsivity (uncontrolled eating) has been shown to mediate the relationship between general impulsivity and obesity (BMI), suggesting that brain volume alterations relate to differences in general impulsivity, which indirectly affect BMI through eating-specific impulsivity⁵². Future neuroimaging studies should measure both general and eating-specific impulsivity to disentangle their independent and shared contribution to the pathophysiological mechanisms of obesity.

Our findings of observed correlations between percent body fat and regional brain volumes (i.e., cerebellar, medial OFC) extend previous neuroimaging work in several important ways. First, we used percent body fat as a more proximal measure of excess weight compared to BMI and waist-to-hip ratio used in previous work, which allows us to make more sensitive assessments of the pathophysiology of obesity⁷. Second, we controlled for important confounders such as total ICV, which was not accounted for in numerous previous studies. Third, we carefully examined the role of age by stratifying our analyses using sample ages as cut-offs, and via controlling for age in overall group analyses.

Despite the above strengths, the current study has several limitations. First, the cross-sectional design prevents the determination of whether regional brain alterations precede or follow obesity and impulsivity. Nevertheless, as impulsivity is a trait measure, it likely precedes obesity, which is supported by both preclinical⁵⁶ and clinical⁵⁷ research. However, longitudinal designs are required to establish cause and effect relationships between body fat and brain structural alterations. Second, the different MRI data pre-processing steps, analysis methods, toolboxes (and the specific versions) and metrics (i.e., grey matter density, volume, cortical thickness) used between the current study (i.e., Freesurfer version 4.1.0, volumes) and past studies may have contributed to the inconsistent results. One minor limitation of the Freesurfer toolbox is that it only computes WM for the cerebellum and total cortical volume. Third, we used percent body fat as a proximal indicator of body composition, but we did not measure Fat Free Mass (FFM) as it is typically measured using a different technique, namely, dual energy x-ray absorptiometry (DXA) scans. However, FFM is also increased in obesity and has been shown to have differential effects on brain structure to fat mass and percent body fat⁵⁸. Fourth, we controlled for a number of potential confounders (i.e., age, gender, ICV), except for 'Years of education', which reflects distinct underlying constructs in adolescents versus adults. Specifically, in adolescents, education should be mainly predicted by age, while in adults, education should more closely reflect intelligence. Thus, the 'Years of Education' variable was removed to run more comparable analyses in adolescents and adults. Finally, this study allowed for an exploratory cross-sectional comparison of adults and adolescents, which revealed emerging effects linked to developmental stage. Nevertheless, longitudinal, repeated-measures studies are also required to determine individual developmental trajectories of body fat, personality and neuroanatomical fluctuations across the lifespan.

In summary, aside from the above limitations, we demonstrated a positive association between accumulation of body fat and the volume of cerebellar, frontal and striatal brain regions; the latter specific to adolescents, and a novel association between impulsivity and frontal and amygdala volumes in a relatively large cohort of community-recruited participants. The current findings are adequately controlled and representative of the body fat-brain health association in the general population.

Methods

Participants. The sample comprised 127 individuals (50.4% female) aged between 14 and 45 years with a wide range in SES (monthly income: <600€ to >2500€). BMI values spanned the three intervals of the continuum, that is, normal weight ($n = 65$, 51.2%), overweight ($n = 34$, 27%), and obese ($n = 28$, 22%) based on cut-offs from the International Obesity Task Force (IOTF) for adolescents⁵⁹ and the World Health Organisation (WHO) for adults³. Given the association between developmental stage, body composition, and brain volumes, participants were classified as either adolescents ($n = 63$, age range: 14–19 years) or adults ($n = 64$; age range: 25–45 years), based on a standard definition of adolescence (i.e., 11–19 years)⁶⁰, which resulted in equal numbers of participants in the two groups.

The sample includes participants from the projects BRAINOBE, INTEROBE and NEUROECOB, conducted between 2010 and 2015, of which we have previously reported findings for functional MRI^{23,61,62}. Participants were recruited from the general community and from specialised services of the University Hospital “Virgen de las Nieves” in Granada, Spain, as well as schools located in the same geographical area (adolescents with normal weight). The inclusion criteria were as follows: (i) aged between 12 and 45 years old; (ii) absence of history or current eating disorder, assessed by the Eating Disorder Inventory (EDI-2); (iii) absence of history or current neurological or psychiatric disorders (including depression and substance-related disorders), as assessed by participant or participant/parent (for adolescents) interviews based on DSM-IV criteria; (iv) no contraindications to MRI (Magnetic Resonance Imaging) scanning (including claustrophobia and implanted ferromagnetic objects); (v) absence of significant abnormalities on MRI; and (vi) absence of history of brain injury involving loss of consciousness for longer than 5 minutes. All participants had normal or corrected-to-normal vision. For participants under 18 years of age, we obtained consent from a parent and/or legal guardian and assent from participants. The study was approved by the Human Research Ethics Committee of the University of Granada (ethics approval number: 1792/10).

Measures. *Body composition.* A Body Composition Analyser (TANITA SC-330 Scale) was used to measure percent body fat (total body fat/total mass) with bioelectrical impedance analysis (BIA). This method has been shown to provide reliable and valid measures of fatness as illustrated by stronger associations between MRI measurements and BIA than between MRI measurements and waist circumference or BMI⁶³.

