Supplemental results

Latent Change Score Model: BMI percentile

To evaluate the relationship between change in NAcc cellularity and body mass index (BMI), a separate, but otherwise identical, latent change score model was run using BMI in place of waist circumference. This model produced a good overall fit with the data (CFI = 0.978; Root Mean Square Error of Approximation [RMSEA] = 0.039; 90% CI: [0.036, 0.041]; $p <= 0.05 = 1.0$) (Figure S6). Baseline measures of both BMI percentile and NAcc cellularity negatively predicted two-year changes in respective measures (BMI percentile: $\beta = -0.32$; $p < 0.0001$; NAcc cellularity: $\beta = -0.43$; $p < 0.0001$), such that higher estimates at baseline corresponded with smaller change scores. Cross-domain paths demonstrated that baseline BMI percentile predicted two-year change in NAcc cellularity ($\beta = 0.10$; 95% CI = [0.06, 0.14]; $p < 0.0001$) and that NAcc cellularity predicted two-year change in BMI percentile ($\beta = 0.04$; 95% CI = [0.01, 0.08]; $p = 0.03$). Although the effect size for the relationship between BMI percentile and change in NAcc cellularity was stronger, bootstrapped confidence intervals indicate no difference in strength of cross-domain parameter estimates. Using the likelihood ratio test, model fit significantly decreased when either cross-domain path was constrained to zero (baseline BMI percentile: $\Delta\chi2(1) = 22.67$; $p < 0.0001$; baseline NAcc cellularity: $\Delta\chi2(1) = 4.65$; $p < 0.05$).

Consistent with previous work [24], BMI percentile and NAcc cellularity were significantly associated at baseline ($\beta = 0.15$; $p < 0.0001$). Moreover, there was a significant association between latent change scores for BMI percentile and NAcc cellularity ($\beta = 0.07$; $p < 0.001$). The removal of all covariates from the LCSM yielded almost identical results (Figure S3), suggesting that these effects are robust and independent of the inclusion of covariates.

Association with diet at Year 2: BMI percentile

Dietary fat was significantly associated with BMI percentile at Year 2 (total effect [path c]: $\beta = 0.07$; 95% CI = [0.03, 0.11]; $p < 0.001$) and was partially mediated by NAcc cellularity (direct effect [path c’]: β = 0.038; 95% CI = [0.0006, 0.07]; $p = 0.04$). Dietary fat was associated with NAcc cellularity (path a: β = 0.049; 95% CI = [0.02, 0.08]; $p = 0.008$), and consistent with previous findings at baseline and Year 1 [24], NAcc cellularity was associated with BMI percentile at Year 2 (path b: β = 0.16; 95% CI = [0.13, 0.21]; $p < 0.0001$). The indirect effect of NAcc cellularity on the relationship between dietary fat and BMI percentile was significant (a*b: β = 0.01; 95% CI = [0.002, 0.014]; $p < 0.01$; proportion mediated = 0.18), suggesting a role of NAcc cell density in mediating diet-induced weight gain in youth.

Association with diet at Year 2: Non-fat macronutrients

As a comparison to the model with dietary fat as the independent variable, additional mediation models were tested using non-fat macronutrients (dietary carbohydrates, protein, fiber—each normalized by total caloric consumption) and total caloric intake as independent variables, respectively. Dietary carbohydrate intake was negatively associated with WC percentile (total effect [path c]: β = –0.07; $p < 0.001$) and NAcc cellularity (path a: β = –0.05; $p < 0.01$) (Figure S9). NAcc cellularity significantly partially mediated the relationship between dietary carbohydrates and WC percentile (indirect effect [a*b]: β = –0.01; $p = 0.01$; proportion mediated = 0.14; direct effect [path c’]: β = –0.06; $p < 0.005$).

By contrast, NAcc cellularity did not mediate the relationship between WC percentile and dietary fiber, protein, or overall caloric intake. Fiber intake was negatively associated with NAcc cellularity (path a: β = –0.05; $p < 0.02$) but was not related to WC percentile (total effect [path c]: $p = 0.28$). Conversely, dietary protein was not associated with NAcc cellularity (path a: $p = 0.14$) but was positively associated with WC percentile (total effect [path c]: β = 0.07; $p < 0.001$). Daily caloric intake was not associated with NAcc cellularity ($p = 0.86$) nor WC percentile ($p = 0.25$) at Year 2.

