Role of the JAKs/STATs pathway in the intracellular calcium changes induced by interleukin-6 in hippocampal neurons

Orellana, Daniel I.

Quintanilla, Rodrigo A.

Gonzalez-Billault, Christian

Maccioni, Ricardo B.

Recent studies show that inflammation has an active role in the onset of neurodegenerative diseases. It is known that in response to extracellular insults microglia and/or astrocytes produce inflammatory agents. These contribute to the neuropathological events in the aging process and neuronal degeneration. Interleukin-6 (IL-6) has been involved in the pathogenesis of neurodegenerative disorders, such as Alzheimer's and Parkinson's diseases. Here, we show that IL-6 treatment of rat hippocampal neurons increases the calcium influx via NMDA-receptor, an effect that is prevented by the specific NMDA receptor antagonist MK-801 (dizocilpine). We also show that this calcium influx is mediated by the JAKs/STATs pathway, since the inhibitor of JAKs/STATs pathway, JAK 3 inhibitor, blocks calcium influx even in the presence of IL-6. This increase in calcium signal was dependent on external sources, since this signal was not observed in the presence of EGTA. Additional studies indicate that the i