Anti-melanocortin-4 receptor autoantibodies in obesity

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Background: The melanocortin-4 receptor (MC4R) is part of an important pathway regulating energy balance. Here we report the existence of autoantibodies (autoAbs) against the MC4R in sera of obese patients. Methods: The autoAbs were detected after screening of 216 patients' sera by using direct and inhibition ELISA with an N-terminal sequence of the MC4R. Binding to the native MC4R was evaluated by flow cytometry and pharmacological effects by measuring adenylyl cyclase activity. Results: Positive results in all tests were obtained in patients with overweight or obesity (prevalence: 3.6%) but not in normal weight patients. The selective binding properties of anti-MC4R autoAbs were confirmed by surface plasmon resonance and by immunoprecipitation with the native MC4R. Finally it was demonstrated that these autoAbs increased food intake in rats after passive transfer via intracerebroventricular injection. Conclusion: These observations suggest that inhibitory anti-MC4R autoAbs might contribute to the development of obesity in a small subpopulation of patients.
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