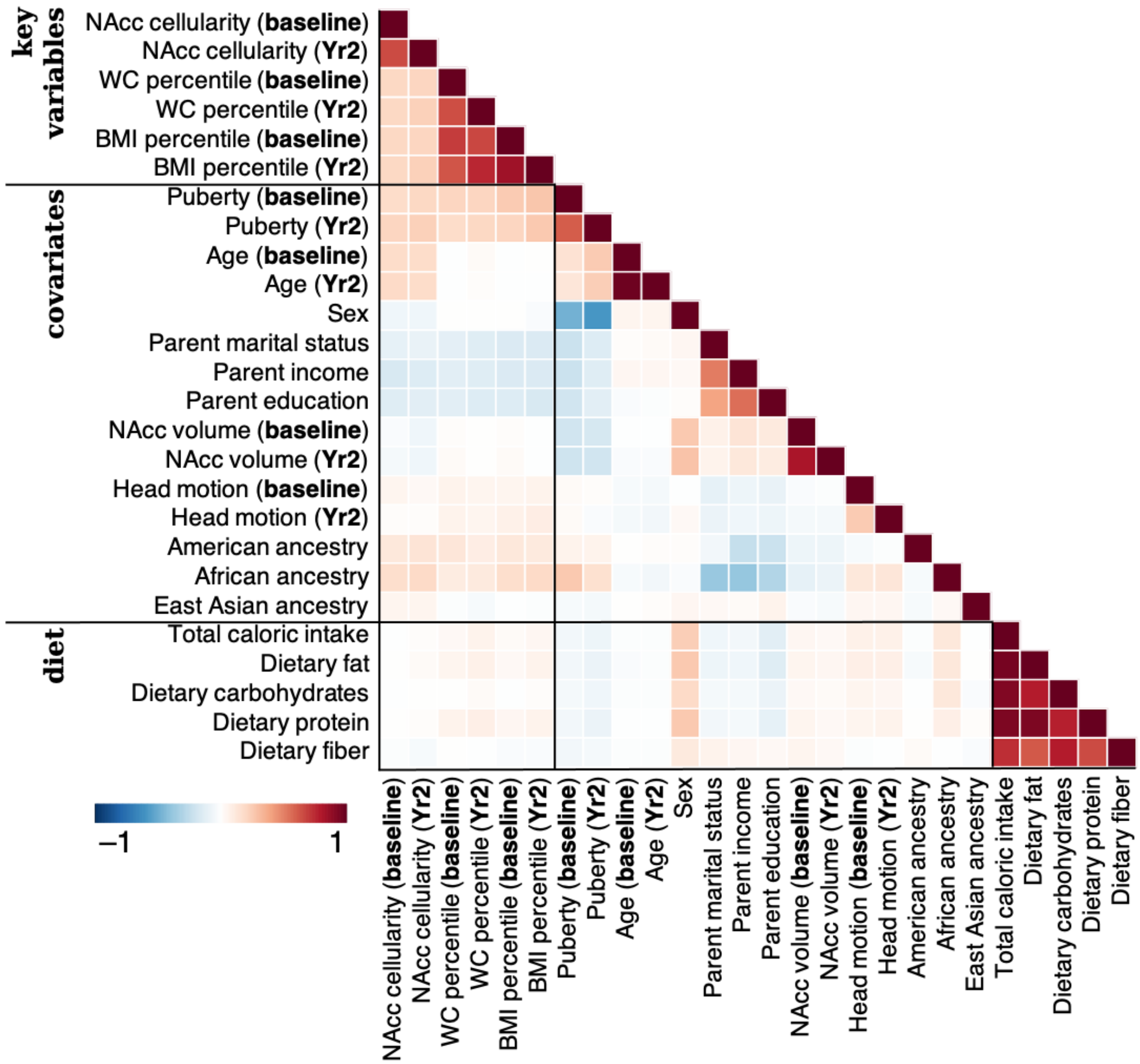

Figure S1. Correlation matrix representing pairwise associations across all variables of interest and covariates.

