

Publication

Antibodies raised against different extracellular loops of the melanocortin-3 receptor affect energy balance and autonomic function in rats

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Melanocortin receptors (MCR) play an important role in the regulation of energy balance and autonomic function. In the present studies, we used active immunization against peptide sequences from the first and the third extracellular loop (EL1 and EL3) of the MC3R to generate selective antibodies (Abs) against this MCR subtype in rats. Immunization with the EL1 peptide resulted in Abs that enhanced the effects of the endogenous ligand alpha-melanocyte-stimulating hormone (alpha-MSH), whereas immunization with the EL3 peptide resulted in Abs acting as non-competitive antagonists. The phenotype of immunized rats chronically instrumented with telemetry transducers was studied under four different conditions: a high-fat diet was followed by standard lab chow, by fasting, and finally by an intraperitoneal injection of lipopolysaccharide (LPS). Under high-fat diet, food intake and body weight were higher in the EL3 than in the EL1 or the control group. Blood pressure was increased in EL3 rats and locomotor activity was reduced. Plasma concentrations of triglycerides, insulin, and leptin tended to rise in the EL3 group. After switching to standard lab chow, the EL1 group showed a small significant increase in blood pressure that was more pronounced and associated with an increase in heart rate during food restriction. No differences between the EL1 or the EL3 group were observed after LPS injection. These results show that immunization against the MC3R resulted in the production of Abs with positive or negative allosteric properties. The presence of such Abs induced small changes in metabolic and cardiovascular parameters.

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