Supplemental Materials:

Methods:

Exclusion criteria: A full list of exclusion criteria determined by the ABCD Study® are listed elsewhere (Garavan et al., 2018), but additional exclusion criteria were applied to obtain a sample that was acceptable for these analyses and hypotheses (e.g., BMI measurement error, failed MRI preprocessing; see Table S1). Youth were excluded if they met the following at any of the time points (e.g., baseline, one-year or two-year follow-up): (1) Underweight (according to the Center for Disease Control's (CDC's) age-sex-height-weight-specific growth curves (Kuczmarski et al., 2002)) possibly due to restrictive eating or medical issues; (2) taking medications known to alter food intake (e.g., antipsychotics, insulin); (3) had caregiver report of neurological, psychiatric, or learning disabilities; (4) met diagnostic criteria for eating disorders (e.g., anorexia, binge eating disorder) as assessed by the caregiver-reported Kiddie Schedule for Affective Disorders and Schizophrenia (Kaufman et al., 1997); (5) mislabeled sex-assigned at birth and/or mismatched sex-specific pubertal questionnaires or transgender youth (i.e., due to sex-specific effects on brain function); (6) height measurement error (e.g., height year 2 < baseline); (7) invalid residential address (necessary for ADI metrics); (8) failed FreeSurfer segmentation; (9) failed T₁ quality control; and/or (10) missing ROI or covariate tabulated data from the National Institutes of Mental Health databases. Siblings were excluded to avoid issues with independence. The final sample consisted of 3,087 youth. Table S2 displays the participant characteristics of the sample included in the analyses to the rest of the youth in ABCD.

Table S1. The number of subjects available based on each exclusion criterion applied.

| | n |
|--|--------|
| Number of subjects at Y2 | 10,415 |
| Y2 available BMI data | 7,702 |
| Overlap with BMI data at Y2 | 6,779 |
| No BMI measurement errors or outliers | 6,553 |
| Not underweight | 6,224 |
| No medications known to affect food intake | 5,800 |
| No eating disorders | 5,093 |
| Complete covariate data | 4,801 |
| Valid residential address | 4,528 |
| Passed T1 QC at Y2 | 4,111 |
| Passed above criteria also at baseline | 3,422 |
| No siblings | 3,087 |
| Final sample | 3,087 |

Note. Metrics were generated starting with a dataframe that consisted of baseline demographics and year 2 neuroimaging data. After quality control assessments of the year 2 data, the dataframe was merged with all available demographic and neuroimaging data from the baseline assessment (see line "Available data for all metrics ..."). Y2= years 2; BMI = Body mass index.

Table S2. Participant characteristics

| | Subsa (n=3 | | The rest (n=8 | | |
|--|---------------|------|---------------|------|---------|
| Variable | Mean | SD | Mean | SD | p |
| Age | | | | | |
| Baseline | 118.9 | 7.4 | 119.4 | 7.5 | 0.001 |
| <i>Y2</i> | 142.8 | 7.6 | 143.4 | 7.8 | < 0.001 |
| Puberty | | | | | |
| Baseline | 2 | 0.8 | 1.9 | 0.8 | 0.264 |
| <i>Y2</i> | 2.7 | 1 | 2.7 | 1 | 0.162 |
| BMI | | | | | |
| Baseline | 18.7 | 3.1 | 18.7 | 4 | 0.663 |
| <i>Y2</i> | 20.5 | 3.7 | 20.5 | 4.8 | 0.785 |
| Area deprivation index | 38.5 | 25.9 | 38.8 | 26.1 | 0.499 |
| | n | % | | | |
| Sex | | | | | |
| Male | 1575 | 51 | 3919 | 52.6 | 0.139 |
| Female | 1512 | 49 | 3528 | 47.4 | |
| Race | | | | | |
| White | 2163 | 70.1 | 5049 | 68.6 | 0.047 |
| Black | 337 | 10.9 | 940 | 12.8 | |
| Asian | 62 | 2 | 174 | 2.4 | |
| AIAN/NHPI | 26 | 0.8 | 48 | 0.7 | |
| Other | 147 | 4.8 | 303 | 4.1 | |
| Multi-race | 352 | 11.4 | 843 | 11.5 | |
| Ethnicity | | | | | |
| Hispanic | 621 | 20.1 | 1433 | 19.5 | 0.476 |
| Non-Hispanic | 2466 | 79.9 | 5921 | 80.5 | |
| Education | | | | | |
| <hs< td=""><td>116</td><td>3.8</td><td>299</td><td>4</td><td>< 0.001</td></hs<> | 116 | 3.8 | 299 | 4 | < 0.001 |
| HS/GED | 223 | 7.2 | 555 | 7.5 | |
| Some College | 763 | 24.7 | 1814 | 24.4 | |
| BA degree | 838 | 27.1 | 1981 | 26.6 | |
| Postgraduate degree | 1147 | 37.2 | 2629 | 35.3 | 0.476 |
| Missing | | | 168 | 2.3 | |
| Baseline Weight Class | | | | | |
| Underweight | | | 468 | 5.2 | < 0.001 |
| Healthy Weight | 2126 | 68.9 | 5702 | 63.3 | ***** |
| Overweight | 547 | 17.7 | 1312 | 14.6 | |
| Obese | 414 | 13.4 | 1508 | 16.7 | |
| Missing | | | 16 | 0.2 | |
| Y2 Weight Class | | | 10 | V.2 | |
| Underweight | | | 286 | 3.8 | < 0.001 |
| Healthy Weight | 2034 | 65.9 | 3008 | 39.9 | -0.001 |

