Universität Basel

Research Project

Understanding gut-brain interactions and the effect of dietary measures in obesity and depression: a translational study

Third-party funded project

Project title Understanding gut-brain interactions and the effect of dietary measures in obesity and depression: a translational study
Principal Investigator(s) Inta, Dragos ;
Co-Investigator(s) Borgwardt, Stefan ; Wölnerhanssen, Bettina ;
Project Members Zajac-Bakri, Kilian ; Bordier, Valentine ; Smolenskii, Ilia ;
Organisation / Research unit
Bereich Psychiatrie (Klinik) / Neuropsychiatrie (Borgwardt)
Department
Project start 01.01.2020
Probable end 31.12.2023
Status Completed

Obesity and major depressive disorders (MDD) are among the most challenging public health problems with a rapidly increasing prevalence worldwide. MDD and obesity are highly comorbid, the “metabolic” (obese) subtype of MDD affects about one third of all individuals with MDD. Therefore, there is an urgent need to develop better preventive and therapeutic strategies, which may include specific dietary measures. Preclinical studies show that a diet low in carbohydrates (low-carb), effective in obesity and associated metabolic disorders, may be beneficial also in MDD. However, no clinical trials on the role of low-carb diet in MDD have been performed to date. Furthermore, while clinical data on the effects of a low-carb diet in obese and diabetic patients is available, the underlying mechanisms were not yet studied. Recent data suggest a key role of factors acting that may act synergistically: i) gut microbiota, ii) neuroplasticity and iii) neuroinflammation in both obesity and MDD, but their role in “metabolic” vs. “lean” (non-obese) MDD is unclear. Exciting clinical and preclinical results suggest that obesity and even MDD-like features can be “transferred” from humans to humans or rodents by fecal material transplantation (FMT). Mice deficient for the key neuroplasticity, MDD-associated marker brain derived neurotrophic factor (BDNF) display are susceptible to both stress/depression-like behavior and obesity (“vulnerability”). Conversely, mice lacking the microglial fractalkine receptor CX3CR1, a main modulator of neuroinflammation, are resistant to both stress and obesity, when exposed to fat-enriched diet (“resilience”). However, the mechanistic interplay between these factors and their specific contribution to each disorder are not yet understood. To clarify these aspects we aim: a) to evaluate the therapeutic potential of dietary microbiome-influencing interventions (low-carb diet) on disease-associated parameters (psychometry, brain network activity, hypothalamic-pituitary-adrenal - hypothalamic-pituitary-adrenal (HPA) axis, plasma BDNF/fractalkine levels, cytokines, gut microbiota composition, leaky gut and metabolic markers, metabolomics) in individuals suffering from MDD with or without obesity, towards better nosology of disease subtypes based on mechanisms and validation of possible new biomarkers (plasma BDNF/fractalkine, neuroimaging parameters); b) to assess molecular determinants of their effect in selected mouse models with deficiency of BDNF or CX3CR1; c) to clarify the contribution of changes in gut microbiota composition to the psychiatric/metabolic pathology by fecal material transplantation (FMT) of samples from patients with MDD, obesity or “metabolic” MDD, to the mouse lines upon microbiome depletion. The analysis in rodents will comprise similar approaches as in humans, together with investigations at cellular level regarding changes in the function of microglia, neurogenesis in MDD/obesity-relevant brain regions (hypothalamus, hippocampus) and inflammation in visceral adipose tissue, which

cannot be performed in living humans. In all paradigms, we seek to unravel relevant gender-specific effects. Our project is highly innovative: it represents the first attempt to study translationally using a multidisciplinary approach the preventive/therapeutic potential of a diet in obesity/MDD. We will use innovative experimental devices like an ultrasensitive approach to detect in real-time BDNF changes in the cerebrospinal fluid (CSF) in rodents, overcoming current difficulties in assessing in vivo cerebral levels. Our project may be important for several biological and medical disciplines, facilitating better understanding of the mechanisms of obesity /MDD, towards novel early and cost-efficient interventions.

Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners