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Topic: AS07 Aging and Neurodegenerative Disorders

## ASRIJ/OCIAD1 DEPLETION RESULTS IN REDUCED GLIAL ACTIVATION AND DECREASES NEUROINFLAMMATION

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Neuroinflammation, driven by activation of astrocytes and microglia, progressively increases with age and is associated with neurodegenerative disorders such as Alzheimer's disease (AD). While the role of microglia and inflammatory pathways is well-known, mechanisms that control neuroinflammation are not well understood. Recent studies show that mitochondria serve as regulatory hubs for the assembly and activation of inflammatory pathways. Mitochondrial homeostasis also impacts glial activation and neuroinflammation. We previously showed that the mitochondrial protein Asrij/OCIAD1 (Ovarian Carcinoma Immunoreactive Antigen Domain containing 1) regulates mitochondrial homeostasis and stem cell aging. Recent reports show increased Asrij levels in the brains of AD patients and AD mouse models. Hence, we examined the status of Asrij in the mouse brain. Immunoblotting analysis showed that aged wild type mice had increased Asrij protein in the cortex. Upregulation of Asrij may promote neuroinflammation or be a protective response during aging. Hence, we used *asrij* knock-out (KO) mice and checked the effect on appearance of hallmarks of aging. Interestingly, immunofluorescence staining of brain cryosections showed that unlike wild type aged mice, aged *asrij* KO mice had no reduction in neuronal numbers and dendritic coverage. Further, the number of reactive $GFAP^+$ astrocytes and $Iba1^+$ microglia was reduced. In addition, astrocyte activation assessed by S100B expression and microglial activation assessed by CD68 levels, was reduced. Additionally, aged KO mice had reduced IL-6/STAT3 and TNFα/NF-KB inflammatory signalling as seen by immunoblotting. Also, qRT-PCR shows increased microglial homeostatic and anti-inflammatory gene expression and reduced pro-inflammatory gene expression. This suggests that increase in Asrij levels during aging in the mouse brain promotes astrocyte and microglial activation and thereby neuroinflammation. Asrij level is elevated in APP/PS1 AD mice, which show increased neuroinflammation. Hence, we are testing whether reducing Asrij levels (KO) in a neuroinflammatory disease model such as AD would help curtail the disease.

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## DIFFERENCES IN WCST ASSOCIATED WITH CHRONIC PAIN IN AGING: A VBM PILOT STUDY

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Chronic pain and aging are causes of cognitive decline. Thus, chronic pain may particularly exacerbate cognitive conditions in aging but the analysis of their interaction with brain atrophy is particularly unknown. Cognitive neuropsychological performance associated with aging may serve to dissociate brain´s aging effects on cognition and pain. The aim of this study was to analyze how neuropsychological performance in the Wisconsin Card Sorting test (WCST) in musculoskeletal pain condition associates to brain regions showing alterations in both pain and aging. Thirty older adults with chronic musculoskeletal pain (69,5 ± 6.58 years; 14 males), 29 healthy older adults (70.483 ± 4.60years; 15 males) and 30 younger adults (20.0 ± 1.58 years; 15 males) participated in the study. T1-weighted MRI scans were preprocessed for voxel-based morphometry analysis. WCST performance was compared between groups. Finally, WCST performance´s variables in the chronic pain older adult group were correlated with brain volumes in the anterior cingulate cortex (ACC) and the insula as brain regions affected by pain and aging. Our results showed that, whole brain voxel-wise analysis showed widespread atrophy associated with aging involving different portions of frontal, parietal and temporal regions when young adults were compared to older adults, including both with and without musculoskeletal pain condition. Second, chronic pain older adults showed poorer performance in the WCST in comparison to the healthy older adults, in the percentage of trials executed to complete the test, the percentage of errors and the percentage of conceptual level responses. Third, correlational analyses showed that the left ACC was negatively associated with the number of trials, while the left insula was associated with the percentage of errors and the percentage of conceptual level. Therefore, the sum of our results suggests the interaction between chronic pain and cognitive decline in aging.Supported by the Spanish Ministry (PID2019-110096GB-I00/AEI /10.13039/501100011033).

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