| Overweight | 582 | 18.9 | 694 | 9.2 |
|------------|-----|------|-----|------|
| Obese | 471 | 15.3 | 841 | 11.1 |

Note. Baseline was assessed when the youth were 9- to 10-years-old. Y2= two-year follow up (age 9-10-years-old). BMI=Body mass index. AIAN/NHPI=American Indian, Alaskan Native/Native Hawaiian and Pacific Islanders. HS=high school; GED=Generalized education diploma. BA=Bachelor's degree. SD=standard deviation. *P*-values were generated from *t*-tests and chi-square analyses were appropriate.

Anthropometrics. Yearly height (nearest 0.1inch) and weight (nearest 0.1lb) assessments (measured twice, a third was collected in cases of large discrepancy) were gathered by a trained researcher. The closest two measurements were averaged and converted into BMI (kg/m²) and BMI percentiles according to the CDC's sex-age-height-weight specific growth charts (Kuczmarski et al., 2002) for clinical interpretations, only as they are prone to several biases (Hendrickson & Pitt, 2021; Palmer et al., 2021).

Pubertal assessment. Puberty was assessed via caregiver and youth self-report sex-specific questionnaires and then averaged. Scores were converted into sex-specific Tanner staging categories (1=Prepubertal, 2=Early puberty; 3=Mid puberty; 4=Late puberty; 5=Postpubertal).

Demographic assessments. The caregiver reported the child's race, ethnicity, date of birth, and sex at birth. Race had 22 options, which were collapsed into six groups: White, Black, Asian, American Indian, Alaskan Native/Native Hawaiian, Pacific Islander (AIAN/NHPI), Other and multi-race. Ethnicity was assessed with two options: Hispanic or Non-Hispanic. Age at each visit was recorded in months. Highest household education was assessed by caregiver report across 29 education levels and collapsed into five groups: <High school (HS), HS/Generalized Education Diploma, Some college, Four-year degree (Bachelor's degree), Postgraduate education.

Pubertal assessment. Puberty was assessed via caregiver and self-report sex-specific questionnaires and then averaged. Scores were converted into sex-specific Tanner staging categories (1=Prepubertal, 2=Early puberty; 3=Mid puberty; 4=Late puberty; 5=Postpubertal).

Confirmatory Analysis, healthy weight subjects: Having overweight or obesity is associated with underlying differences in brain structure. Therefore, to ensure that our results were not being driven by youth with higher BMIs, we reran our analyses but excluded youth who were overweight or obese at baseline. This resulted in a new group of youth (n=2,162).

Results:

<u>Confirmatory analysis – only health weight subjects</u>. After removing youth who had overweight or obesity at baseline, the Ventral DC was still associated with ADI and BMI but only in the neuronal stress model (e.g., ADI → Brain structure → Δ BMI; see **Tables S7-S8**). In this model, the Ventral DC fully mediated the effect between ADI at 9/10 -years-old and BMI at 11/12-years-old (B=- 0.01, Bootstrapped 95% CI=[-0.03, -0.003]) and the direct effect of ADI on BMI at 11/12 was no longer significant (B=0.005, p=0.9, c path). ADI was negatively associated with subcortical volume of the Ventral DC (B=0.08, p=0.007, a path) while the Ventral DC was

positively associated with BMI at 11/12-years-old (B=0.15, p=0.002, b path).

