

Effects on the hippocampal microglia after acute treatment of a psychological stressor associated with depressive-like behaviours

Andrea Nieto-Quero^{1,2}, María Inmaculada Infantes-López^{2,3}, Emma Zambrana-Infantes^{1,2}, Patricia Chaves-Peña^{1,3}, Sara Tabbai^{1,2}, Margarita Pérez-Martín^{2,3}, Carmen Pedraza^{1,2}

¹ *Department of Psychobiology and Methodology of Behavioral Sciences. University of Malaga. Malaga, Spain*

² *Instituto de Investigación Biomédica de Málaga (IBIMA). University of Malaga. Malaga, Spain*

³ *Department of Cell Biology, Genetics and Physiology. University of Malaga. Malaga, Spain*

Abstract

Stressful life events may have a negative impact on mental health compromising people's well-being, so knowing the neurobiological changes that occur after psychosocial stressors can have an impact on overall health. However, the neurobiological mechanisms responsible for the negative effects are not known in detail, and the initial changes that take place after the initiation of a stress protocol are much less well understood. Hippocampus constitutes a target structure of the adverse effects of stress. Among the possible mechanisms involved, the response of microglia to stress is receiving increasing interest. For this reason, after 1 and 24 hours of submitted C57BL/6J mice to acute and intense stress procedure denominated WIRS (water immersion restraint stress), the microglial response were analysed using a set of morphofunctional parameters. Then, the levels of the cytokines: IL-6, IFN-gamma and TNF-alpha cytokine were measured. Furthermore, a complementary proteomic analysis based on the principle of mass spectrometry was carried out. Results reveal that acute stress increased the number of microglia and induced microglial morphofunctional changes. Regarding cytokines, acute stress only increased IL-6 levels, which remained elevated at 24 h. Proteomic analysis, over time (in 24 h post-stress), showed an increase in proteins associated with the intracellular calcium metabolism. These findings suggest a neuroinflammatory response after acute stress observed at one hour after the application of the WIRS protocol and maintained at least 24 hours after the end of the stressor.

Funding: This study was supported by FEDER/Ministerio de Ciencia, Innovación y Universidades – Agencia Estatal de Investigación from Spain (PSI2017-83408-P to C. Pedraza), and Ministerio de Universidades from Spain (FPU16/05308 to A. Nieto-Quero and FPU19/03629 to M.I. Infantes-López).