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# Body weight-related alterations in white matter functional connectivity in children: An fMRI study

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## Abstract

**Background** Childhood obesity is linked to altered brain functional connectivity (FC) in brain gray matter (GM), with potential implications on changes in cognition function. This study investigates white matter – white matter (WM-WM) and WM-GM FC differences between children with normal-weight (NW) and overweight/obese (OW/OB) using functional Magnetic Resonance Imaging (fMRI).

**Methods** Resting-state fMRI data from 68 children aged 10–12 years (32 OW/OB, 36 NW) were analyzed. FC matrices were constructed using predefined WM and GM region of Interest (ROI). Group differences and correlations with body mass index (BMI) were analyzed using t-test and Pearson correlation.

**Results** The OW/OB group exhibited increased WM-WM FC between the middle cerebellar peduncle (m.CBLP) and right uncinate fasciculus (r.UF), which was also positively correlated with BMI ($R = 0.47$, $p = 0.0001$). Meanwhile, reduced WM-GM FC was observed between the body of the corpus callosum (b.CC) and right dorsolateral prefrontal cortex (r.DLPFC), which was also negatively correlated with BMI ($R = -0.44$, $p = 0.0002$).

**Conclusions** Our findings suggest that childhood obesity is associated with changes in WM-WM and WM-GM FC, potentially impacting motor coordination (via m.CBLP-r.UF) and executive function (via b.CC-r.DLPFC), contributing to cognitive regulation differences.

**Keywords** fMRI, White matter, Functional connectivity, Obesity, Adolescents

## Introduction

Obesity has become a major public health concern worldwide. The prevalence of childhood obesity has risen significantly over the past few decades [1, 2]. In addition to increased risk of many other health conditions, childhood obesity may also impact the normal development of brain structure and function, potentially impairing cognitive function and emotional regulation [3–5].

Functional magnetic resonance imaging (fMRI) is a useful tool for studying the effects of obesity on brain function, which can capture brain activity during different tasks or stimuli, and can provide detailed information on brain functional connectivity [6, 7]. Recent

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neuroimaging studies have shown that obesity is associated with alterations in brain function, particularly in the fronto-mesolimbic system, which governs reward processing and self-regulation [7–10]. These findings indicate the potential of fMRI in uncovering the complex neural mechanisms associated with obesity and offer important insights for developing targeted interventions.

Current fMRI research on obesity primarily focuses on the brains cortical and subcortical gray matter regions, revealing associations between obesity and functional abnormalities in these areas [6–8, 11]. For example, our previous study used fMRI scans to compare brain activation in normal-weight and obese children (ages 8–10) while viewing high-calorie food images, finding that normal-weight children showed stronger activation in memory-related regions (posterior parahippocampal gyrus) and cognitive control regions (dorsomedial prefrontal cortex) [12]. Most research on potential effects of obesity on brain white matter utilized diffusion magnetic resonance imaging (dMRI) [13, 14]. For example, a meta-analysis by Daoust et al. provides strong evidence that obesity is associated with reduced white matter integrity, particularly in the genu of the corpus callosum, which connects frontal regions involved in executive function [14]. In recent years, there has been a notable increase in fMRI studies in white matter, an area that was historically less explored in functional neuroimaging [15, 16]. Gore and Ding et al. have demonstrated that white matter tracts are actively involved in functional connectivity, challenging the traditional view of white matter as merely passive conduits for signal transmission [16–21]. These studies have shown that white matter can exhibit synchronous activity during both resting states and task performance, which has important implications for understanding brain function in health and disease. Moreover, research led by D'Arcy and colleagues has revealed white matter functional signals should not be dismissed as noise as they are related to brain functional activation [22–25]. Research has shown that task performance or pathological conditions can influence or alter white matter functional signals [26–28]. These studies suggest that the white matter signal of fMRI data plays a more dynamic role in cognitive processes than previously understood.

Recent work has established that BOLD signals in white matter (WM) are physiological, stimulus-locked, and reproducible, with hemodynamic characteristics that differ from those of gray matter (GM), including smaller amplitude, a delayed peak, and a prolonged initial dip [29, 30]. These WM signals exhibit clear neurovascular coupling and reflect synchronous activity across distributed axonal pathways. Moreover, WM functional connectivity (FC) is strongly constrained by the underlying structural connectivity (SC) of fiber tracts, as demonstrated by diffusion tractography and intracranial electrophysiology, yet the correspondence is not strictly one-to-one [31]. Differences in tract architecture, brain state, and individual variability can influence the strength and topology of WM FC. This converging evidence supports the biological relevance of WM FC derived from fMRI and provides an important context for interpreting the present study's WM–WM and WM–GM connectivity findings.

Converging evidence suggests that stronger WM–WM or WM–GM FC generally reflects greater inter-areal synchrony and communication efficiency along the supporting pathways, whereas reduced FC can indicate impaired conduction or desynchronization, often arising from microstructural compromise or neuro-glio-vascular changes [32]. At the same time, WM–GM FC can increase in a compensatory fashion when alternative loops (e.g., cerebello–thalamo–cortical or fronto-limbic circuits) are up-weighted to maintain cognitive or motor control. These patterns have been linked to downstream effects on executive function, interhemispheric communication, and sensorimotor integration, thereby offering an interpretive framework for the relevance of WM–WM and WM–GM connectivity changes to cognition and behavior.

Given the reported association between childhood obesity and specific changes in white matter microstructures, we hypothesize that significant alterations in white matter fMRI signals may also occur in children with overweight/obesity. Specifically, we aim to (1) identify brain regions with significant differences in WM-WM FC between children with overweight/obesity and children with normal weight and investigate the relationship between BMI and WM-WM FC; and (2) compare the WM-GM FC between groups and its relationship with BMI. The significance of this study lies in expanding the scope of research on the impact of childhood obesity on brain development, moving from traditional GM FC studies to the domain of WM FC based on fMRI data. This provides new insights into how childhood body weight status may impact brain function.