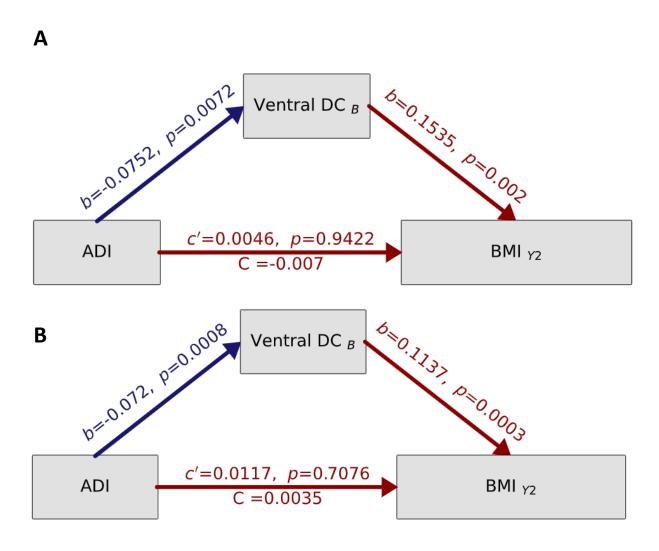


Figure S1. Testing the causal pathway of the neuronal stress theory of overeating in only healthy weight youth at baseline. **A)** Mediation models where the colored arrows reflect the strength (and direction) of the indirect effects, while controlling for sex, age, race, ethnicity, education, handedness and scanner ID. Total effects are represented by c', direct effects of ADI are represented by C while a and b values refer to the association of ADI on brain structure at 9/10-years-old and brain structure at 9/10-years-old on BMI at 11/12-years-old, respectively. All a, b, c, and c' values are unstandardized regression coefficients. Significance testing was carried out by bias-corrected bootstrapping (n=10,000) 95% confidence intervals. **B)** The results of the mediation analyses while controlling for a difference in BMI and Ventral DC subcortical volume as well as sex, age, race, ethnicity, education, handedness and scanner ID. B=baseline (aged 9/10-years-old). Y2=two-year follow-up (aged 11/12-years-old). ADI = area deprivation index. BMI = body mass index

| Immunologic model of self-re | egulation fa | ailure | | | | | |
|------------------------------|--------------|-------------------|---------------|-----------------------------------|-----------------|----------|--|
| | Asse | ociations with BM | I at 9/10-yrs | Associations with ADI at 9/10-yrs | | | |
| ROI (11/12-yrs) | Beta | 95%CI | p | Beta | 95%CI | p | |
| Anterior cingulate (Caudal) | -0.001 | [-0.006,0.005] | 0.794 | -0.002 | [-0.009,0.005] | 0.566 | |
| Anterior cingulate (Rostral) | 0.005 | [-0.0,0.01] | 0.058 | 0.003 | [-0.004,0.009] | 0.44 | |
| Caudal middle frontal | -0.001 | [-0.005,0.003] | 0.537 | 0 | [-0.006,0.005] | 0.863 | |
| Cuneus | -0.002 | [-0.007,0.002] | 0.274 | -0.008 | [-0.014,-0.003] | 0.003**a | |
| Entorhinal | -0.001 | [-0.01,0.007] | 0.781 | 0.003 | [-0.007,0.014] | 0.543 | |
| Frontal pole | -0.012 | [-0.019,-0.006] | <0.001***a | 0 | [-0.009,0.009] | 0.947 | |
| Fusiform | 0 | [-0.004,0.003] | 0.97 | 0 | [-0.005,0.004] | 0.874 | |
| Inferior parietal | 0 | [-0.003,0.004] | 0.785 | -0.005 | [-0.009,0.0] | 0.055 | |
| Inferior temporal | -0.001 | [-0.005,0.003] | 0.766 | -0.003 | [-0.008,0.003] | 0.319 | |
| Insula | 0.005 | [0.001,0.009] | 0.021* | 0.006 | [-0.0,0.011] | 0.055 | |
| Isthmus cingulate | -0.005 | [-0.01,-0.001] | 0.019* | -0.003 | [-0.009,0.002] | 0.207 | |
| Lateral occipital | -0.002 | [-0.005,0.002] | 0.388 | -0.008 | [-0.013,-0.003] | 0.002**a | |
| Lateral orbitofrontal | -0.005 | [-0.009,-0.002] | 0.005**a | -0.001 | [-0.006,0.003] | 0.583 | |
| Lingual | -0.005 | [-0.009,-0.001] | 0.02* | -0.006 | [-0.011,-0.0] | 0.033* | |
| Medial orbitofrontal | -0.005 | [-0.008,-0.001] | 0.016* | 0 | [-0.005,0.005] | 0.927 | |
| Middle frontal (Rostral) | -0.009 | [-0.013,-0.005] | <0.001***a | -0.001 | [-0.006,0.004] | 0.615 | |
| Middle temporal | -0.005 | [-0.01,-0.001] | 0.02* | -0.005 | [-0.011,0.001] | 0.105 | |
| Paracentral | -0.007 | [-0.011,-0.003] | 0.001**a | -0.007 | [-0.013,-0.002] | 0.008** | |
| Parahippocampus | 0.003 | [-0.005,0.01] | 0.489 | -0.009 | [-0.018,-0.0] | 0.049* | |
| Parsopercularis | -0.001 | [-0.005,0.003] | 0.587 | 0 | [-0.005,0.005] | 0.864 | |
| Parsorbitalis | -0.01 | [-0.015,-0.005] | <0.001***a | -0.001 | [-0.008,0.005] | 0.714 | |
| Parstriangularis | -0.007 | [-0.011,-0.003] | <0.001***a | -0.001 | [-0.006,0.004] | 0.679 | |
| Pericalcerine | 0.001 | [-0.004,0.005] | 0.831 | -0.01 | [-0.016,-0.003] | 0.002** | |
| Postcentral | 0.001 | [-0.004,0.005] | 0.741 | -0.007 | [-0.013,-0.001] | 0.018* | |
| Posterior cingulate | -0.003 | [-0.007,0.0] | 0.087 | -0.003 | [-0.007,0.002] | 0.238 | |
| Precentral | 0 | [-0.004,0.004] | 0.951 | -0.006 | [-0.012,-0.001] | 0.025* | |
| Precuneus | -0.003 | [-0.006, 0.0] | 0.085 | -0.002 | [-0.007,0.002] | 0.328 | |
| Superior frontal | -0.009 | [-0.013,-0.005] | <0.001***a | -0.001 | [-0.007,0.004] | 0.621 | |
| Superior parietal | -0.001 | [-0.004,0.003] | 0.698 | -0.003 | [-0.008,0.001] | 0.161 | |
| Superior temporal | -0.005 | [-0.01,-0.001] | 0.027* | -0.004 | [-0.01,0.002] | 0.242 | |
| Superior temporal (Banks) | 0.001 | [-0.003,0.006] | 0.549 | -0.009 | [-0.015,-0.003] | 0.004**a | |
| Supramarginal | 0.003 | [-0.001,0.006] | 0.191 | -0.004 | [-0.009,0.001] | 0.115 | |
| Temporal pole | -0.001 | [-0.009,0.007] | 0.737 | 0.002 | [-0.009,0.012] | 0.749 | |
| Transverse temporal | -0.001 | [-0.006,0.005] | 0.839 | 0.001 | [-0.006,0.007] | 0.862 | |

Table S3. Parameter estimates from the immunologic model of self-regulation failure (ADI → BMI_B → Brain_{Y2}) assessing the associations between ADI and BMI at 9/10-years-old and cortical thickness at 11/12-years-old. Linear random mixed effects covaried for puberty, sex, Race/ethnicity and education with a random effect of scanner type to identify ROIs at 11/12-years-old that were significantly associated with ADI and BMI at 9/10-years-old. Correction was conducted separated by model (e.g., ADI, BMI). ^asurvived multiple correction testing using the Benjamini-Hochberg method. Salmon-colored rows highlight the ROIs that showed significant associations with BMI and ADI.

| Immunologic model of self-regulation failure | | | | | | | |
|--|--------|-------------------|-------------|-----------------------------------|-------------------|------------|--|
| | Asso | ciations with BMI | at 9-10-yrs | Associations with ADI at 9-10-yrs | | | |
| ROI (11-12-yrs) | Beta | 95%CI | p | Beta | 95%CI | p | |
| Accumbens area | 0.367 | [-2.985,3.719] | 0.83 | -7.239 | [-11.583,-2.895] | 0.001**a | |
| Amygdala | -1.329 | [-8.26,5.603] | 0.707 | -16.689 | [-26.055,-7.324] | <0.001***a | |
| Caudate | 3.347 | [-13.134,19.829] | 0.691 | -22.871 | [-43.751,-1.991] | 0.032*a | |
| Hippocampus | 3.584 | [-9.855,17.023] | 0.601 | -34.164 | [-51.51,-16.817] | <0.001***a | |
| Pallidum | 9.031 | [1.656,16.406] | 0.016* | -17.02 | [-26.894,-7.147] | 0.001**a | |
| Putamen | -4.672 | [-24.025,14.68] | 0.636 | -33.534 | [-56.795,-10.273] | 0.005**a | |
| Thalamus | 29.595 | [4.699,54.491] | 0.02* | -46.191 | [-79.136,-13.246] | 0.006**a | |
| Ventral DC | 27.956 | [14.992,40.921] | <0.001***a | -24.828 | [-40.985,-8.671] | 0.003**a | |

