

The Brain-Derived Neurotrophic Factor / TrkB-Receptor Pathway as a Possible New Target for the Pharmacotherapy of Anorexia Nervosa (2)

(project no. 04-10 A)

Authors

Karl G. Hofbauer, *Biozentrum, University of Basel, CH*

Martien J.H. Kas, *Rudolf Magnus Institute, University of Utrecht, NL*

Aim

To validate and compare the therapeutic potential of antibodies against the melanocortin-4 receptor (MC4R) and the TrkB-receptor for the indication of anorexia nervosa in an animal model.

Background

In a specific rodent model of anorexia, food restriction leads to a paradoxical increase in physical activity and further suppression of food intake. Reminiscent to anorexia nervosa, rodents exposed to this so-called activity-based anorexia (ABA) model show accelerated body weight loss. Pharmacologically active monoclonal antibodies against the MC4R and the TrkB receptor will be tested in this model for their possible therapeutic effects in anorexia nervosa.

Method

Certain inbred strains of mice show differences in ABA susceptibility. For example, DBA/2J mice show behavioral hyperactivity and accelerated body weight loss when compared to C57BL/6J mice. For that reason, the active monoclonal antibodies will be studied in the sensitive DBA/2J mouse strain.

Execution

For the anti-MC4R monoclonal antibody, 3 different doses will be tested (0.01, 0.03, and 0.1 µg/ 2µl) against a vehicle control group (BSA or the inactive mAb 2G2) in a pilot experiment during *ad libitum* food access. The purpose of these dose finding studies is the confirmation of the efficacy of the doses previously used in rat experiments. If positive, these dose levels will be used for the final studies in the ABA model and evaluated for their effects on food intake and physical activity.

The project is financed by the Swiss Anorexia Nervosa Foundation.