Abstract booklet

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proinflammatory cytokines and chemokines including TNF-α, IFN-γ and CCL2. Moreover, evidence for synaptic stripping was detected in the hippocampus by increased phagocytic microglia engulfment of the postsynaptic compartment (IBA-1/ LAMP-1/Homer-1+ puncta). While neuroinflammation induced by the neurotropic H7N7 IAV showed the strongest effect, systemic infection with both non-neurotropic H1N1 and H3N2 subtypes also resulted in long-term impairments in synapse number and hippocampal function. Interestingly, at 120 dpi, a severe spatial learning deficit was still detectable in aged H7N7 IAV-infected mice which was not the case in young adult individuals. These results clearly demonstrate that IAV infection can lead to prolonged and more severe impacts on hippocampal function in older animals representing highly vulnerable individuals, reminiscent of the cognitive impact of "long COVID-19" symptoms.

T14-068D

Coexistance of different damage-associated myeloid populations in the hippocampus of Alzheimer's patients

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Parenchymal microglia are the brain-resident immune cells capable of responding to damage and disease. Though the role of microglial cells in the development/progression of AD is still unknown, a dysfunctional response has recently gained support since the identification of several genetic risk factors related to microglial function. In this sense, and clearly in contrast to that observed in amyloidogenic models, we have reported an attenuated microglial activation associated to amyloid plaques in the hippocampus of AD patients, including a prominent degenerative process of the microglial population in the dentate gyrus. On the other hand, it is also known that others myeloid components, apart from microglia, could also be involved in the neurodegenerative process. However, these different phenotypes and the implication of the diverse immune cells in the human pathology have not been determined yet. In this work, we analyzed the phenotypic profile displayed by damage-associated myeloid cells in the hippocampus of AD brains. For this purpose, immunohistochemistry and image analysis approaches have been carried out in p*ostmortem* frontal cortex from non-demented controls (Braak II) and AD cases (Braak V-VI). Damage-associated myeloid cells from Braak II and Braak VI individuals were clustered around amyloid plaques and expressed Iba1, TMEM119, CD68, Trem2 and $CD45^{high}$. A subset of these cells also expressed ferritin. However, and even though some Braak II individuals accumulated CD45-positive plaques, only AD patients exhibited parenchymal infiltration of CD163-positive cells (Iba1+/$CD45^{high}$/CD163+/MCR1-), along with a decrease of the resident microglial marker TMEM119. Moreover, a negative correlation was observed between CD163 and TMEM119 intensities in Braak VI patients, showing a functional cooperation among these different myeloid populations. The homeostatic and ramified microglial like cells of non-demented Braak II cases were characterized by Iba1, CX3CR1, P2ry12, TMEM119 and $CD45^{low}$ expression. Taken together, these findings suggest the existence of different populations of amyloid-associated myeloid cells in the hippocampus during disease progression. The differential contribution of these myeloid populations to the pathogenesis of the disease remains to be elucidated. The dynamic of the myeloid molecular phenotypes associated to AD pathology needs to be considered for better understand the disease complexity and, therefore, guarantee clinical success. Correcting dysregulated brain inflammatory responses might be a promising avenue to prevent/slow cognitive decline.

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Essential omega-3 fatty acids tune microglial phagocytosis of synaptic elements in the mouse developing brain

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Omega-3 fatty acids (n-3 PUFAs) are essential for the functional maturation of the brain. Westernization of dietary habits in both developed and developing countries is accompanied by a progressive reduction in dietary intake of n-3 PUFAs. Low maternal intake of n-3 PUFAs has been linked to neurodevelopmental diseases in Humans. However, the n-3 PUFAs deficiency-mediated mechanisms affecting the development of the central nervous system are poorly understood. Active microglial engulfment of synapses regulates brain development. Impaired synaptic pruning is associated with several neurodevelopmental disorders. We identify a molecular mechanism for detrimental effects of low maternal n-3 PUFA intake on hippocampal development in mice. Our results show that maternal dietary n-3 PUFA deficiency increases microglia-mediated phagocytosis of synaptic elements in the rodent developing hippocampus, partly through the activation of 12/15-lipoxygenase (LOX)/12-HETE signaling, altering neuronal morphology and affecting cognitive performance of the offspring. DHA, the main n-3 PUFA, highly accumulates in the brain over the perinatal period. Using genetically engineered mice allowing to increase n-3 PUFA in microglia (iFAT1:Cx3cre1creERT2), we investigate how early-life n-3 PUFAs impacts postnatal brain and establish a causal link between n-3 PUFA action on microglia and miswiring of the brain.

T14-070D

Involvement of neuroinflammation processes in nociceptive defects of *Fmr1* KO mice, model of Fragile X syndrome.

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Fragile X Syndrome (FXS) is the most common inherited cause of intellectual disability. FXS is due to large expansions of CGG repeat in *Fmr1* causing loss of FMRP (fragile X mental retardation protein) expression. Among the wide range of associated abnormalities, inadequate responses to environmental stimuli are described and could explain self-injurious behavior related to 60% of FXS patients. Although these sensorial disturbing features could contribute to the cognitive deficits and affect social interactions, the cellular and molecular processes involved are still poorly understood. To this purpose, our experiments using the *Fmr1* knockout mouse model (*Fmr1* KO) focused on tactile sensitivity in normal and inflammatory conditions.
In our experiments, *Fmr1* KO mice shown a hypersensitivity in chronic inflammatory condition. This inflammation