Table S4. Parameter estimates from the Immunologic model of self-regulation failure looking at the associations between ADI and BMI at 9/10-years-old and subcortical volume at 11/12-years-old. Associations were tested using linear random mixed effects covaried for puberty, sex, Race/ethnicity and education with a random effect of scanner type was utilized to identify ROIs at 11/12-years-old that were significantly associated with ADI and BMI at 9/10-years-old. Significant effects were corrected separated by modality (e.g., cortical thickness, volume) and model (e.g., ADI, BMI). ^asurvived multiple correction testing using the Benjamini-Hochberg method. Salmon-colored rows highlight the ROIs that showed significant associations with BMI and ADI. Blue rows highlight regions that were significant but there was no overlap between BMI and ADI. Gray rows had no significant associations.

| Neuronal stress theory of over | Neuronal stress theory of overeating | | | | | | |
|--------------------------------|--------------------------------------|-------------------|--------------|-----------------------------------|-----------------|------------|--|
| | Asso | ciations with BMI | at 11/12-yrs | Associations with ADI at 9/10-yrs | | | |
| ROI (9/10-yrs) | Beta | 95%CI | p | Beta | 95%CI | p | |
| Anterior cingulate (Caudal) | -0.078 | [-0.201,0.044] | 0.21 | 0.014 | [-0.03,0.058] | 0.545 | |
| Anterior cingulate (Rostral) | 0.06 | [-0.066,0.186] | 0.348 | 0.051 | [0.005, 0.097] | 0.031* | |
| Caudal middle frontal | -0.158 | [-0.284,-0.033] | 0.013*a | -0.022 | [-0.068,0.025] | 0.363 | |
| Cuneus | -0.16 | [-0.286,-0.034] | 0.013*a | -0.122 | [-0.168,-0.077] | <0.001***a | |
| Entorhinal | -0.011 | [-0.134,0.112] | 0.859 | -0.003 | [-0.049,0.043] | 0.912 | |
| Frontal pole | -0.145 | [-0.267,-0.022] | 0.02* | 0.027 | [-0.018,0.073] | 0.242 | |
| Fusiform | -0.047 | [-0.171,0.077] | 0.459 | -0.044 | [-0.089,0.001] | 0.056 | |
| Inferior parietal | -0.062 | [-0.191,0.066] | 0.342 | -0.049 | [-0.095,-0.003] | 0.036* | |
| Inferior temporal | -0.09 | [-0.214,0.034] | 0.155 | -0.032 | [-0.078,0.014] | 0.175 | |
| Insula | 0.143 | [0.015,0.27] | 0.028* | 0.029 | [-0.017,0.075] | 0.218 | |
| Isthmus cingulate | -0.136 | [-0.258,-0.015] | 0.028* | -0.057 | [-0.107,-0.008] | 0.024* | |
| Lateral occipital | -0.187 | [-0.332,-0.042] | 0.011*a | -0.098 | [-0.139,-0.057] | <0.001***a | |
| Lateral orbitofrontal | -0.102 | [-0.227,0.023] | 0.11 | -0.006 | [-0.052,0.04] | 0.803 | |
| Lingual | -0.175 | [-0.302,-0.048] | 0.007**a | -0.111 | [-0.157,-0.065] | <0.001***a | |
| Medial orbitofrontal | -0.055 | [-0.182,0.072] | 0.398 | 0.03 | [-0.016,0.077] | 0.203 | |
| Middle frontal (Rostral) | -0.402 | [-0.528,-0.277] | <0.001***a | -0.01 | [-0.056,0.037] | 0.683 | |
| Middle temporal | -0.2 | [-0.331,-0.07] | 0.003**a | -0.058 | [-0.104,-0.013] | 0.012*a | |
| Paracentral | -0.155 | [-0.28,-0.031] | 0.014*a | -0.082 | [-0.126,-0.038] | <0.001***a | |
| Parahippocampus | 0.034 | [-0.092,0.16] | 0.597 | -0.074 | [-0.116,-0.032] | 0.001**a | |
| Parsopercularis | -0.061 | [-0.186,0.064] | 0.337 | 0.035 | [-0.011,0.081] | 0.135 | |
| Parsorbitalis | -0.168 | [-0.292,-0.044] | 0.008**a | 0.018 | [-0.026,0.062] | 0.434 | |
| Parstriangularis | -0.278 | [-0.401,-0.155] | <0.001***a | 0.022 | [-0.024,0.068] | 0.345 | |
| Pericalcerine | -0.093 | [-0.223,0.036] | 0.158 | -0.101 | [-0.146,-0.056] | <0.001***a | |
| Postcentral | -0.14 | [-0.267,-0.014] | 0.03* | -0.098 | [-0.143,-0.052] | <0.001***a | |
| Posterior cingulate | -0.047 | [-0.169,0.076] | 0.455 | -0.02 | [-0.065,0.024] | 0.37 | |
| Precentral | -0.057 | [-0.183,0.069] | 0.378 | -0.071 | [-0.117,-0.025] | 0.002**a | |
| Precuneus | -0.087 | [-0.211,0.037] | 0.17 | -0.06 | [-0.106,-0.015] | 0.009**a | |
| Superior frontal | -0.32 | [-0.445,-0.195] | <0.001***a | 0.002 | [-0.045,0.049] | 0.937 | |
| Superior parietal | -0.135 | [-0.263,-0.008] | 0.037* | -0.061 | [-0.107,-0.015] | 0.01*a | |
| Superior temporal | -0.21 | [-0.336,-0.084] | 0.001**a | -0.039 | [-0.085,0.007] | 0.1 | |
| Superior temporal sulcus | -0.019 | [-0.143,0.104] | 0.758 | -0.094 | [-0.14,-0.049] | <0.001***a | |
| Supramarginal | -0.029 | [-0.164,0.106] | 0.671 | -0.045 | [-0.089,-0.0] | 0.048* | |
| Temporal pole | -0.077 | [-0.201,0.046] | 0.218 | 0.013 | [-0.032,0.059] | 0.568 | |
| Transverse temporal | -0.099 | [-0.223,0.025] | 0.117 | -0.033 | [-0.077,0.011] | 0.137 | |

