the impact of AβOs on neurons has been extensively studied, only recently have the possible effects of AβOs on astrocytes begun to be investigated. Given the key roles of astrocytes in synapse formation, plasticity, and function, we sought to investigate the impact of AβOs on astrocytes and to determine whether this impact is related to the deleterious actions of AβOs on synapses. We found that AβOs interact with astrocytes, cause astrocyte activation, and trigger abnormal generation of reactive oxygen species, which is accompanied by impairment of astrocyte neuroprotective potential *in vitro*. We further show that both murine and human astrocyte conditioned media increase synapse density, reduce AβOs binding, and prevent AβO-induced synapse loss in cultured hippocampal neurons. Both a neutralizing anti-transforming growth factor-β1 (TGF-β1) antibody and siRNA-mediated knockdown of TGF-β1 previously identified as an important synaptogenic factor secreted by astrocytes, abrogated the protective action of astrocyte conditioned media against AβO-induced synapse loss. Notably, TGF-β1 prevented hippocampal dendritic spine loss and memory impairment in mice that received an intracerebroventricular infusion of AβOs. Results suggest that astrocyte-derived TGF-β1 is part of an endogenous mechanism that protects synapses against AβOs. By demonstrating that AβOs decrease astrocyte ability to protect synapses, our results unravel a new mechanism underlying the synaptotoxic action of AβOs in AD.

Astrocytes as Active Players of the Innate Immune System: Another Layer of Astroglial Heterogeneity?

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Reactive gliosis involving activation and proliferation of astrocytes and microglia is a widespread but largely complex and graded glial response to brain injury. Astroglial population has a previously underestimated high heterogeneity with cells differing in their morphology, gene expression profile, and response to injury. Over the last years, we have been studying whether astrocytes may behave as facultative innate immunity cells after central nervous system injury. Classical innate immunity activation in the absence of infection relies on the damage-associated molecular patterns (DAMP) release by dying cells. DAMPs behave as ligands of the pattern recognition receptors, such as Toll-like receptor, RAGE, and others. Using a combination of mathematical modeling, *in vitro* and *in vivo* experimentation, we have been able to show that astrocytes essentially behave as facultative cells of the innate immunity response that classically follows brain damage. While classical innate immunity pathways such as those involving RAGE, Toll-like receptor 4/nuclear factor-κB, and TREM-2 are activated by released DAMPs, astrocytes are also key players in determining the interaction with local and peripheral professional immune cells. Moreover, detailed histological studies and *ex vivo* culture experiments have shown that only a subset of astrocytes seems to have the immune and neuroinflammatory role in experimental focal brain lesions and they can be specifically targeted by dendrimeric nanoparticles. This additional layer of neurobiological complexity can also be explored for therapeutic purposes oriented toward controlling neuroinflammation in the injured brain.

Are Neuroinflammation and Astrocytes Key Elements in L-DOPA-Induced Dyskinesia in Parkinson's Disease?

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Inflammation in Parkinson's disease (PD) is a new concept that has gained ground due to the potential of mitigating dopaminergic neuron death by decreasing inflammation. The solution to this question is likely to be complex. We propose here that the significance of inflammation in PD may go beyond the nigral cell death. The pathological process that underlies PD requires years to reach its full extent. A growing body of evidence has been accumulated on the presence of multiple inflammatory signs in the brain of PD patients even in very late stages of the disease. Because neuron–microglia–astrocyte interactions play a major role in the plasticity of neuronal response to l-DOPA in post-synaptic neurons, we focused this review on our recent results of l-DOPA-induced dyskinesia in rodents correlating it to significant findings regarding glial cells and neuroinflammation. We showed that in the rat model of PD/l-DOPA-induced dyskinesia, there was an increased expression of inflammatory markers, such as the enzymes COX2 in neurons and iNOS in glial cells, in the dopamine-denervated striatum. The gliosis commonly seem in PD was associated with modifications in astrocytes and microglia that occur after chronic treatment with l-DOPA. Either as a cause, consequence, or promoter of progression of neuronal degeneration, inflammation plays a role in PD. The key aims of current PD research ought to be to elucidate (a) the time sequence in which the inflammatory factors act in PD patient brain and (b) the mechanisms by which