## Materials and methods

### Participants

All study procedures were approved by the Institutional Review Board of the University of Arkansas for Medical Sciences, and assents/consents were obtained from the participants/guardians. School age children were recruited for this study at the Arkansas Children's Nutrition Center. Participants with BMI above the 85th percentile were categorized as OW/OB, while children with BMI between the 5th and 85th percentile were categorized as NW. Exclusion criteria included: full-scale intelligence quotient < 80 on the Wechsler Abbreviated Scale of Intelligence (Second Edition); taking medications or

having chronic illnesses or disorders that may independently affect brain development; implant or other foreign object in the body which may be an MRI safety concern; and dental work which may cause artifacts in MRI. Those who were not able to complete the MRI scan and/or did not have valid structural and functional images were also excluded. A total of 68 participants were included in this study, including 32 children in the OW/OB group and 36 children in the NW group. The demographic information of the research subjects is summarized in Table 1.

#### MRI data acquisition

All children underwent an MRI examination of the brain on a Siemens Prisma 3T scanner at the Arkansas Children's Hospital, Department of Radiology. A 20-channel head coil was used. The MRI protocol included a high resolution MPRAGE 3D T1-weighted brain structural scan using with the following parameters: TR 2400 ms, TE 2.24 ms, 1 average, voxel size 0.8*0.8*0.8 $mm^3$, 8° flip angle, turbo factor 256, 208 sagittal slices; and a resting-state fMRI scan for functional imaging with TR 800ms, TE 37ms, voxel size 2*2*2 $mm^3$, matrix size 104*104, 72 axial slices, multi-band factor 8, and 420 dynamics in both AP and PA direction (when possible), corresponding to approximately 5.6 min per direction. For the present analyses, we used the AP run because of high incidence of missing PA data and discarded the first five volumes to allow for magnetic field stabilization, leaving 415 volumes (≈5.5 min) for preprocessing and subsequent connectivity analyses. The participants were instructed to close their eyes but do not fall asleep during the fMRI scan.

#### MRI data preprocessing

The brain structural and functional images were preprocessed by the fMRIPrep toolbox [33], which includes tools from FSL [34], AFNI [35], and ANTs [36]. The pipeline in our study includes (1) head motion correction; (2) slice timing correction; (3) correction for susceptibility distortions induced by magnetic field inhomogeneity and multi-band EPI; (4) co-registration of the functional data to the structural image, then normalize the structural image, as well as the functional data, to the MNI standard space. The fMRI data were partitioned into white matter and gray matter volumes using the T1-weighted segmentation. To minimize partial-volume contamination from adjacent tissues, the WM mask was restricted to voxels with a T1-derived WM probability greater than 0.8. Spatial smoothing was then performed only within this WM mask using a 4 mm full-width-at-half-maximum (FWHM) Gaussian kernel. Global signal regression was not applied, in order to preserve the relative BOLD fluctuations across WM and GM compartments. Head motion for all participants was carefully inspected, and only datasets with maximal frame-wise translation < 3.0 mm and maximal rotation < 3° across all volumes were retained. The six rigid-body motion parameters and their temporal derivatives were regressed out immediately prior to temporal band-pass filtering to further reduce motion-related artifacts. After that further de-spiking and filtering of the data were performed, with a passband between 0.01 and 0.10 Hz.

#### Functional connectivity analysis

We analyzed the fMRI data from the OW/OB and NW groups and extracted regions of interest (ROIs) for constructing WM-WM FC and WM-GM FC, respectively. Specifically, based on the preprocessed MRI data, we defined 48 WM ROI regions using the JHU white matter atlas [37] and identified 84 GM ROI regions using the Brodmann atlas. Abbreviations for WM bundles are listed in Supplementary Table S1. We utilized Brodmann atlas regions 1 to 47, excluding regions 12, 14, 15, 16, and 26. In total, there are 42 pairs, resulting in 84 brain regions. We then extracted the average time series signals for each ROI and calculated the Pearson correlation coefficients between each pair of ROIs. The WM-WM FC matrix (48*48) was constructed based on the average time series from 48 WM regions. Similarly, the WM-GM FC matrix (48*84) was constructed from each pair of WM ROIs and GM ROIs [17].

We conducted independent t-tests to compare the WM–WM FC matrices between the two groups to identify brain regions with FC differences. The potential confounding effects of sex and age were regressed out. Additionally, we further analyzed the Pearson correlation between WM–WM FC and BMI for the 68 subjects (also with the effects of sex and age regressed out) to examine whether there is a linear relationship between WM–WM FC and BMI. A similar scheme was applied to compare the WM-GM FC matrices of the two groups and to analyze the correlation between WM-GM FC and BMI.

Multiple comparisons correction: To correct for multiple comparisons, we adopted a heuristic false-positive control strategy that has been widely used in previous fMRI functional-connectivity studies [34–38].

**Table 1** Demographic information of subjects included in this study

| Group | Age(mean) | Age (std) | Age (range) | Sex | Hispanic | Non-Hispanic |
|---|---|---|---|---|---|---|
| OW/OB | 11.1 | 0.6 | 9.5–12.1 | 16 M/16F | 7 | 25 |
| NW | 10.7 | 0.7 | 9.5–11.7 | 15 M/21F | 3 | 33 |

*NW* Normal-weight, *OW/OB* Overweight/obese

Specifically, the significance threshold was set at p < (1/N), where N is the number of nodes (ROIs) included in the network analysis, rather than the total number of edge-wise comparisons. This yielded the following thresholds in our data: $p < 0.0208$ for WM–WM ($N = 48$ WM nodes), $p < 0.0119$ for GM–GM ($N = 84$ GM nodes), and $p < 0.0076$ for WM–GM ($N = 48 + 84 = 132$ nodes). This method has been explicitly adopted in the previous literature to balance false-positive control and statistical sensitivity in large network analyses [38–42].

Power analysis: We also performed a sensitivity-based power analysis using G*Power to evaluate whether the current sample size ($n = 68$; 32 OW/OB and 36 NW) provided adequate power to detect the observed effects. Using the above thresholds ($p < 0.0208$ for WM–WM, $p < 0.0119$ for GM–GM, and $p < 0.0076$ for WM–GM), our analysis indicated that this sample size yields 80% power (two-tailed) to detect correlations of $|r| \geq 0.33$–0.36 and group differences with Cohen's $d \geq 0.73$–0.80. The observed effects in this study (e.g., the m.CBLP–r.UF correlation with BMI, $r = 0.47$, $p = 0.0001$; the b.CC–r.DLPFC correlation, $r = -0.44$, $p = 0.0002$) exceeded these thresholds and thus were sufficiently powered (> 90%).

