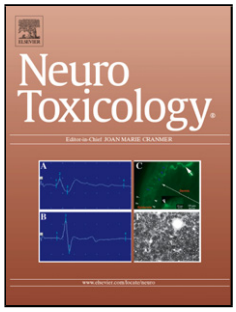

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PII: S0161-813X(18)30081-0
DOI: https://doi.org/10.1016/j.neuro.2018.03.003
Reference: NEUTOX 2309

To appear in: *NEUTOX*

Received date: 13-10-2017
Revised date: 6-3-2018
Accepted date: 6-3-2018

Please cite this article as: Chen X, Nie X, Mao J, Zhang Y, Yin K, Jiang S, Perfluorooctanesulfonate induces neuroinflammation through the secretion of TNF-α mediated by the JAK2 / STAT3 pathway, *Neurotoxicology* (2010), https://doi.org/10.1016/j.neuro.2018.03.003

Perfluorooctanesulfonate induces neuroinflammation through the secretion of TNF-α mediated by the JAK2 / STAT3 pathway

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Highlights

- PFOS promote the expression and secretion of TNF-a in C6 astrocyte.
- PFOS promote STAT3 signaling activation in primary astrocytes and C6 cells.
- Astrocytic TNF-α secretion contributes to PFOS-mediated neuronal apoptosis.

Abstract

Perfluorooctanesulfonate (PFOS)-containing compounds are widely used in all aspects of industrial and consumer products. Recent studies indicated that PFOS is ubiquitous in environments and is considered to be a new type of persistent organic pollutant (POP). This has raised concerns regarding its adverse effects on human health. The nervous system is regarded as a sensitive target of environmental contaminants, including PFOS. Previous findings showed that PFOS can induce neurobehavioral deficits. However, the molecular mechanism underlying PFOS neurotoxicity remains obscure. Astrocyte activation and the resulting pro-inflammatory cytokine release play an integral role in protecting neurons from neurotoxin-mediated damage. If uncontrolled, sustained astrocyte activation may cause the secretion of excessive levels of pro-inflammatory cytokines that exacerbate the initial damage. In this study, we showed that PFOS could promote excessive secretion of tumor necrosis factor-α (TNF-α) in dose- and time-dependent manners in astrocytes. Furthermore, PFOS exposure could induce the phosphorylation of Janus kinase 2 (JAK2)/signal transducer and activator of transcription 3 (STAT3). This suggests that the JAK2/STAT3 signal transduction pathway is involved in PFOS-mediated astrocyte activation and secretion of TNF-α. Indeed, targeted blockage of the JAK2/STAT3 pathway prevented the phosphorylation of JAK and STAT3, and it also caused abnormal expression of TNF-α. Finally, we demonstrated that SH-SY5Y neuronal cells underwent