

Neuroscience Seminar

Friday 26 April 2019
11.00 – 12.00

Lille Anatomisk Auditorium, building 1231, room 424

Anne M. Klawonn

Postdoc by Professor Robert C. Malenka, Stanford Universitet

Title of talk:

“Neuromodulators of Motivational and Affective Neurocircuits – Aversive, Rewarding and anhedonic features”

Abstract:

Various molecular pathways in the brain shape our understanding of good and bad, as well as our motivation to seek and avoid such stimuli. My work evolves around the brain circuits responsible for signaling negative affect, with a particular emphasis on how systemic inflammation causes aversion and why general unpleasant states such as sickness, stress, pain and nausea are encoded by our brain as undesirable. A common feature of various disease states is involvement of the motivational neurocircuitry - from mesolimbic to striatonigral pathways. Having an intact motivational system is what helps us evade negative outcomes and approach natural positive reinforcers, which is essential for our survival. During disease-states the motivational and affective neurocircuitry may be overthrown by the molecular mechanisms that originally were meant to aid us. We uncovered that during systemic inflammation the innate immune-system employs specific signaling cascades recruiting the striatonigral system for signaling aversion. Furthermore, by employing DREADDs for simulating microglial activation and inhibition, we found that striatal microglia constitute a critical hub for regulating affective state and encoding inflammation induced aversion by regulating the excitability of medium spiny neurons. Finally, we elucidated a more general mechanisms for the regulation of aversion: Melanocortin 4 receptors are responsible for encoding aversion to various types of negative stimuli -from stress to pain. When melanocortin 4 receptors are absent from striatal dopamine D1-receptor expressing neurons, mice will surprisingly perceive aversive stimuli as rewarding - this dichotomous behavior is mirrored in an inverted dopamine response to aversive stimuli. Though these pathways are central players in aversion and depression behaviors, a central question remains: How does affective and motivational circuits connect to regulate the aversive features of disease?

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