## Results

### WM-WM FC between the OW/OB and NW groups

Figure 1 shows the mean WM-WM FC for OW/OB and NW groups, with each cell representing a mean group correlation coefficient between WM ROIs. To explore the differences in WM-WM FC between the two groups, we performed independent t-test on each WM-WM FC value. To account for multiple comparisons, the significance threshold was set at p < (1/N), and N denotes the total number of comparisons. A significant difference was observed in the fFC between the middle cerebellar peduncle (m.CBLP) and the right uncinate fasciculus (r.UF), with $p = 0.0003$. A corresponding boxplot illustrating this difference is shown in Fig. 2. A Pearson correlation analysis revealed a significant positive association between m.CBLP-r.UF FC and BMI ($R = 0.47$, $p = 0.0001$), and A scatter plot depicting this correlation is presented in Fig. 3.

### WM-GM FC between the OW/OB and NW groups

The mean WM-GM FC for the OW/OB and NW groups is presented in Fig. 4, where each cell represents the mean group correlation coefficient between a WM ROI and a GM ROI. To examine the differences in WM-GM FC between the two groups, we conducted independent t-tests for each WM-GM FC value. A significant difference was observed in the FC between the body of the corpus callosum (b.CC) and the right Brodmann area 46 (also known as the right dorsolateral prefrontal cortex, r.DLPFC), with $p = 0.0002$. A corresponding boxplot illustrating this difference is shown in Fig. 5. In addition, the WM-GM FC between the b.CC and r.DLPFC exhibited a significant negative correlation with BMI ($R = -0.44$, $p = 0.0002$). A scatter plot visualizing this correlation is shown in Fig. 6.

To complement the WM-based analyses, we also constructed a conventional GM–GM FC matrix using the same participants, preprocessing, and statistical framework (see Supplementary Methods and Figures S1–S3). BA35.L–BA34.R (left perirhinal cortex – right piriform cortex) showed a significant group difference (age/sex-adjusted $p = 0.0002$) and was positively correlated with BMI (partial $R = 0.41$, $p = 0.0007$). Connectivity was higher in the OW/OB group compared to the NW group, consistent with the positive BMI association.

## Discussion

Our study leveraged resting-state fMRI data from 68 children to explore alterations in WM-WM and WM-GM functional connectivity associated with BMI. We performed independent t-tests to assess group differences in connectivity and conducted Pearson correlation analyses

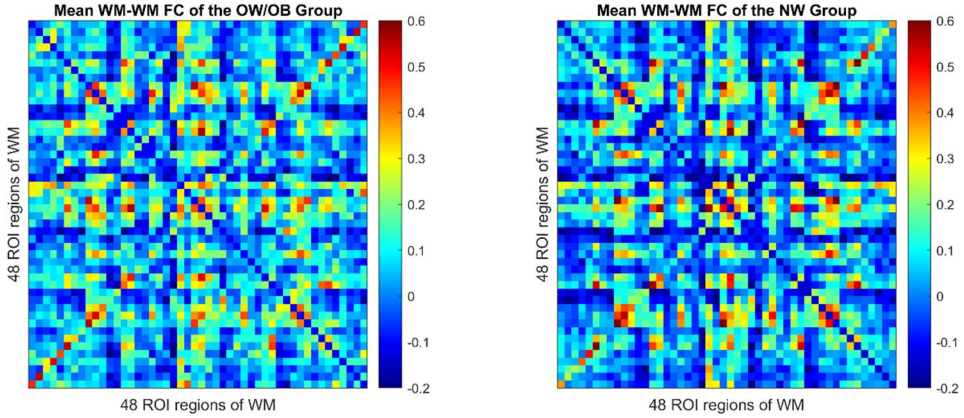


**Fig. 1** The mean WM-WM FC Patterns in (left) the OW/OB group and (right) the NW group. Each cell of this FC matrix represents the mean Pearson correlation coefficient of the time series between two WM ROIs

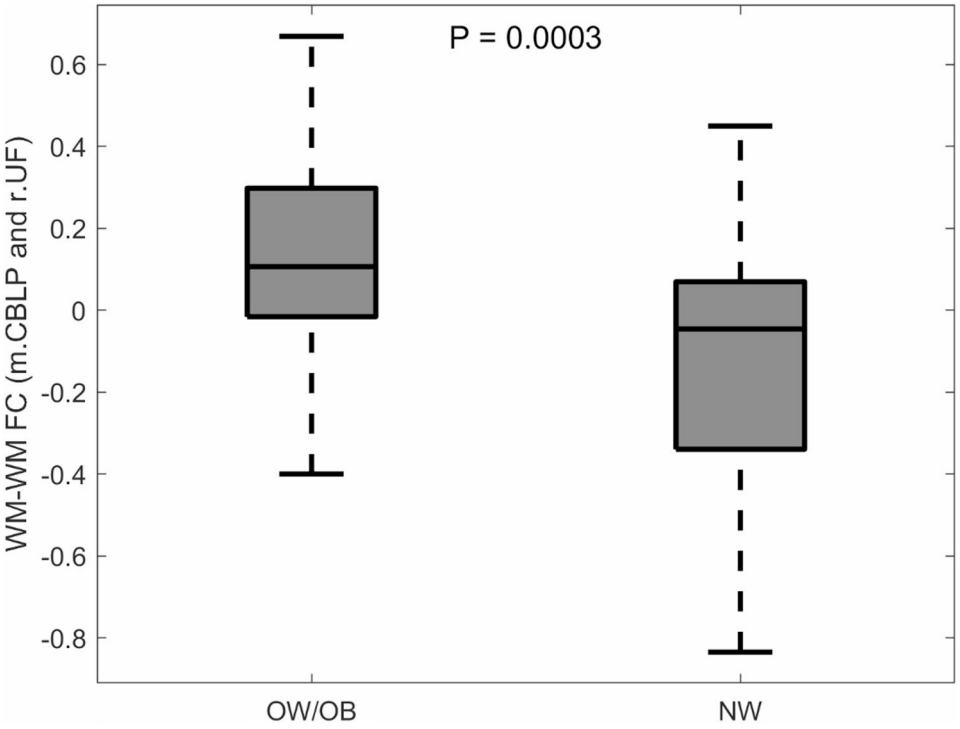


**Fig. 2** Comparison of WM-WM FC between OW/OB and NW Groups. Middle cerebellar peduncle (m.CBLP); right uncinate fasciculus (r.UF)

