Abstract of dissertation: Coding of innate behaviours by neural subpopulations of the reward circuitry

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Adequate coordination of innate behaviours – such as feeding, drinking, locomotion and social interaction – by the brain is crucial for survival and for mental health. The brain circuitry driving these behaviours largely consists of hypothalamic areas, involved in homeostasis, and the dopaminergic reward system with the ventral tegmental area (VTA) at its core, providing motivational drive, and their connections to cortical and limbic areas including the lateral septum. Yet the specific functions of the components within this circuitry need clarification. For example, it is known that Neurotensin, a neuropeptide widely expressed in the brain, can modulate various innate behaviours, but its region-specific functions are largely unknown. Similarly, VTA dopamine neurons respond to rewards and reward predictive cues, yet individual neurons do not signal reward anticipation uniformly. Additionally, subsets of kinematic and behavioural variables are encoded by separate neurons. The question remains whether individual VTA dopamine neurons encode different reward types heterogeneously as well or not.

Here, I studied the contribution of different genetically defined subpopulations within the lateral hypothalamus (LH), lateral septum (LS) and the VTA in driving innate behaviours. In the first part, I used chemogenetics to activate Nts-expressing (Nts) neurons in either the LH or LS and assessed behavioural responses to water, food and conspecifics in detail using an unsupervised machine learning method for behavioural classification. Additionally, I quantified behavioural transitions with this method.
In the second part, I recorded the activity of single VTA dopamine neurons using *in vivo* 1-photon calcium imaging in mice that were freely exploring an arena containing multiple rewards: food, water, a conspecific, a running wheel and a novel object. First, I assessed the responses of individual neurons to these different types of rewards. Second, I studied how the activity dynamics of VTA dopamine neurons changes during increased motivation for voluntary exercise and feeding, as well as during altered metabolic states (e.g. after exposure to a high-fat diet).

I found that Nts neurons in the lateral hypothalamus (LH) and lateral septum (LS) control food seeking and social behaviour in an opposite manner. Specifically, Nts neurons in the LH suppress social interaction in favour of behaviour directed to drinking and intake of high-fat food, while Nts neurons in the LS reduce consumptive behaviours to facilitate social approach. Furthermore, at 2 seconds before transition to social interaction small changes in behavioural syllables became apparent.
In addition, I found that approximately 75% of VTA dopamine neurons are modulated by at least one reward. Individual neurons respond differently to distinct rewards, and most encode food and voluntary exercise in an orthogonal manner, further supporting the heterogeneous nature of VTA dopamine neurons. On average, the strongest responses were to food. Additionally, reward responses changed during altered motivational and metabolic states. Together, these results contribute to the understanding of how neural circuits control innate behaviour.