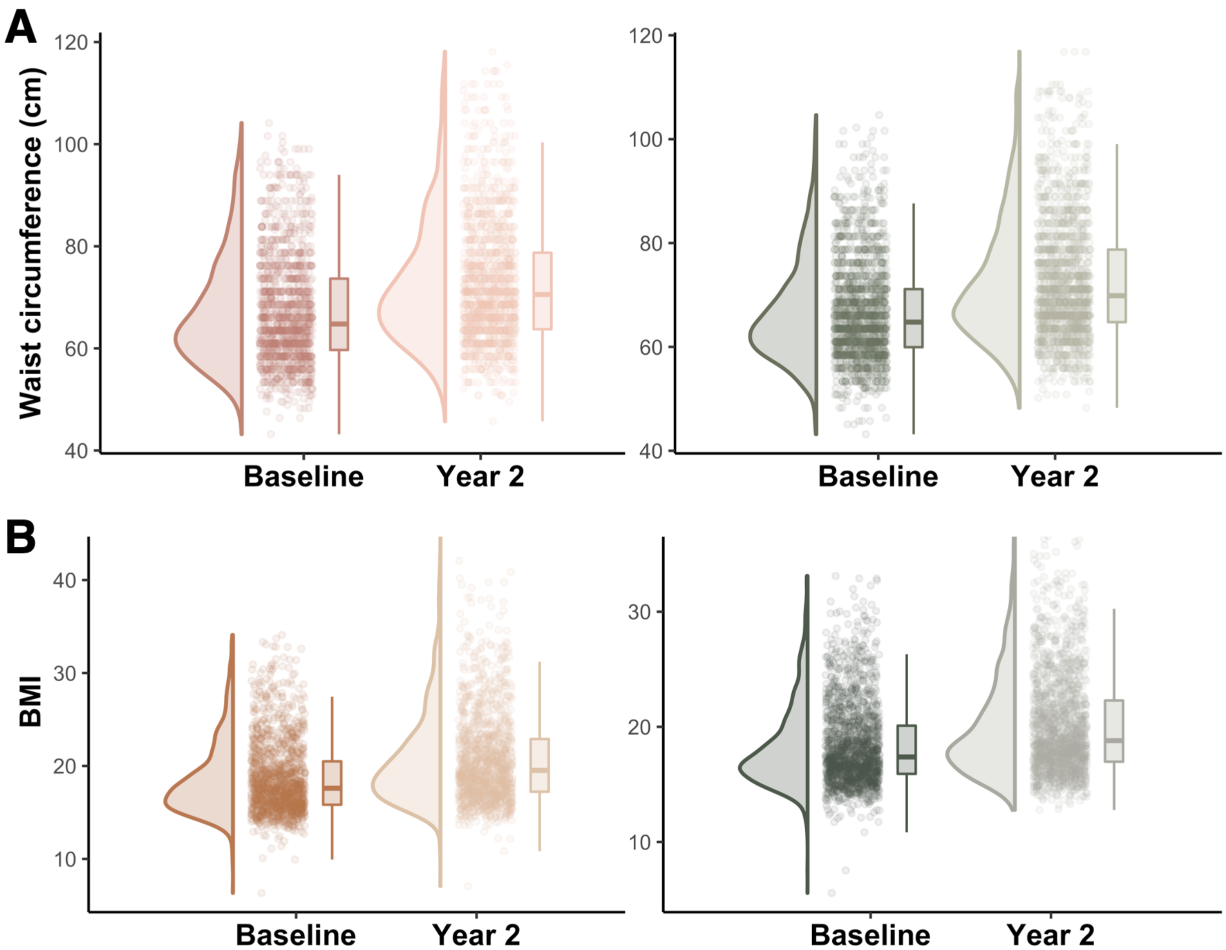

Figure S2. Sex-specific anthropometric distributions. A) Raincloud plots demonstrating raw waist circumference values at baseline and Year 2 follow-up for females (left) and males (right). B) Raincloud plots demonstrating raw BMI values at baseline and Year 2 follow-up for females (left) and males (right).