Table S5. Parameter estimates from the neuronal stress theory of overeating (ADI \rightarrow Brain_B \rightarrow BMI_{Y2}) assessing the associations between ADI and cortical thickness at 9/10-years-old and BMI at 11-to-12-year-old. Linear random mixed effects covaried for puberty, sex, race/ethnicity and education, scanner type (random effect) to identify ROIs at 9/10-years-old that were significantly associated with ADI at 9/10-years-old and BMI at 11/12-years-old. Correction was conducted separately by model (e.g., ADI, BMI). ^asurvived multiple correction via the Benjamini-Hochberg method. Salmon-colored rows highlight the ROIs that were significantly associated with BMI and ADI.

| Neuronal stress theory of overeating | | | | | | | |
|--------------------------------------|--------|-------------------|--------------|--------|--------------------|-------------|--|
| | Asso | ciations with BMI | at 11-12-yrs | Ass | ociations with ADI | at 9-10-yrs | |
| ROI (9-10-yrs) | Beta | 95%CI | p | Beta | 95%CI | p | |
| Accumbens area | -0.027 | [-0.156,0.102] | 0.684 | -0.114 | [-0.158,-0.07] | <0.001***a | |
| Amygdala | -0.11 | [-0.248,0.027] | 0.115 | -0.152 | [-0.195,-0.11] | <0.001***a | |
| Caudate | -0.051 | [-0.177,0.075] | 0.426 | -0.123 | [-0.171,-0.075] | <0.001***a | |
| Hippocampus | -0.026 | [-0.158,0.106] | 0.699 | -0.153 | [-0.195,-0.11] | <0.001***a | |
| Pallidum | 0.117 | [-0.015,0.249] | 0.083 | -0.102 | [-0.146,-0.058] | <0.001***a | |
| Putamen | -0.056 | [-0.187,0.075] | 0.401 | -0.118 | [-0.164,-0.072] | <0.001***a | |
| Thalamus | 0.115 | [-0.019,0.249] | 0.092 | -0.107 | [-0.149,-0.064] | <0.001***a | |
| Ventral DC | 0.226 | [0.091,0.361] | 0.001**a | -0.121 | [-0.164,-0.078] | <0.001***a | |

