

Sex and obesity differentially influence central insulin action to food cues

Lore Wagner¹, Ralf Veit¹, Christian Kübler^{1,2}, Andreas L. Birkenfeld^{1,2}, Martin Heni^{1,2,3}, Hubert Preissl^{1,2}, Stephanie Kullmann^{1,2}

¹Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tübingen; German Center for Diabetes Research (DZD), Tübingen, Germany

²Department of Internal Medicine IV, University of Tübingen, Germany

³Institute for Clinical Chemistry and Pathobiochemistry, University Hospital Tübingen, Germany

Central insulin action influences cognitive processes, peripheral metabolism and eating behavior. However, the contribution and interaction of obesity, age and sex on central-insulin action still remain unclear.

In a randomized within-subject design, we measured neural reactivity to food cues in 60 participants (30 women, BMI 18-32 kg/m², age 21-69 years) on two separate days. After intranasal insulin (INI) or placebo (PL) spray administration, visual food cues were presented during functional magnetic resonance imaging. Afterwards, participants were asked to rate the presented food cues for wanting (“how much they want to eat the presented food cues”).

In response to high versus low caloric food, INI evoked higher activity in the amygdala compared to PL. Furthermore, 3-way interactions between sex, BMI status and nasal spray were identified in multiple cortical regions. Women with overweight and obesity and men of normal weight showed higher cortical activity in response to INI compared to PL. Higher central insulin responsiveness in the insular cortex was associated with better peripheral insulin sensitivity and higher cognitive restraint. Moreover, neural activity parametrically modulated by wanting ratings revealed a significant interaction between sex and nasal spray. In response to INI compared to PL, men showed lower dorsolateral prefrontal cortex (DLPFC) activity with increasing wanting ratings, whereas women showed higher DLPFC activity.

Obesity and sex, but not age, influenced the central-insulin mediated neural activity to visual food cues in brain regions implicated in reward and cognitive control. These findings show that central insulin action differentially affect men and women, which may have consequences for metabolism and eating behavior.