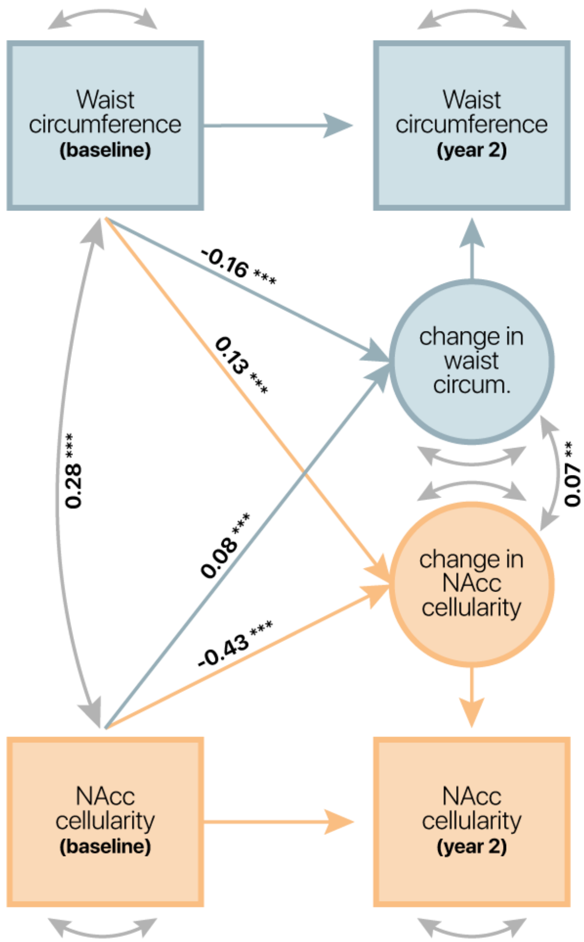

Figure S3. Waist circumference latent change score model without the inclusion of covariates. Standardized coefficients plotted for paths of interest. Significance represented as $p < 0.0001$ (***); $p < 0.005$ (**).