Table S6. Parameter estimates from the neuronal theory of overeating (ADI \rightarrow Brain_B \rightarrow BMI_{Y2}) looking at the associations between ADI and subcortical volume at 9/10-years-old and BMI at 11-to-12-year-old. Associations were tested using linear random mixed effects covaried for puberty, sex, Race/ethnicity and education with a random effect of scanner type was utilized to identify ROIs at 9/10-years-old that were significantly associated with ADI at 9/10-years-old and BMI at 11/12-years-old. Significant effects were corrected separated by modality (e.g., cortical thickness, volume) and model (e.g., ADI, BMI). asurvived multiple correction testing using the Benjamini-Hochberg method. Salmon-colored rows highlight the ROIs that showed significant associations with BMI and ADI.

| Neuronal stress theory of overeating – healthy weight subjects at baseline | | | | | | | |
|--|--------|-------------------|--------------|--------|-------------------|---------------|--|
| | Asso | ciations with BMI | at 11/12-yrs | Ass | ociations with AD | I at 9/10-yrs | |
| ROI (9/10-yrs) | Beta | 95%CI | p | Beta | 95%CI | p | |
| Anterior cingulate (Caudal) | -0.007 | [-0.094,0.079] | 0.871 | -0.002 | [-0.059,0.054] | 0.932 | |
| Anterior cingulate (Rostral) | 0.069 | [-0.021,0.159] | 0.132 | 0.027 | [-0.031,0.085] | 0.364 | |
| Caudal middle frontal | -0.057 | [-0.146,0.032] | 0.209 | -0.015 | [-0.073,0.044] | 0.621 | |
| Cuneus | -0.089 | [-0.179,0.002] | 0.054 | -0.091 | [-0.146,-0.035] | 0.001**a | |
| Entorhinal | 0.05 | [-0.038,0.138] | 0.266 | 0.013 | [-0.044,0.071] | 0.647 | |
| Frontal pole | -0.05 | [-0.137,0.037] | 0.258 | 0.036 | [-0.021,0.094] | 0.211 | |
| Fusiform | 0 | [-0.087,0.088] | 0.996 | -0.022 | [-0.077,0.032] | 0.422 | |
| Inferior parietal | -0.022 | [-0.112,0.069] | 0.641 | -0.02 | [-0.078,0.037] | 0.485 | |
| Inferior temporal | 0.035 | [-0.053,0.123] | 0.439 | -0.018 | [-0.074,0.039] | 0.541 | |
| Insula | 0.001 | [-0.086,0.088] | 0.983 | 0.009 | [-0.048,0.067] | 0.747 | |
| Isthmus cingulate | -0.003 | [-0.089,0.083] | 0.95 | 0.012 | [-0.038,0.062] | 0.628 | |
| Lateral occipital | -0.023 | [-0.127,0.082] | 0.669 | -0.049 | [-0.1,0.002] | 0.061 | |
| Lateral orbitofrontal | 0.001 | [-0.087,0.089] | 0.988 | 0.013 | [-0.045,0.07] | 0.661 | |
| Lingual | -0.045 | [-0.136,0.045] | 0.327 | -0.044 | [-0.101,0.013] | 0.127 | |
| Medial orbitofrontal | 0.017 | [-0.072,0.106] | 0.709 | 0.021 | [-0.038,0.079] | 0.491 | |
| Middle frontal (Rostral) | -0.137 | [-0.226,-0.048] | 0.003** | -0.004 | [-0.062,0.054] | 0.896 | |
| Middle temporal | -0.043 | [-0.133,0.048] | 0.358 | -0.016 | [-0.074,0.041] | 0.579 | |
| Paracentral | -0.004 | [-0.093,0.084] | 0.925 | -0.059 | [-0.115,-0.004] | 0.037* | |
| Parahippocampus | 0.044 | [-0.045,0.133] | 0.33 | -0.045 | [-0.096,0.007] | 0.088 | |
| Parsopercularis | -0.008 | [-0.095,0.08] | 0.863 | 0.023 | [-0.034,0.081] | 0.428 | |
| Parsorbitalis | -0.012 | [-0.099,0.075] | 0.785 | 0.016 | [-0.037,0.07] | 0.551 | |
| Parstriangularis | -0.031 | [-0.118,0.056] | 0.482 | 0.029 | [-0.029,0.086] | 0.332 | |
| Pericalcerine | -0.027 | [-0.115,0.061] | 0.551 | -0.077 | [-0.133,-0.02] | 0.008** | |
| Postcentral | 0.015 | [-0.078,0.108] | 0.751 | -0.072 | [-0.128,-0.015] | 0.013* | |
| Posterior cingulate | -0.054 | [-0.141,0.033] | 0.225 | -0.008 | [-0.065,0.049] | 0.789 | |
| Precentral | 0.005 | [-0.084,0.094] | 0.906 | -0.06 | [-0.117,-0.003] | 0.039* | |
| Precuneus | -0.013 | [-0.101,0.075] | 0.775 | -0.032 | [-0.087,0.024] | 0.269 | |
| Superior frontal | -0.066 | [-0.154,0.022] | 0.143 | -0.008 | [-0.067,0.051] | 0.781 | |
| Superior parietal | 0.015 | [-0.075,0.105] | 0.737 | -0.032 | [-0.09,0.025] | 0.268 | |
| Superior temporal | -0.023 | [-0.111,0.066] | 0.615 | -0.012 | [-0.069,0.045] | 0.676 | |
| Superior temporal sulcus | 0.011 | [-0.076,0.098] | 0.802 | -0.057 | [-0.112,-0.002] | 0.042* | |
| Supramarginal | -0.032 | [-0.128,0.063] | 0.504 | -0.024 | [-0.079,0.032] | 0.404 | |
| Temporal pole | -0.037 | [-0.125,0.05] | 0.402 | -0.003 | [-0.06,0.054] | 0.912 | |
| Transverse temporal | -0.039 | [-0.126,0.049] | 0.384 | 0.004 | [-0.049,0.057] | 0.885 | |

