## Neural Self- Manipulation of Food Reward with Real- Time fMRI Neurofeedback

## Project: 511

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Obesity is a pandemic that necessitates innovative interventions. Fuelled by an unfavourable interaction between the human predisposition to consume food when it is available and to prefer calorie-rich options, and the environment offering a constant flow of highly appetising, affordable, energy-dense foods that are available around the clock, the global prevalence of overweight and obesity in humans has had a stark in- crease. Human food reward and its regulation are orchestrated to a great extent by the brain, and here, in large part by the dopaminergic system and associated brain regions. However, non-invasive interventions that directly target the neural reward system do not exist as yet, revealing a strong need for their development. Real-time fMRI (rt-fMRI) neurofeedback training (NFT) is a recently developed non-invasive technology with great potential for clinical applications. It may function as such a targeted neuro-intervention for food-related behaviour.

In this thesis, two projects are reported. The Neural Self-Regulation of Food Reward project (NeuroFoodReg project) was an ambitious and high-risk project developed to examine rt-fMRI NFT as a potential intervention in this context with a specific focus on the role of the dopaminergic midbrain. In preparation for these rt-fMRI NFT measurement campaign, the available options for quantifying incentive motivation in humans were examined to inform on the choice of an adequate measure in the NeuroFoodReg project.

Regarding quantifying incentive motivation in humans this thesis found that an implicit drive is difficult to quantify in humans because conscious thought is an always present confounder in the most often used measures. Also, this work shows that ratings placed on two distinct measures (grip force and ratings placed on a visual analogue scale (VAS)) do not capture fundamentally different information. Therefore, it was concluded that the choice between measures for the following and future studies can be based on what suits an experimental paradigm. The VAS should be favoured whenever the paradigm permits it given that it is easier to setup, does not require training the subjects, and the output is straight-forward to analyse.

The NeuroFoodReg project tested the feasibility of real-time fMRI neurofeedback as an intervention for changing reward-related eating behaviour and people's ability to self- regulate the dopaminergic midbrain. While the NeuroFoodReg project's paradigm did not induce learning of ventral tegmental area and substantia nigra (VTA/SN) self-regulation in subjects, its core protocol was deemed feasible for re-use in future studies. This conclusion was made on the basis of adequate training intensity and agreeableness to the subjects. It is rather uncommon to have a pre-training session with a mock-up scanner in NFTs, but it may be a time investment worth considering as it proved to be a helpful addition to reduce cognitive load on the training days and pre-emptively address any scanner-related anxiety. Another insight gained through this project by means of the experiment's results and studying the relevant peer-reviewed literature was that VTA/SN-activity arising in response to food reward may not be robust enough for practicing neurofeedback-guided self-regulation.

The studies in this thesis approach their respective research questions holistically. An attempt was made to capture as many as possible accompanying variables that may have an influence on the outcome. For example, potentially relevant personality traits were captured alongside brain signals. Also, the reaction of participants to the food pictures was captured on multiple levels, namely that of the brain, by means of skin conductance, and in the participants' subjective ratings. This should become a more commonplace practice to enable taking into account the multidimensional and idiosyncratic nature of human experience in scientific experiments