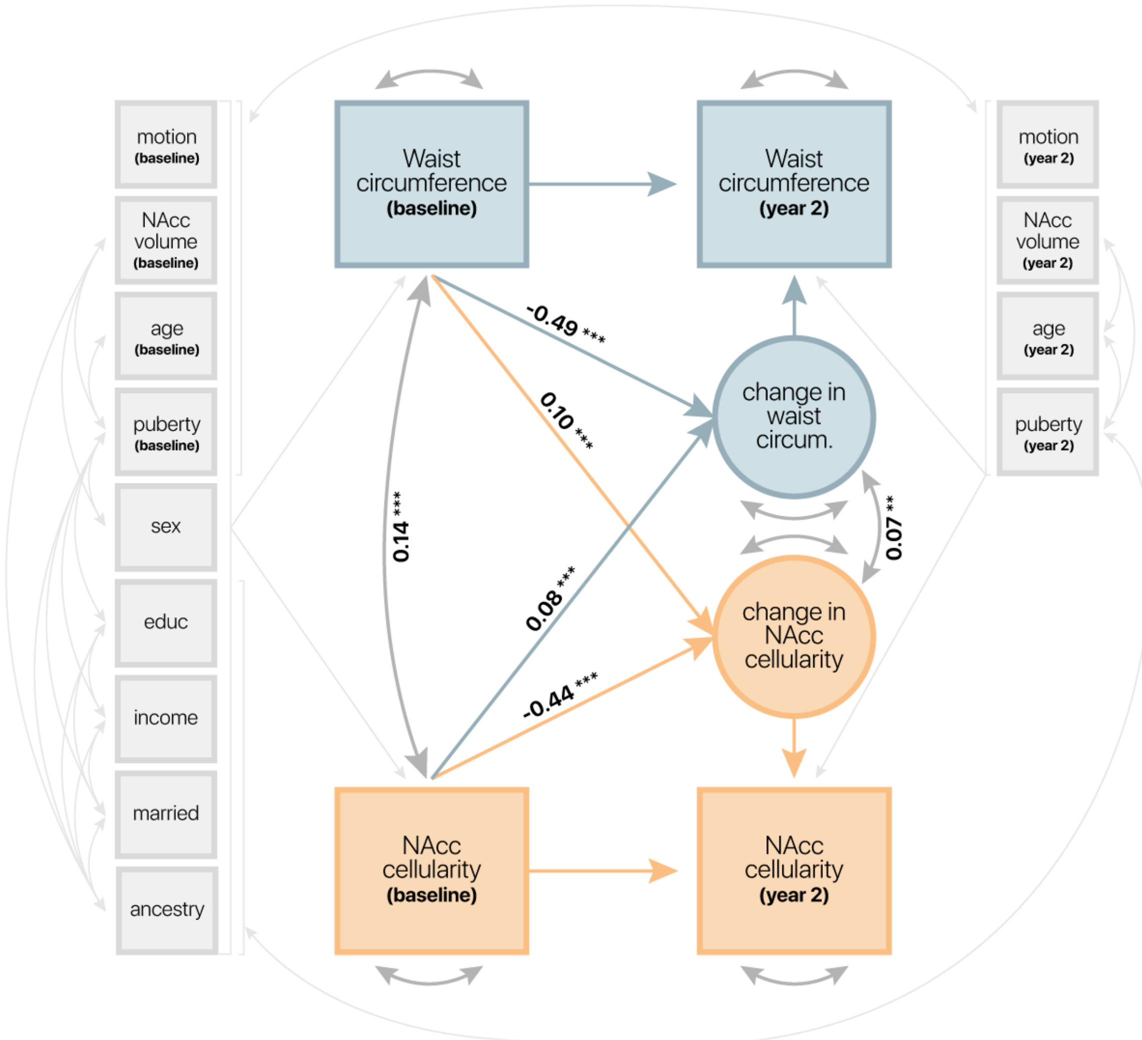

Figure S4. Latent change score model demonstrating relationships between waist circumference percentile and NAcc cellularity over two years without the inclusion of siblings. Standardized coefficients plotted for paths of interest. Significance represented as $p < 0.0001$ (***); $p < 0.001$ (**).