Table S7. Parameter estimates from the neuronal stress theory of overeating (ADI \rightarrow Brain_B \rightarrow BMI_{Y2}) assessing the associations between ADI and cortical thickness at 9/10-years-old and BMI at 11-to-12-year-old in subjects who at baseline, were of a healthy weight. Linear random mixed effects covaried for puberty, sex, race/ethnicity and education, scanner type (random effect) to identify ROIs at 9/10-years-old that were significantly associated with ADI at 9/10-years-old and BMI at 11/12-years-old. Correction was conducted separately by model (e.g., ADI, BMI). ^asurvived multiple correction via the Benjamini-Hochberg method. Salmon-colored rows highlight the ROIs that were significantly associated with BMI and ADI.

| Neuronal stress theory of overeating – healthy weight subjects at baseline | | | | | | | | |
|--|--------|-------------------|--------------|--------|--------------------|-------------|--|--|
| | Asso | ciations with BMI | at 11-12-yrs | Ass | ociations with ADI | at 9-10-yrs | | |
| ROI (9-10-yrs) | Beta | 95%CI | p | Beta | 95%CI | p | | |
| Accumbens area | -0.025 | [-0.115,0.065] | 0.592 | -0.076 | [-0.131,-0.022] | 0.006**a | | |
| Amygdala | 0.015 | [-0.083,0.112] | 0.768 | -0.068 | [-0.121,-0.014] | 0.013*a | | |
| Caudate | 0.027 | [-0.062,0.115] | 0.554 | -0.093 | [-0.154,-0.032] | 0.003**a | | |
| Hippocampus | -0.018 | [-0.112,0.076] | 0.707 | -0.071 | [-0.124,-0.019] | 0.008**a | | |
| Pallidum | 0.033 | [-0.06,0.126] | 0.491 | -0.064 | [-0.119,-0.009] | 0.023*a | | |
| Putamen | 0.031 | [-0.061,0.123] | 0.509 | -0.041 | [-0.091,0.01] | 0.113 | | |
| Thalamus | 0.085 | [-0.009,0.18] | 0.076 | -0.046 | [-0.099,0.007] | 0.092 | | |
| Ventral DC | 0.152 | [0.056,0.248] | 0.002**a | -0.058 | [-0.108,-0.009] | 0.021*a | | |

Table S8. Parameter estimates from the neuronal theory of overeating (ADI \rightarrow Brain_B \rightarrow BMI_{Y2}) looking at the associations between ADI and subcortical volume at 9/10-years-old and BMI at 11-to-12-year-old in subjects who at baseline, were of a healthy weight. Associations were tested using linear random mixed effects covaried for puberty, sex, Race/ethnicity and education with a random effect of scanner type was utilized to identify ROIs at 9/10-years-old that were significantly associated with ADI at 9/10-years-old and BMI at 11/12-years-old. Significant effects were corrected separated by modality (e.g., cortical thickness, volume) and model (e.g., ADI, BMI). ^asurvived multiple correction testing using the Benjamini-Hochberg method. Salmon-colored rows highlight the ROIs that showed significant associations with BMI and ADI.