Role of the inflammation in the control of the GABA switch in cultured hippocampal neurons

1)Desiato G. 2)Mirabella F. 3)Filipello F. 4)Matteoli M. 5)Pozzi D.

Hunimed

The transition of GABA signalling from excitatory to inhibitory represents a critical process of brain development. The process is determined by a change in intracellular chloride concentration, through the activity of two chloride cotransporters, NKCC1 and KCC2. An altered GABA switch is associated with different neurodevelopmental disorders, including autism, which are frequently related to inflammatory states. Hence, we investigated whether immune molecules produced during inflammation can impinge the GABA switch during neuronal development. Using a combination of calcium and chloride imaging techniques, we found that IL-6, a major pro-inflammatory cytokine, is able to accelerate the GABA switch in neuronal cultures by potentiating GABAergic transmission. This effect involved STAT-3 activation, a transcription factor activated by IL-6 signalling, as the STAT3 inhibitor Stattic prevented the IL-6–mediated GABA switch potentiation. Moreover, qRT-PCR analysis revealed that KCC2, but not NKCC1, gene was upregulated upon IL-6 treatment thus suggesting a possible effect of this cytokine specifically on KCC2 expression. Taken together, these results show that IL6 may regulate the developmental GABAergic switch through STAT3 activation and REST-mediated gene regulation. Further experiments will allow to clarify the role of IL-6 as a critical player in such a crucial process.