**Reciprocal influence between APP expression and glucose metabolism in the hippocampus**

Nowadays, there is evidence that brain glucose metabolism and Alzheimer’s disease are linked. Patients suffering from type II diabetes present a higher risk to develop AD while in AD patients but also in preclinical stage (MCI) the brain glucose metabolism is reduced, leading to a general hypometabolism. Our hypothesis is that glucose metabolism disruption occurring during ageing or in disease condition like insulin resistance could lead to a compensatory increase in the expression of APP. This increase could in turn be the starting point of metabolic and neurotransmitter homeostasis disruption leading to cognitive impairments and AD. The aim of this project is to better understand the link between APP expression and brain glucose metabolism and its impact on neuronal activity and synaptic connections.

Three levels of APP expression are investigated thanks to APP WT, HT and KO mice. The neurophysiological impact of the genotype, of the glucose restriction and of the interaction between these two parameters is studied by extracellular electrophysiological recordings of cell excitability and synaptic activity in acute hippocampal slices incubated in control condition, mild and severe glucose deprivation. The metabolic profile in the hippocampus is studied by 1H-NMR spectroscopy in control and in hypoglycemic conditions.

Results highlight differences between WT and KO mice in metabolic profiles, sensitivity to glucose deprivation and susceptibility to hyperexcitability. Interestingly, HT present an intermediate phenotype confirming the importance of the level of expression of APP for the regulation of the metabolism.