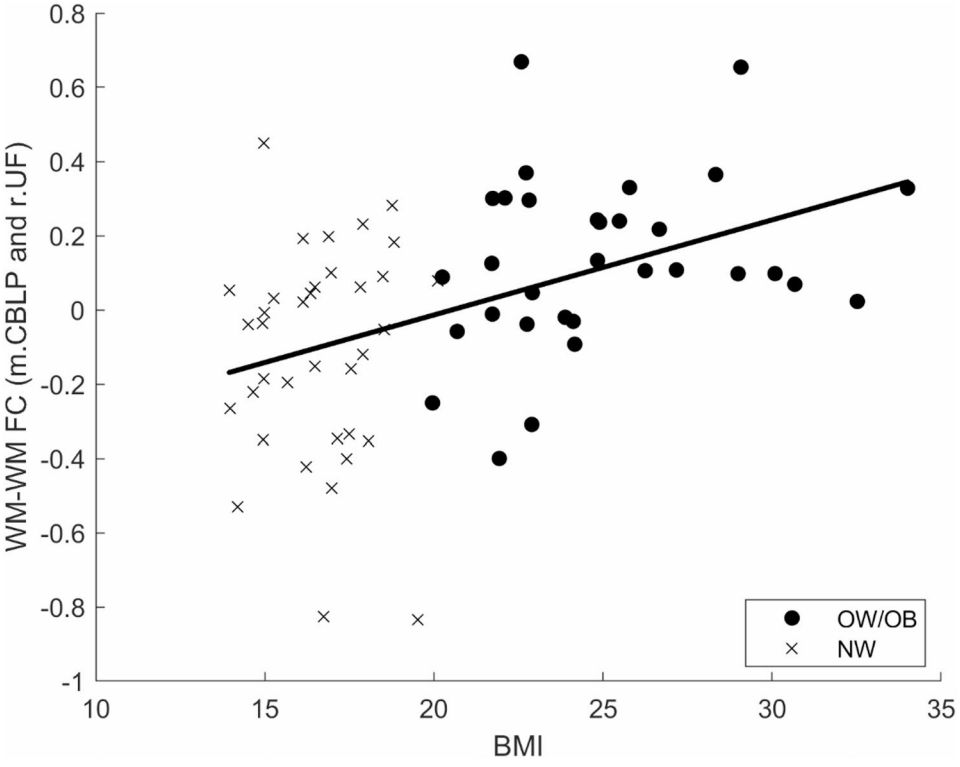


**Fig. 3** Correlation between WM-WM FC and BMI. ($R = 0.47$, $p = 0.0001$, with the effects of sex and age regressed out). Middle cerebellar peduncle (m.CBLP); right uncinate fasciculus (r.UF)

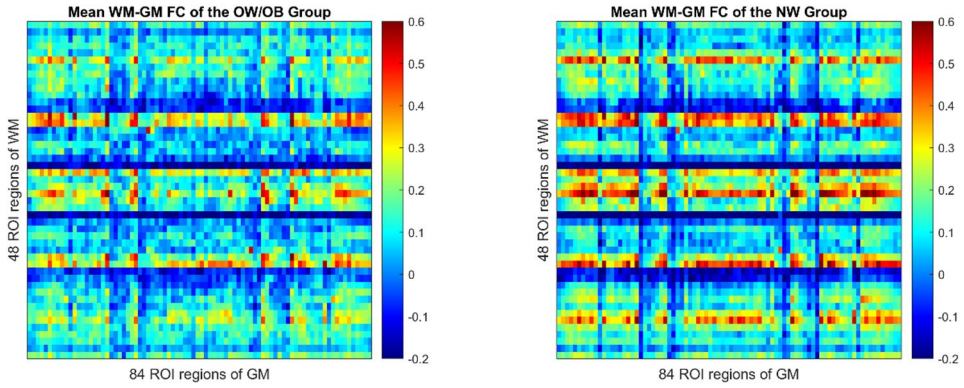


**Fig. 4** The mean WM-GM FC Patterns in (left) the OW/OB group and (right) the NW group. Each cell of this FC matrix represents the mean Pearson correlation coefficient of the time series between one WM and one GM ROIs

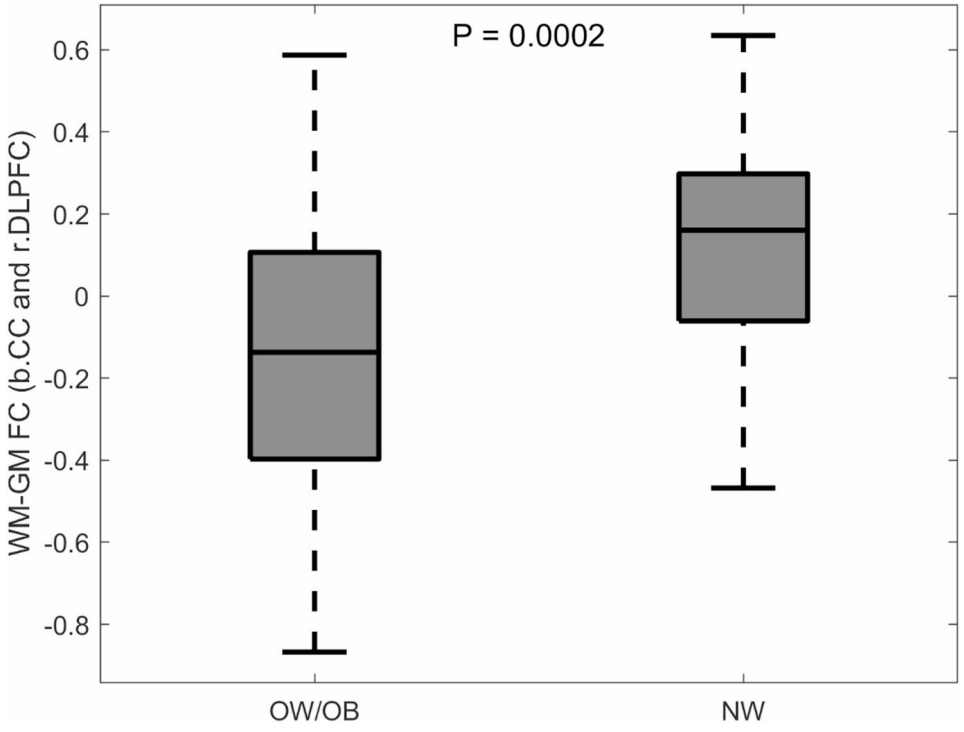


**Fig. 5** Comparison of WM-GM FC between OW/OB and NW Groups. Body of the corpus callosum (b.CC); right dorsolateral prefrontal cortex (r.DLPFC)