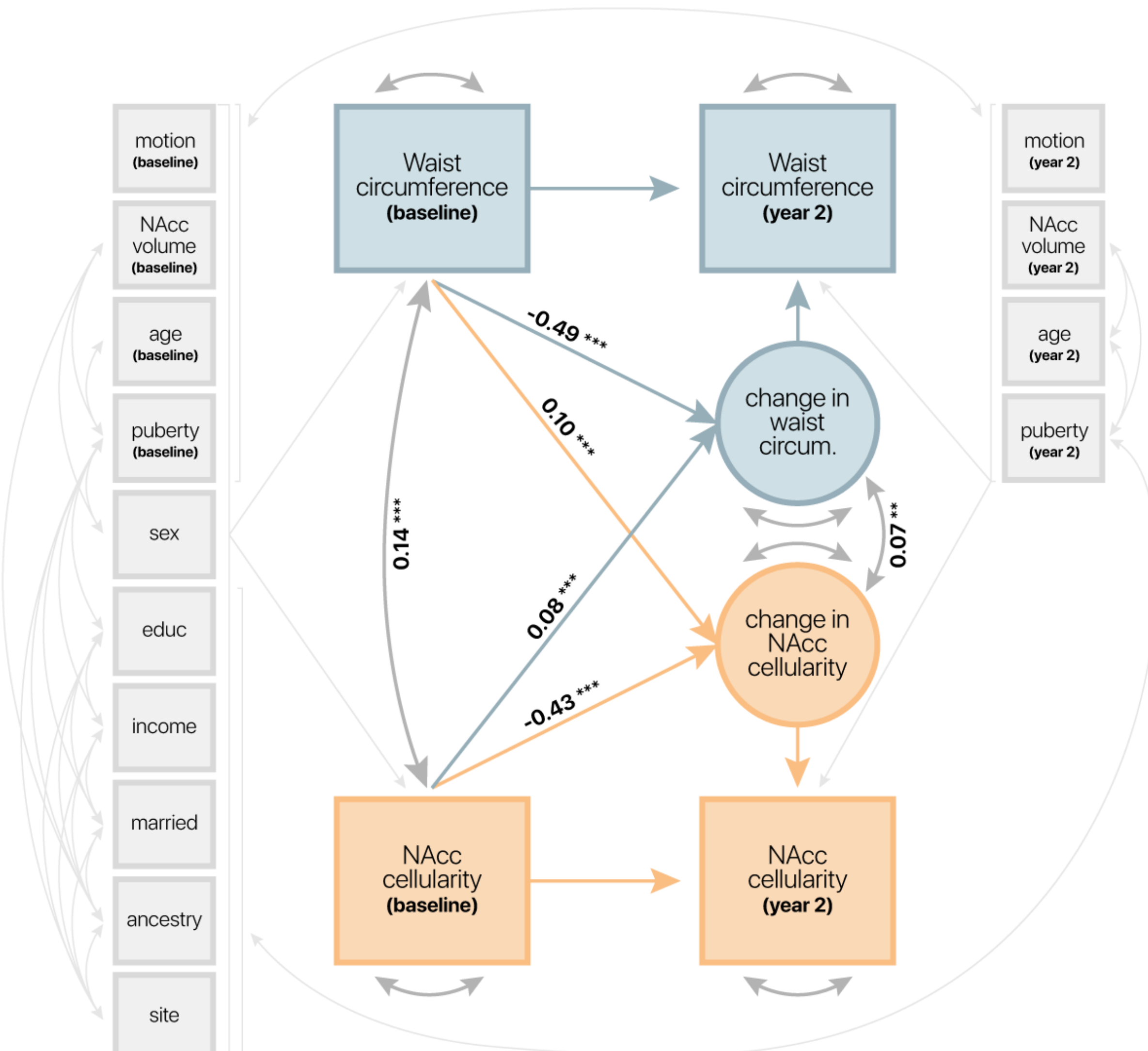

Figure S5. Latent change score model demonstrating relationships between waist circumference percentile and NAcc cellularity over two years with the inclusion of site-wise regressors. Standardized coefficients plotted for paths of interest. Significance represented as $p < 0.0001$ (***); $p < 0.001$ (**).