UPPS-P Impulsive Behaviour Scale. The UPPS-P⁶⁴ is a 59-item questionnaire designed to measure five distinct personality facets associated with impulsive behaviour: negative urgency, lack of perseverance, lack of premeditation, sensation seeking, and positive urgency. Urgency (26 items) refers to the tendency to experience strong impulses under conditions of negative affect (negative urgency – 12 items) or positive affect (positive urgency – 14 items); (lack of) perseverance (10 items) refers to the individual’s ability to remain focused on a task that may be boring or difficult; (lack of) premeditation (11 items) refers to the tendency to think and reflect on the consequences of an act before engaging in that act; and finally, sensation seeking (12 items) incorporates two aspects: (a) a tendency to enjoy and pursue activities that are exciting and (b) an openness to trying new experiences that may or may not be dangerous. Each item on the UPPS-P is rated on a four-point scale ranging from 1 (strongly agree) to 4 (strongly disagree). Total scores were obtained for each of the five UPPS-P facets, with higher scores indicating higher levels of impulsivity.

MRI Data Acquisition and Processing. Participants were scanned with a 3T Phillips Achieva X-series scanner at Centro Diagnostico Granada in Spain. For each participant, a 3D volume was acquired using a T1-weighted turbo-gradient-echo sequence (3D-TFE) in the sagittal plane, with a $0.94 \times 0.94 \times 1.0$ mm resolution (160 slices, FOV = 240×240 mm², matrix 256×256), TR = 8.3 ms, TE = 3.8 ms, and flip angle = 8°). MRI images were transferred to a Linux workstation for pre-processing and regional brain volumes were extracted using the automated FreeSurfer image analysis suite version 4.1.0 (<http://surfer.nmr.mgh.harvard.edu/>). The automated FreeSurfer pipeline included motion correction⁶⁵, non-uniform intensity normalisation (N3) at 500 iterations to correct for intensity non-uniformity artefacts (increased from the default number of iterations of 4)⁶⁶, automated Talairach transformation, removal of non-brain tissue⁶⁷, and parcellation of neuroanatomical measures, which were extracted for further statistical analysis.

Statistical Analyses. Data was analysed using the Statistical Package for the Social Sciences version 25 (SPSS; Chicago, IL, USA). All variables met assumptions for multiple regression, including linear independence of predictors as assessed by the Durbin-Watson statistic (range = 1.89 to 2.12). We also found adequate levels of collinearity between predictors as assessed by tolerance (range = 0.22 to 0.97) and VIF values (range = 1.02 to 1.34). Homoscedasticity was assessed via visual inspection of scatterplots (residuals versus predicted values). The variance and co-variance matrices were assessed to check whether the predictors were correlated. BMI and % body fat were highly correlated ($r = 0.696$, $p < 0.001$). For this reason, we included % body fat, but not BMI, in the regression models as we were interested in the former as it is a more proximal measure of body composition⁷. Furthermore, we assessed correlations between the continuous socio-demographic variables (i.e., age, SES) and the brain regions of interest. We found that SES was not significantly correlated with any of the brain volumes of interest (all p 's > 0.05). Thus, SES was not included in the regression analyses to increase power.

We restricted our analyses to cortical (i.e., insula, OFC, PFC [medial and dorsolateral]) and subcortical (i.e., striatum, hippocampus, amygdala, and cerebellum) brain regions that have been previously associated with body fat and/or impulsivity. Additionally, white matter estimates were available for the cerebellum and total cortical volume. First, to examine which cortical and subcortical brain regions were associated with body composition and/or impulsivity, we ran partial correlations between brain volumes, % body fat and UPPS-P impulsivity facets (negative urgency, positive urgency, sensation seeking, lack of premeditation, lack of perseverance) controlling for

ICV²⁸. Second, we ran hierarchical regression analyses with % body fat and impulsivity as predictors and volumes of the brain regions linked to adiposity and/or impulsivity as dependent variables, controlling for confounders (i.e., ICV in Step 1, and in Step 2, age, developmental age group, and gender). We run these analyses in both the whole sample and each developmental group separately. In the latter case, we did not include age group as a predictor. For partial correlations, the significance threshold was set at $p < 0.01$ to protect against Type I error due to multiple comparisons. For regression analyses, $p < 0.05$ was considered significant.

Finally, we conducted four hierarchical multiple regression analyses via the SPSS macro PROCESS⁶⁸. These analyses tested the hypothesis that impulsivity moderates the association between % body fat and brain volumes for those regions that were significantly associated with body fat in the partial correlations (i.e., bilateral cerebellum WM, left mOFC, and left NAcc). For each analysis, % body fat was a predictor, UPPS-P total score was the moderator, brain volumes were the dependent variables, and ICV was a covariate. The continuous variables (i.e., % body fat, UPPS-P total score and ICV) were centered to avoid high multicollinearity. We created a product term between impulsivity and % body fat to examine the interaction. To estimate the conditional effects, 5,000 bootstrap samples were used.

Compliance with Ethical Standards. Research involving Human Participants and/or Animals: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study and/or their legal guardians.

Data Availability

The datasets generated during and/or analysed during the current study are available in the figshare repository, <https://figshare.com/>.

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Acknowledgements

This study has been funded by project grants from the Andalusian Health Service (Consejería de Salud) [PI 0416/2008 (BRAINOBE) and P-10-HUM-6635 (NEUROECOBEBE)] and the Spanish Ministry of Innovation and Science (MICINN) [PSI2010-17290 (INTEROBE)] awarded to Dr Verdejo-García.

Author Contributions

N.K. analysed the data; N.K. wrote the paper; N.K., V.L., K.C. and A.V.-G. had primary responsibility for final content. All authors read and approved the final manuscript.

Additional Information

Supplementary information accompanies this paper at <https://doi.org/10.1038/s41598-019-38846-7>.

Competing Interests: The authors declare no competing interests.

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