to examine the relationship between FC and BMI, while controlling for potential confounding effects of age and sex. Our findings indicate that WM-WM FC between the m.CBLP and r.UF was significantly enhanced in the OW/OB group and positively correlated with BMI across all subjects. This increased connectivity may reflect a neuroadaptive compensatory mechanism, potentially facilitating the integration of motor and cognitive functions in response to obesity-related challenges. Additionally, we observed a significant reduction in WM-GM FC between the b.CC and r.DLPFC in the OW/OB group, with this connectivity showing a negative correlation with BMI. This inverse relationship may suggest disruptions in the modulatory interaction between these regions, potentially impairing executive function, cognitive control, and interhemispheric communication.

The m.CBLP is primarily involved in motor coordination and cognitive functions. It plays a crucial role in fine motor control, balance, and postural maintenance. Studies have shown that individuals with obesity exhibit a certain degree of motor impairment in tasks requiring complex motor coordination, which may be related to altered m.CBLP function [9]. A previous study provided support for the notion that the cerebellum may be involved in fat mass and obesity associated gene-related risk for obesity [43]. The r.UF connects the anterior temporal lobe and orbitofrontal cortex, playing a crucial role in the emotional empathy network, socio-emotional

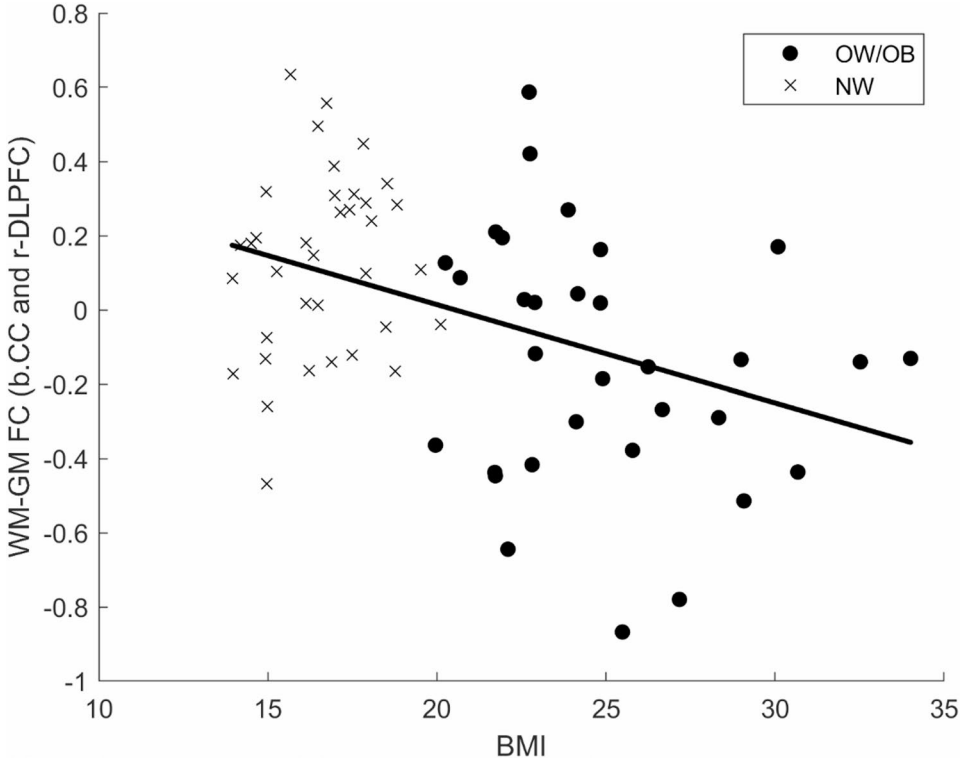


**Fig. 6** Correlation between WM-GM FC and BMI. ($R$ = -0.44, $p$ = 0.0002, with the effects of sex and age regressed out). Body of the corpus callosum (b.CC); right dorsolateral prefrontal cortex (r.DLPFC)

processing, decision-making, memory functions, emotional regulation, and cognitive control [44]. Previous studies have found that obese individuals exhibit significantly increased activation in the prefrontal cortex and amygdala when exposed to food-related stimuli, suggesting heightened sensitivity to food cues and altered functional connectivity in these regions [11]. Other studies suggested that changes in the function of the uncinate fasciculus in individuals with obesity may be associated with an exaggerated response to high-calorie food during food-related decision-making [45]. The m.CBLP and r.UF play crucial roles in motor and cognitive functions, respectively. Individuals with obesity may face greater challenges in tasks requiring the coordination of these functions, prompting the brain to potentially enhance connectivity between these two regions to facilitate more effective motor-cognitive integration. As a neuroadaptive compensation mechanism, the brain may strengthen the connectivity between the m.CBLP—which is primarily responsible for motor coordination and cognitive functions—and the r.UF, which plays a key role in emotional regulation, decision-making, and cognitive control, to help maintain normal function. Furthermore, increased connectivity between emotional decision-making and motor-related regions may contribute to more spontaneous motor responses driven by food-seeking emotions, potentially influencing eating behaviors in individuals with obesity.