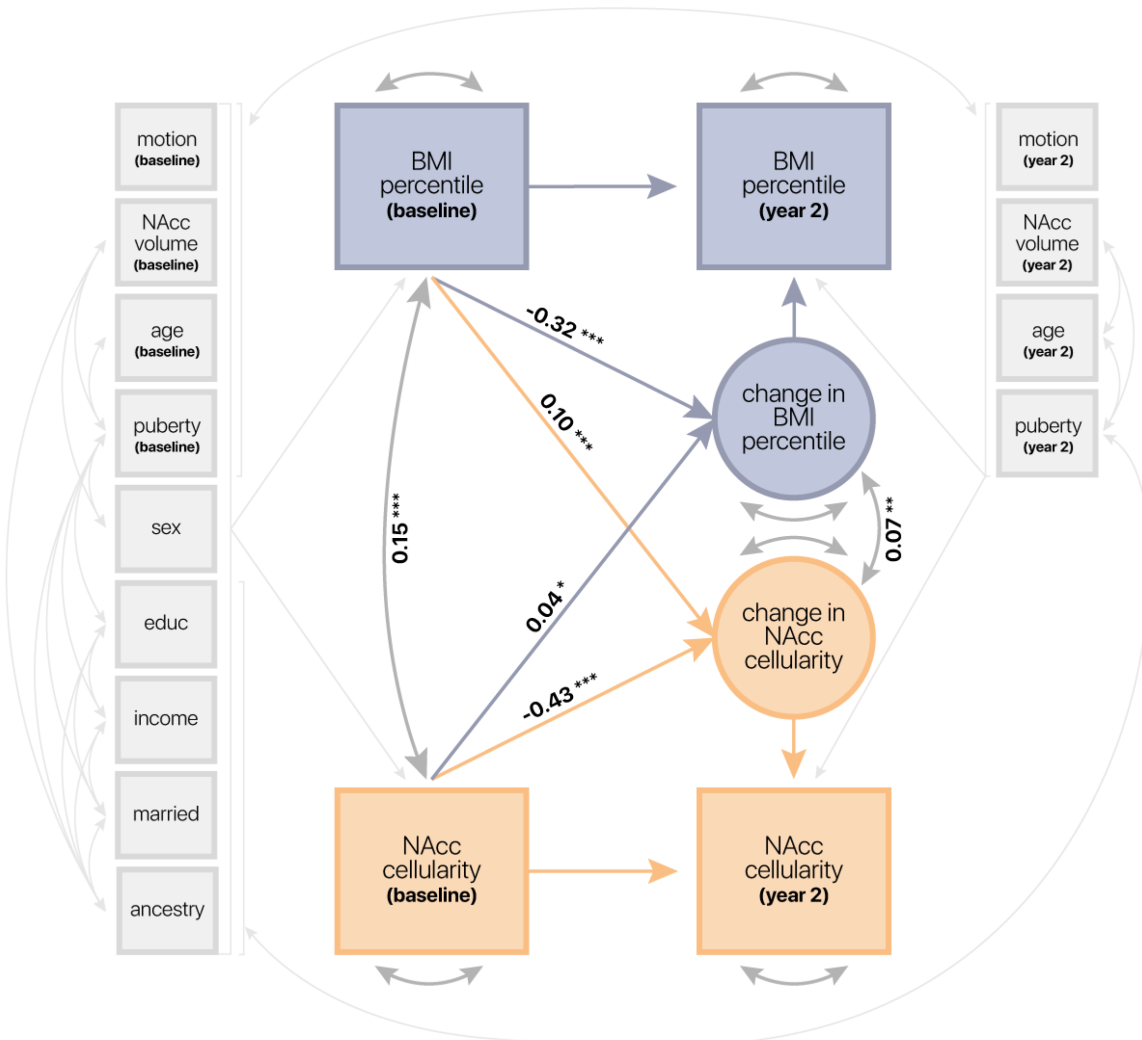

Figure S6. BMI percentile latent change score model. Standardized coefficients plotted for paths of interest. Significance represented as $p < 0.0001$ (***); $p < 0.001$ (**); $p < 0.05$ (*). Thin light gray arrows represent covariate paths of no interest.

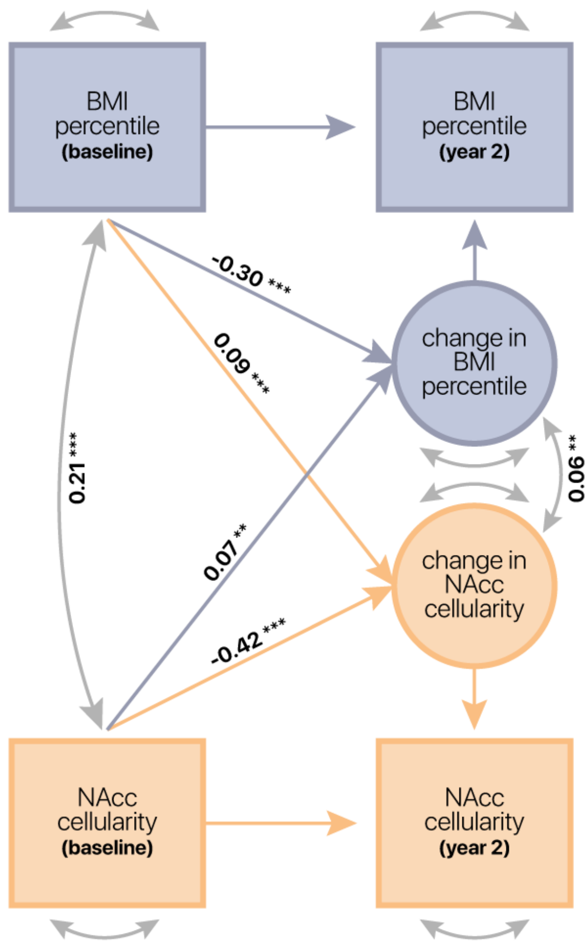

Figure S7. BMI percentile latent change score model without the inclusion of covariates. Standardized coefficients plotted for paths of interest. Significance represented as $p < 0.0001$ (***); $p < 0.001$ (**).

