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Supplementary information

MC3R links nutritional state to childhood growth and the timing of puberty

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Supplementary Information

The effect of *MC3R* complete Loss-of-function (cLoF) mutations on trajectories of BMI and height in the Avon Longitudinal Study of Parents and Children (ALSPAC)

Associations of *MC3R* mutations with trajectories of BMI and height were performed using linear splines multilevel models. These models can estimate mean trajectories of the outcomes while accounting for the non-independence or clustering of repeated measurements within individuals, change in scale and variance of measures over time, and differences in the number and timing of measurements between individuals (using all available data from all eligible participants under a missing at-random assumption). Given the lack of individuals carrying a cLoF mutation before the age of 8 years, longitudinal models were restricted to represent ages 8 to 24 years, with a knot point placed at age 15. Interaction terms between *MC3R* cLoF and each spline were included in the models to estimate the difference in the intercepts (mean at the earliest anthropometric trait measurement) and slopes (change in anthropometric trait from the earliest measure to 24 years across splines) between *MC3R* cLoF carriers and non-carriers. The models were adjusted for sex. Carriers of *MC3R* mutations had lower height, such that at age 8, they were on average 6.79cm (95% CI -11.06, -2.52) shorter, but there was little evidence of differences between the groups in linear growth between 8-15 years and between 15-24 years (**Table S14**). Conversely, there was little evidence of association between cLoF *MC3R* mutations and BMI trajectories. (**Table S15**)

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