The dorsolateral prefrontal cortex is involved in complex cognitive processes, including executive control, attention, and inhibitory control. This region is recognized for its role in goal-directed behavior, particularly in conflict and self-monitoring, error detection, executive control, and decision-making related to risk and reward [46], which also has been identified in previous studies as a critical region for diet success [47, 48]. The importance of the dorsolateral prefrontal cortex as a behavioral control area is underscored by its chronic activation in overweight and obese individuals, which may reflect compensatory processes used to regulate eating behavior and appetite hormones [49, 50]. On the other hand, the body of the corpus callosum is essential for interhemispheric communication, facilitating the integration of motor, sensory, and cognitive information between the hemispheres. Yang Hu et al. found that alterations in white matter anatomical connectivity between corpus callosum and other brain regions involved in reward and executive control are associated with abnormal eating behaviors [51]. Carbine et al. investigated differences in white matter integrity between normal-weight and overweight/obese adolescents, and found that overweight and obese adolescents exhibited reduced white matter integrity in key regions such as the corpus callosum

and cingulum [52]. Other studies have also shown that obesity is associated with reduced integrity and altered connectivity in the corpus callosum, and these reductions may be linked to deficits in cognitive functions and behavioral control [13, 14, 53]. The observed reduction in WM-GM FC between the b.CC and r.DLPFC in the OW/OB group may be attributed to obesity-induced white matter alterations, which disrupt normal brain connectivity. This disruption suggests a potential underlying mechanism by which obesity affects brain function—specifically through impaired connectivity between decision-making processes and motor-cognitive control, potentially leading to deficits in behavioral regulation and cognitive control.

Our WM–GM findings align with previous structural studies reporting obesity-related alterations in callosal and fronto-limbic white matter microstructure [14]. The reduced b.CC–rDLPFC WM–GM FC observed in the present study may reflect impaired interhemispheric conduction and synchrony, consistent with prior reports of decreased callosal integrity in overweight and obese cohorts [54]. In contrast, the elevated m.CBLP–r.UF WM–WM FC could represent compensatory up-weighting of cerebello-fronto-limbic communication loops that support motor-cognitive integration [51]. Mechanistically, reduced WM–GM FC may arise from microstructural compromise, neuro-glio-vascular changes, or timing desynchronization along affected pathways, whereas increased FC may reflect re-routing or compensatory recruitment of alternative networks. These interpretations highlight the need for multimodal studies that integrate diffusion tractography, electrophysiology, and fMRI to clarify the biological underpinnings of altered WM connectivity in pediatric obesity. The GM findings complement the main-text WM results, supporting the view that obesity is associated with selective re-weighting across pathways.

Emerging evidence supports the interpretation that increased WM–WM FC in specific pathways may reflect neuroadaptive re-weighting in the context of obesity. For example, resting-state fMRI studies have shown that stronger cerebellar–cerebral connectivity predicts higher BMI, and monozygotic twin data indicate that the heavier co-twin exhibits heightened cerebellar–insula coupling [55]. Interventional work further demonstrates that dual-site transcranial magnetic stimulation targeting the dorsolateral prefrontal cortex (DLPFC) and cerebellum acutely reduces appetite in obese individuals, suggesting that this loop can be recruited to compensate for dysregulated eating drives [56]. Meta-analytic and task-based fMRI studies consistently report enhanced DLPFC/orbitofrontal activation in response to food cues among people with obesity, particularly in those who succeed at dietary self-control, supporting the idea of prefrontal up-regulation as a compensatory mechanism [57]. These convergent findings reinforce our interpretation that increased m.CBLP–r.UF WM–WM FC may index compensatory recruitment of cerebello–fronto-limbic pathways to maintain behavioral regulation.

Limitations. This study has several limitations. First, the sample size ($n = 68$) is modest. Although we did a power analysis before the conduct of this study which has showed that the sample size was adequate, the power analysis was focusing on other imaging features (e.g., structural differences) and not for the novel analysis of the WM FC. Therefore, the study may be underpowered to detect small effects, and the findings should be interpreted as exploratory and hypothesis-generating. Second, cognitive, behavioral, or motor assessments measured at the same time of the MRI would have strengthened the functional interpretation of the observed connectivity changes. Third, handedness information was not collected for participants, which may constrain the interpretation of connectivity patterns, particularly in regions affected by hemispheric lateralization. Finally, while we used a $p < 1/N$ edge-wise threshold commonly adopted in WM-fMRI studies, our main effects do not survive stricter false-discovery-rate or Bonferroni corrections; future studies with larger samples will be required to replicate these results.

## Conclusions

Our study showed significant alterations in WM-WM FC and WM-GM FC in children with OW/OB, indicating the impact of body weight status of children on brain connectivity, even in WM. These findings suggested the previously unknown impact of childhood obesity on white matter functional connectivity, emphasizing the need for further research on its neurodevelopmental consequences.

**Abbreviations**

| | |
|---|---|
| BBMI | Body mass index |
| FC | Functional connectivity |
| WM-WM | White matter – white matter |
| WM-GM | White matter – gray matter |
| NW | Normal-weight |
| OW/OB | Overweight/obese |
| m.CBLP | The middle cerebellar peduncle |
| r.UF | The right uncinate fasciculus |
| b.CC | The body of the corpus callosum |
| r.DLPFC | The right dorsolateral prefrontal cortex |
| DMPFC | Dorsomedial prefrontal cortex |
| ROI | Region of interest |
| TE | Echo time |
| TR | Repetition time |
| fMRI | Functional magnetic resonance imaging |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-026-04804-w.

Supplementary Material 1.

Supplementary Material 2.

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**Authors' contributions**
Yali Huang: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing. Xiaoxu Na: MR data preprocessing. Linda Larson-Prior: Supervision; Writing – review & editing. Xiawei Ou: Conceptualization; Funding acquisition; Supervision; Writing – original draft; Writing – review & editing.

**Data availability**
The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**
All experimental procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Institutional Review Board of the University of Arkansas for Medical Sciences (Approval No. 206464). Written informed consent was obtained from the parents or legal guardians of all participants under the age of 16 prior to study participation. Assent was also obtained from the children.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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**References**

1. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes and consequences. J family Med Prim care. 2015;4(2):187–92.
2. Kumari S, Shukla S, Acharya S. Childhood obesity: prevalence and prevention in modern society. Cureus. 2022;14(11):e31640.
3. Pearce AL, Mackey E, Cherry JBC, Olson A, You X, Magge SN, Mietus-Snyder M, Nadler EP, Vaidya CJ. Effect of adolescent bariatric surgery on the brain and cognition: a pilot study. Obesity. 2017;25(11):1852–60.
4. Brooks SJ, Smith C, Stamoulis C. Excess BMI in early adolescence adversely impacts maturating functional circuits supporting high-level cognition and their structural correlates. Int J Obes. 2023;47(7):590–605.
5. Li ZA, Cai Y, Taylor RL, Eisenstein SA, Barch DM, Marek S, Hershey T. Associations between socioeconomic status, obesity, cognition, and white matter microstructure in children. JAMA Netw Open. 2023;6(6):e2320276–2320276.
6. Drelich-Zbroja A, Matuszek M, Kaczor M, Kuczyńska M. Functional magnetic resonance imaging and obesity—Novel ways to seen the unseen. J Clin Med. 2022;11(12):3561.
7. Szmygin H, Szmygin M, Cheda M, Kłobuszewski B, Drelich-Zbroja A, Matyjaszek-Matuszek B. Current insights into the potential role of fMRI in discovering the mechanisms underlying obesity. J Clin Med. 2023;12(13):4379.
8. Legget KT, Wylie KP, Cornier M-A, Berman BD, Tregellas JR. Altered between-network connectivity in individuals prone to obesity. Physiol Behav. 2021;229:113242.
9. Schmahmann JD, Pandya DN. The cerebrocerebellar system. Int Rev Neurobiol. 1997;41:31–60.
10. Li G, Hu Y, Zhang W, Wang J, Ji W, Manza P, Volkow ND, Zhang Y, Wang G-J. Brain functional and structural magnetic resonance imaging of obesity and weight loss interventions. Mol Psychiatry. 2023;28(4):1466–79.
11. Tan Z, Li G, Zhang W, Wang J, Hu Y, Li H, Zhang L, Lv S, Jia Z, Li X. Obese individuals show disrupted dynamic functional connectivity between basal ganglia and salience networks. Cereb Cortex. 2021;31(12):5676–85.
12. Samara A, Li X, Pivik R, Badger TM, Ou X. Brain activation to high-calorie food images in healthy normal weight and obese children: a fMRI study. BMC Obes. 2018;5:1–8.
13. Kullmann S, Callaghan MF, Heni M, Weiskopf N, Scheffler K, Häring H-U, Fritsche A, Veit R, Preissl H. Specific white matter tissue microstructure changes associated with obesity. NeuroImage. 2016;125:36–44.
14. Daoust J, Schaffer J, Zeighami Y, Dagher A, García-García I, Michaud A. White matter integrity differences in obesity: a meta-analysis of diffusion tensor imaging studies. Neurosci Biobehavioral Reviews. 2021;129:133–41.
15. Li J, Biswal BB, Wang P, Duan X, Cui Q, Chen H, Liao W. Exploring the functional connectome in white matter. Hum Brain Mapp. 2019;40(15):4331–44.
16. Gore JC, Li M, Gao Y, Wu T-L, Schilling KG, Huang Y, Mishra A, Newton AT, Rogers BP, Chen LM. Functional MRI and resting state connectivity in white matter-a mini-review. Magn Reson Imaging. 2019;63:1–11.
17. Ding Z, Huang Y, Bailey SK, Gao Y, Cutting LE, Rogers BP, Newton AT, Gore JC. Detection of synchronous brain activity in white matter tracts at rest and under functional loading. Proc Natl Acad Sci USA. 2018;115(3):595–600.
18. Schilling KG, Li M, Rheault F, Ding Z, Anderson AW, Kang H, Landman BA, Gore JC. Anomalous and heterogeneous characteristics of the BOLD hemodynamic response function in white matter. Cereb Cortex Commun. 2022;3(3):tgac035.
19. Zhao Y, Gao Y, Zu Z, Li M, Schilling KG, Anderson AW, Ding Z, Gore JC. Detection of functional activity in brain white matter using fiber architecture informed synchrony mapping. NeuroImage. 2022;258:119399.
20. Huang Y, Bailey SK, Wang P, Cutting LE, Gore JC, Ding Z. Voxel-wise detection of functional networks in white matter. NeuroImage. 2018;183:544–52.
21. Huang Y, Yang Y, Hao L, Hu X, Wang P, Ding Z, Gao J-H, Gore JC. Detection of Functional Networks within White Matter Using Independent Component Analysis. *NeuroImage* 2020(222):117278.
22. Grajauskas LA, Frizzell T, Song X, D'Arcy RC. White matter fMRI activation cannot be treated as a nuisance regressor: Overcoming a historical blind spot. Front NeuroSci. 2019;13:1024.
23. Frizzell TO, Grajauskas LA, Liu CC, Ghosh Hajra S, Song X, D'Arcy RC. White matter neuroplasticity: Motor learning activates the internal capsule and reduces hemodynamic response variability. Front Hum Neurosci. 2020;14:509258.
24. Frizzell TO, Phull E, Khan M, Song X, Grajauskas LA, Gawryluk J, D'Arcy RC. Imaging functional neuroplasticity in human white matter tracts. Brain Struct Function. 2022;227(1):381–92.
25. Kirby ED, Frizzell TO, Grajauskas LA, Song X, Gawryluk JR, Lakhani B, Boyd L. D'Arcy RC: Increased myelination plays a central role in white matter neuroplasticity. NeuroImage. 2022;263:119644.
26. Li J, Chen H, Fan F, Qiu J, Du L, Xiao J, Duan X, Chen H, Liao W. White-matter functional topology: a neuromarker for classification and prediction in unmedicated depression. Translational psychiatry. 2020;10(1):365.
27. Ji GJ, Ren C, Li Y, Sun J, Liu T, Gao Y, Xue D, Shen L, Cheng W, Zhu C. Regional and network properties of white matter function in Parkinson's disease. Hum Brain Mapp. 2019;40(4):1253–63.
28. Jiang Y, Song L, Li X, Zhang Y, Chen Y, Jiang S, Hou C, Yao D, Wang X, Luo C. Dysfunctional white-matter networks in medicated and unmedicated benign epilepsy with centrotemporal spikes. Hum Brain Mapp. 2019;40(10):3113–24.
29. Li M, Newton AT, Anderson AW, Ding Z, Gore JC. Characterization of the hemodynamic response function in white matter tracts for event-related fMRI. Nat Commun. 2019;10(1):1140.
30. Li M, Gao Y, Ding Z, Gore JC. Power spectra reveal distinct BOLD resting-state time courses in white matter. *Proceedings of the National Academy of Sciences* 2021, 118(44):e2103104118.
31. Huang Y, Wei P-H, Xu L, Chen D, Yang Y, Song W, Yi Y, Jia X, Wu G, Fan Q. Intracranial electrophysiological and structural basis of BOLD functional connectivity in human brain white matter. Nat Commun. 2023;14(1):3414.
32. Li M, Xu L, Choi S, Qin Y, Gao F, Schilling KG, Gao Y, Zu Z, Anderson AW, Ding Z. Functional contrast across the gray-white matter boundary. Nat Commun. 2025;16(1):6077.
33. Esteban O, Markiewicz CJ, Blair RW, Moodie CA, Isik AI, Erramuzpe A, Kent JD, Goncalves M, DuPre E, Snyder M. fMRIPrep: a robust preprocessing pipeline for functional MRI. Nat Methods. 2019;16(1):111–6.
34. Jenkinson M, Beckmann CF, Behrens TE, Woolrich MW, Smith SM. FSL Neuroimage. 2012;62(2):782–90.

35. Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput Biomed Res. 1996;29(3):162–73.
36. Avants BB, Tustison N, Song G. Advanced normalization tools (ANTS). Insight j. 2009;2(365):1–35.
37. Mori S, Oishi K, Jiang H, Jiang L, Li X, Akhter K, Hua K, Faria AV, Mahmood A, Woods R. Stereotaxic white matter atlas based on diffusion tensor imaging in an ICBM template. NeuroImage. 2008;40:570–82.
38. Lynall M-E, Bassett DS, Kerwin R, McKenna PJ, Kitzbichler M, Muller U, Bullmore E. Functional connectivity and brain networks in schizophrenia. J Neurosci. 2010;30(28):9477–87.
39. Fornito A, Yoon J, Zalesky A, Bullmore ET, Carter CS. General and specific functional connectivity disturbances in first-episode schizophrenia during cognitive control performance. Biol Psychiatry. 2011;70(1):64–72.
40. Liao W, Zhang Z, Mantini D, Xu Q, Wang Z, Chen G, Jiao Q, Zang Y-F, Lu G. Relationship between large-scale functional and structural covariance networks in idiopathic generalized epilepsy. Brain Connect. 2013;3(3):240–54.
41. Liao W, Li J, Duan X, Cui Q, Chen H, Chen H. Static and dynamic connectomics differentiate between depressed patients with and without suicidal ideation. Hum Brain Mapp. 2018;39(10):4105–18.
42. Na X, Glasier CM, Andres A, Bellando J, Chen H, Gao W, Livingston LW, Badger TM, Ou X. Associations between mother's depressive symptoms during pregnancy and newborn's brain functional connectivity. Cereb Cortex. 2023;33(14):8980–9.
43. Lugo-Candelas C, Pang Y, Lee S, Cha J, Hong S, Ranzenhofer L, Korn R, Davis H, McInerny H, Schebendach J. Differences in brain structure and function in children with the FTO obesity-risk allele. Obes Sci Pract. 2020;6(4):409–24.
44. Oishi K, Faria AV, Hsu J, Tippett D, Mori S, Hillis AE. Critical role of the right uncinate fasciculus in emotional empathy. Ann Neurol. 2015;77(1):68–74.
45. Von Der Heide RJ, Skipper LM, Klobusicky E, Olson IR. Dissecting the uncinate fasciculus: disorders, controversies and a hypothesis. Brain. 2013;136(6):1692–707.
46. Nowrangi MA, Lyketsos C, Rao V, Munro CA. Systematic review of neuroimaging correlates of executive functioning: converging evidence from different clinical populations. J Neuropsychiatry Clin Neurosci. 2014;26(2):114–25.
47. Szabo-Reed AN, Martin LE, Hu J, Yeh HW, Powell J, Lepping RJ, Patrician TM, Breslin FJ, Donnelly JE, Savage CR. Modeling interactions between brain function, diet adherence behaviors, and weight loss success. Obes Sci Pract. 2020;6(3):282–92.
48. Neseliler S, Hu W, Larcher K, Zacchia M, Dadar M, Scala SG, Lamarche M, Zeighami Y, Stotland SC, Larocque M. Neurocognitive and hormonal correlates of voluntary weight loss in humans. Cell Metabol. 2019;29(1):39–49. e34.
49. Tataranni PA, Gautier J-F, Chen K, Uecker A, Bandy D, Salbe AD, Pratley RE, Lawson M, Reiman EM, Ravussin E. Neuroanatomical correlates of hunger and satiation in humans using positron emission tomography. Proc Natl Acad Sci. 1999;96(8):4569–74.
50. Del Parigi A, GAUTIER JF, Chen K, Salbe AD, Ravussin E, Reiman E, Tataranni PA. Neuroimaging and obesity: mapping the brain responses to hunger and satiation in humans using positron emission tomography. Ann N Y Acad Sci. 2002;967(1):389–97.
51. Hu Y, Li G, Zhang W, Wang J, Ji W, Yu J, Han Y, Cui G, Wang H, Manza P. Obesity is associated with alterations in anatomical connectivity of frontal-corpus callosum. Cereb Cortex. 2024;34(2):bhae014.
52. Carbine KA, Duraccio KM, Hedges-Muncy A, Barnett KA, Kirwan CB, Jensen CD. White matter integrity disparities between normal-weight and overweight/obese adolescents: an automated fiber quantification tractography study. Brain imaging Behav. 2020;14:308–19.
53. Stanek KM, Grieve SM, Brickman AM, Korgaonkar MS, Paul RH, Cohen RA, Gunstad JJ. Obesity is associated with reduced white matter integrity in otherwise healthy adults. Obesity. 2011;19(3):500–4.
54. Carbine KA, Duraccio KM, Hedges-Muncy A, Barnett KA, Kirwan CB, Jensen CD. White matter integrity disparities between normal-weight and overweight/obese adolescents: an automated fiber quantification tractography study. Brain imaging Behav. 2020;14(1):308–19.
55. Schmidt L, Medawar E, Aron-Wisnewsky J, Genser L, Poitou C, Clément K, Plassmann H. Resting-state connectivity within the brain's reward system predicts weight loss and correlates with leptin. Brain Commun. 2021;3(1):fcab005.
56. Marron EM, Viejo-Sobera R, Cuatrecasas G, Redolar-Ripoll D, Lorda PG, Datta A, Bikson M, Magerowski G, Alonso-Alonso M. Prefronto-cerebellar neuromodulation affects appetite in obesity. Int J Obes. 2019;43(10):2119–24.
57. Pleger B. Invasive and non-invasive stimulation of the obese human brain. Front NeuroSci. 2018;12:884.


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