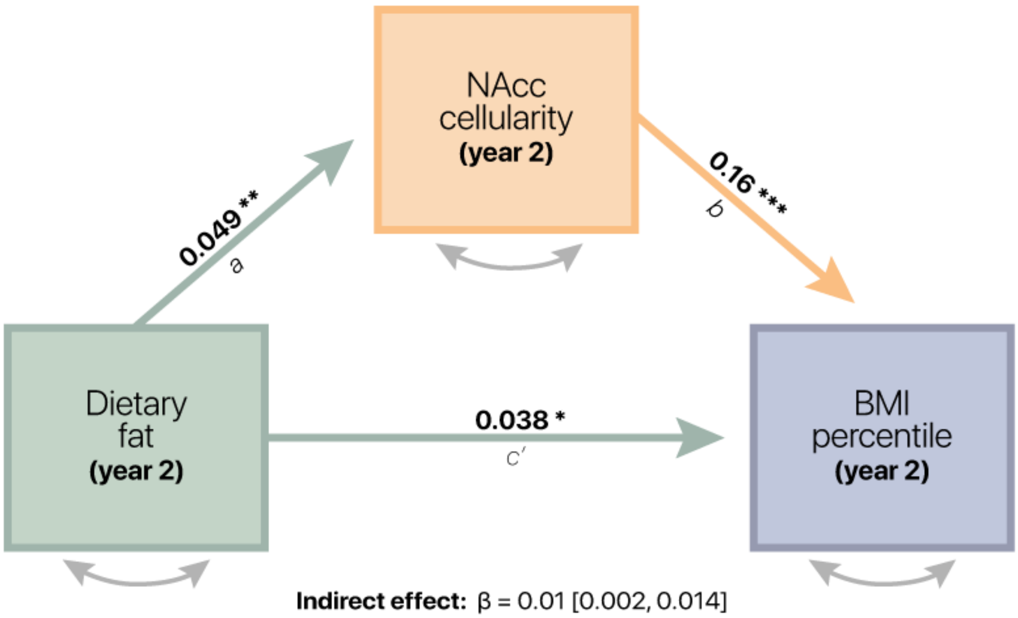

Figure S8. NAcc cellularity significantly mediated the relationship between dietary fat and BMI percentile. Path coefficients are standardized, and significance is represented as $p < 0.0001$ (***); $p < 0.01$ (**); $p < 0.05$ (*). Covariates were consistent with those included in the LCSM at Year 2.

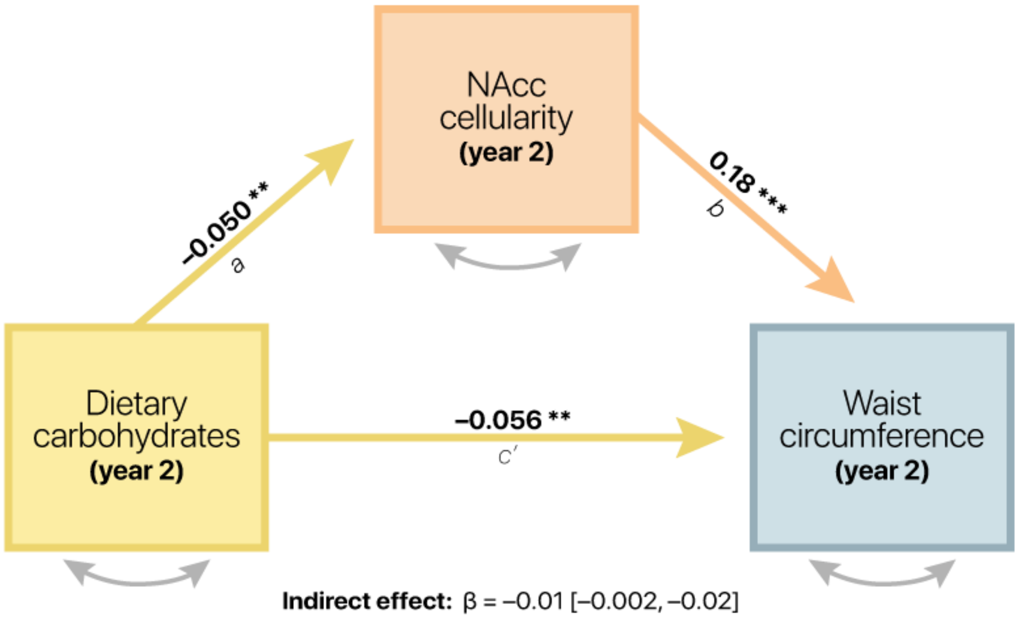

Figure S9. NAcc cellularity significantly mediated the relationship between dietary carbohydrates and waist circumference percentile. Path coefficients are standardized, and significance is represented as $p < 0.0001$ (***); $p < 0.01$ (**). Covariates were consistent with those included in the LCSM at Year 2.