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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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For	all st	atistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a	Cor	nfirmed
	X	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
x		A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	×	The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
	x	A description of all covariates tested
	×	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	×	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	×	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
x		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
X		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
	×	Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
		Our web collection on statistics for biologists contains articles on many of the points above

Software and code

Policy information about availability of computer code

Data collection

We obtained T1-weighted structural MRI and rs-fMRI data from the enhanced Nathan Kline Institute-Rockland Sample (eNKI) database (http://fcon_1000.projects.nitrc.org/indi/enhanced/).

Data analysis

Data preprocessing: https://gitlab.com/by9433/funp
Stepwise functional connectivity: https://sites.google.com/site/bctnet
Full analysis: https://github.com/hebinalee/SFC_obesity

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Data used in this study are available from the enhanced Nathan Kline Institute-Rockland Sample (eNKI-RS) database (http://fcon_1000.projects.nitrc.org/indi/enhanced/access.html). The eNKI-RS Institutional Data Access Committee grants access to researchers who meet the criteria for access to confidential data upon completion of the Data Usage Agreement. Researchers should contact the database administrator to get access to data.

Field-specific reporting			
Please select the o	one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.		
x Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences		
For a reference copy of	the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf		
Life scie	nces study design		
All studies must d	isclose on these points even when the disclosure is negative.		
Sample size	301 neurologically healthy controls		
Data exclusions	Among 650 participants, subjects with medical conditions (e.g., attention-deficit/hyperactivity disorder, depression, migraine, diabetes, and cardiovascular diseases) or related medication (n = 165), and lack of full demographic information and obesity phenotypes (BMI and the waist-to-hip ratio [WHR]; n = 184) were excluded.		
Replication	N/A		
Randomization	Correlation analyses were performed using 5,000 permutation tests by randomly shuffling the participants. A null distribution was constructed, and if the real correlation coefficient did not belong to 95% of the distribution, we considered the correlation to be significant (two-tailed p < 0.05).		
Blinding	N/A		
Donortin	a for specific materials, systems and mathods		
-	ng for specific materials, systems and methods		
	tion from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, sted is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.		
Materials & ex	operimental systems Methods		
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X Antibodie	S ChIP-seq		
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	research of concern		
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Human rese	earch participants		

Policy information about studies involving human research participants

Number of participants: 301

Age: mean (SD) = 40.44 (17.68) years

Sex (male: female): 119:182

BMI (kg/m2): mean (SD) = 27.18 (5.66)

WHR: Male: mean (SD) = 0.88 (0.09); Female: 0.80 (0.07)

Healthy weight (18.5 ≤ BMI < 25): Overweight (25 ≤ BMI < 30): Obesity (BMI ≥ 30) = 123: 97: 81

Recruitment

We obtained T1-weighted structural MRI and rs-fMRI data from the enhanced Nathan Kline Institute-Rockland Sample (eNKI) database.

Ethics oversight

This retrospective study was approved by the Institutional Review Board (IRB) of Sungkyunkwan University and was performed in full accordance with the local IRB guidelines. All participants provided informed consent.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Experimental design			
Design type	Resting-state		
Design specifications	Resting-state		
Behavioral performance measure	s Resting-state		
Acquisition			
Imaging type(s)	T1-weighted, resting-state fMRI		
Field strength	ЗТ		
Sequence & imaging parameters	All imaging data were scanned using a 3-T Siemens Magnetom Trio Tim scanner. The T1-weighted structural data were scanned using magnetization-prepared rapid gradient-echo (MPRAGE) sequence (repetition time [TR] = 1900 ms, echo time [TE] = 2.52 ms, flip angle = 9° , field-of-view [FOV] = $250 \text{ mm} \times 250 \text{ mm}$, 1 mm3 voxel resolution, and 176 slices). The rs-fMRI parameters were scanned using a multiband echo planar imaging (EPI) sequence (TR = 645 ms , TE = 30 ms , flip angle = 60° , FOV = $222 \text{ mm} \times 222 \text{ mm}$, 3 mm3 voxel resolution, 40 slices, and 900 volumes).		
Area of acquisition	whole brain		
Diffusion MRI Used	Not used		
Preprocessing			
Preprocessing software All imaging data were preprocessed using a Fusion of Neuroimaging Preprocessing (FuNP) volume-based pipeline, which integrates AFNI, FSL, and ANTs software.			
Normalization	The cleaned rs-fMRI data were registered onto the T1-weighted data and subsequently onto the 3 mm isotropic Montreal Neurological Institute (MNI) standard space.		
Normalization template	3 mm isotropic Montreal Neurological Institute (MNI) standard space.		
Noise and artifact removal	Nuisance components of head motion, cerebrospinal fluid, white matter, and cardiac- and large-vein-related artifacts were regressed out using the FMRIB's ICA-based Xnoiseifier (FIX).		
Volume censoring	Head motion was corrected using FSL.		
Statistical modeling & infe	rence		
Model type and settings	Linear correlation Two-sample t-tests		
Effect(s) tested	r-values and FDR-corrected p-values t-statistics and FDR-corrected p-values		
Specify type of analysis:	Whole brain ROI-based X Both		
An	atomical location(s) Brainnetome atlas		
Statistic type for inference (See <u>Eklund et al. 2016</u>)	ROI-wise		
Correction	FDR		
Models & analysis			
n/a Involved in the study Functional and/or effect Graph analysis	tive connectivity		

n/a	Involved in the study
	✗ Functional and/or effective connectivity
	✗ Graph analysis
X	Multivariate modeling or predictive analysis
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Functional and/or effective connectivity

Partial correlation with L2-norm (ridge regularization)

Graph analysis

Individual-level weighted graph

We opted for degree centrality, a graph-theoretical measure assessing the total strength of connections of a given region, to associate it with an obesity phenotype.