

## The role of mitochondrial and ER Ca2+ stores in the homeostasis of hippocampal circuits and its failures in Alzheimer's disease

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Age-related diseases, such as Alzheimer's disease (AD), are becoming increasingly common in the society. The AD field is currently changing its approaches from studying the late-stage AD pathology to trying to understand early-stage pathophysiology. This has a greater potential for therapeutic intervention. One key element that is still unknown is the mechanism behind early disease progression, which causes the transition from faulty neuronal circuits to clinically-evident memory decline. The research group hypothesize that failures in neuronal components such as mitochondria and endoplasmic reticulum play a key role in this transition. They have identified key proteins whose manipulation can regulate the mitochondria and endoplasmic reticulum, and will now study their behavior, which probably holds a key to understanding AD pathology. The scientists will combine AD and neuronal analysis, for which the Slutsky laboratory is specialized, with novel imaging tools developed in the Rizzoli laboratory. Their tools include novel optical microscopy approaches, such as 10x-expansion microscopy, in which the neurons are "dilated" 10 times before imaging, to obtain very high imaging detail. They will also use secondary ion mass spectrometry, in which a non-optical machine images the atomic composition of the neurons. By this combination of skills in neurobiology, pathology and technology the hope is to identify new biological mechanisms, and to provide new strategies for preventing memory decline in AD patients.

## Projektbeteiligte

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