University of Fribourg / Faculty of Science and Medicine / Department of Biology

Mechanisms of learning, memory and forgetting in Drosophila melanogaster

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It is fascinating how our brain works and how it stores memories for up to a lifetime. Yet, it is susceptible to a wide range of diseases and disorders. Although the basic mechanisms for learning and memory are highly conserved, there still remain many mysteries. Even less is known about how a healthy brain changes to a diseased brain during aging. Given the high level of evolutionary conservation, simpler model systems can be used to shed light on the blank spaces in neuroscience. This work uses the fruit fly Drosophila melanogaster, a well-established model organism to study different aspects of learning, memory, and forgetting. The focus is on signaling pathways involved in learning and memory and how they change during Alzheimer's disease.

IIn the first part of the thesis – 2. Dopamine, sleep, and neuronal excitability modulate amyloid-β–mediated forgetting in Drosophila – a Drosophila Alzheimer's model, to study early disease stages, was established. In this model, the expression of the toxic Aβ peptides was restricted to the Mushroom body – the brain region where flies form associative memories. Older flies from this model develop memory formation defects. However, younger flies, show pronounced accelerated forgetting. Thus, there is an age-dependent progression in learning and memory phenotypes. Further, this work shows, that sleep, neuronal excitability, and the dopamine-dependent forgetting pathway play an important role in the progression of AD. This model offers the opportunity to look closer at the relationship between sleep, excitability, and forgetting pathways. Moreover, it can be used to test pharmaceutical reagents in Alzheimer's.

In the second part – 3. Generation of tools to study dopamine Receptors in Drosophila – antibodies and transgenic lines were established. Dopamine is a crucial neuromodulator for many brain processes. It acts through an intricated network of different receptors and downstream signaling pathways. Drosophila employs four dopamine receptors, which are all reported to be involved in learning, memory, and forgetting. The focus of this work was to create tools to get a better grip on the individual type of dopamine receptors and how they orchestrate the multiple dopamine function. Therefore, specific antibodies for the individual receptors were generated. Further, transgenic lines were made for three of the dopamine receptors that contained an HA-tag and two FRT sites to inactivate the receptor in neurons of interest.

Jury:
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