Multimodal characterization of the Tg2576 mice model of ad

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In this talk I will show our latest results in the characterization of the Tg2576 mice model of AD. The Tg2576 is a transgenic strain expressing mutant amyloid precursor proteins (APPs) and constitute an opportunity for exploring the pathophysiology and neurobiology of Alzheimer's disease. Although cognitive function has been extensively characterized in this model, the neurophysiological basis of memory impairment is poorly understood. Here we aim at obtaining a full electrophysiological characterization of this model. To do that, we use systems neuroscience tools (chronic electrophysiological recordings and data analyses) to identify functional domains that could be involved in the progression of the cognitive deficit.

Morris water maze (MWM) and fear conditioning (FC) test were used to assess cognitive deficit in the Tg2576 mice. Then, animals were implanted with ECoG screws on prefrontal cortex together with 6 equally spaced deep electrodes in the hippocampal CA1 region and EMG. After recovery, mice were recorded in a freely moving open field and under physiological sleep. Behavioral states were divided into awake rest, awake movement, slow sleep and REM sleep conditions. Raw signals were inspected for the presence of artifacts and segments containing low quality signals were removed from the analyses. Around 75% of the Tg2576 animals (17) showed paroxysmal activities originated in the dentade gyrus that spread into the CA1 region, mostly under sleep conditions. On the contrary, such activities were not detected in any of the wild type (WT) mice recorded (24). Then power spectrum, cross-frequency coupling and imaginary coherence estimates were obtained and compared across conditions and genotypes. Age effect was investigated by means of covariance analyses and detected significant differences between Tg and WT, mainly during sleep. To finish, electrophysiological parameters were correlated with behavioral (MWM, FC) and histopathological (amyloid and tau deposition) markers.

To the best of our knowledge this is one the most detailed characterizations of the Tg2576 electrophysiology that could serve to guide new investigations devoted to bridge the gap between behavioral deficits and histopathological markers present in this mice model for AD.

This is a joint work wit Sandra Arrieta, A. Ricobaraza, M. Nicolás, and J. Artieda.