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Role of melanocortin signalling in the preference for dietary macronutrients in human beings

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Abstract

Background—Signalling through the melanocortin 4 receptor (MC4R), which is widely expressed in the hypothalamus, mediates food intake and macronutrient preference in rodents. Studies in patients with MC4R deficiency can provide insights into the role of this pathway in man. We investigated the role of melanocortin signalling in fat and sucrose preference in human beings by studying patients with loss of function mutations in *MC4R*.

Methods—We studied 24 obese patients with MC4R deficiency, and 80 healthy controls (40 obese, 40 lean). We used an ad-libitum meal protocol consisting of three meals covertly manipulated to provide 20% (low), 40% (medium), and 60% (high) fat content. We used the same procedure for meals manipulated to provide 8% (low), 26% (medium), and 54% (high) sucrose content. We measured food intake and rated liking for the meals with visual analogue scores. Data were analysed by ANOVA and Tukey's post-hoc tests or a linear mixed-effects model with an interaction term for study group and study meal when appropriate.

Findings—Although the liking of the three different fat meals did not differ between the three groups, patients with *MC4R* mutations consumed 95% more of the high fat meal than did lean controls and 65% more of the high fat meal than did obese controls ($p=0.0222$ for the interaction of group by meal). By contrast, although liking ratings for low and medium sucrose meals were comparable in the individuals with MC4R deficiency, liking ratings for the high sucrose meal were significantly reduced ($p=0.0252$ in linear mixed-effects model, intercept 57.8, MC4R group factor -26.2 , factors in the model for MC4R-low sucrose 27.7, MC4R-medium sucrose 22.6). Similarly,

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Contributors

AvdK and SF designed the study, analysed the data, and performed statistical analysis. All authors conducted the research and contributed to and approved the abstract.

Declaration of interests

We declare no competing interests.

patients with MC4R deficiency consumed less of all three sucrose meals than did healthy controls ($p=0.0064$).

Interpretation—Our study shows that the central melanocortin system has divergent effects on macronutrient preference and intake in human beings.

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