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"Maresin1 protection of dopaminergic neurons involves activation of astrocytes in vivo"

Parkinson's disease (PD) is a neurodegenerative disorder that affects the dopaminergic neurons in the Substantia Nigra (SN). Astrocytes, the largest and most abundant type of supporting cells in the central nervous system, participate in the detection and communication of stress signals from neurons to microglial cells. For this purpose, astrocytes change their phenotype, in some cases transforming themselves into reactive types with the subsequent release of cytokines and chemokines with the activation of NFkB/p65 transcription factor. These phenotypes direct the defensive neuroprotective efforts to modulate neuroinflammation. We hypothesize that Maresin1 induces the anti-inflammatory conversion of astrocytes when 6-hydroxydopamine (6HODA) exerts toxicity on dopaminergic neurons to help them survive. This hypothesis was tested in a 6HODA toxicity transgenic rat model that expresses GFP driven by the tyrosine hydroxylase (TH) promoter. The rats were administered 5 µg of Maresin 1 intranasally, pre and post stereotactic injection of 6HODA. We used immunohistochemistry to detect nuclear p65 in glial fibrillary acidic protein positive cells, a marker of astrocytes in different areas of the rat brain. The confocal captured z-stacks were processed using IMARIS 10 and the data was statistically analyzed. The number and intensity of nuclear p65 positive nuclei was obtained. Stereology was used to verify that the Maresin1 treatment protected dopaminergic neurons via the detection of the expression of GFP in the substantia nigra (SN) area. There was no significant difference in the amount of dopaminergic neurons between Ipsilateral side of injection and the contralateral control in the Maresin 1 treated animals. The opposite was observed in the rats that were administered saline intranasally; dopaminergic neurons were completely absent at the site of injection. Astrocytes in the ipsilateral hemisphere of Maresin1-treated animals showed double the intensity of nuclear p65 than the contralateral control, despite the notorious protection elicited by the lipid mediator. We concluded that astrocytic activation took place and did not prevent Maresin1 from protecting the SN. Markers of anti-inflammatory astrocyte phenotypes are needed to determine whether p65 is part of the pro-survival astrocytic program.