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NEUROSCIENCE 2014

Presentation Abstract

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Presentation Title:	Corticosterone enhances chlorpyrifos-induced neuroinflammation
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Topic:	++C.11.g. Neurotoxicity and neurodegeneration

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Abstract: Elevated expression of proinflammatory mediators in the CNS serves as the basis for normal and pathophysiological neuroinflammation. For example, the enhanced expression of proinflammatory cytokines and chemokines such as TNF-α, IL-1β, IL-6 and CCL2 may underlie the general malaise termed sickness behavior as well as depression and can affect and contribute to a risk of neurodegeneration in affected individuals. Chemical exposures that increase the degree or duration of proinflammatory responses in the CNS may lead to more severe symptoms and consequences of neuroinflammation. Our prior data indicate that acute exposure of the C57Bl6/J mouse to the irreversible cholinesterase inhibitor, diisopropylfluorophosphate (DFP), results in a neuroinflammatory response in multiple brain regions, as evidenced by enhanced expression of a large variety of proinflammatory cytokines over a 12-hr post exposure period. Surprisingly, treatment with anti-inflammatory glucocorticoid, corticosterone (CORT), enhanced rather than suppressed DFP-induced

neuroinflammation. These findings suggested that CORT might serve as a stressor surrogate to "prime" the neuroinflammatory response to workplace and environmentally relevant exposures to organophosphates, such as the widely used pesticide, chlorpyrifos (CPF). Here, we administered CPF (8 mg/kg, i.p.) with and without prior CORT (400 μg/ml in the drinking water for 4 days) to C57Bl6/J male mice. As with DFP, CPF alone caused neuroinflammation (increases in mRNA for TNF-α, LIF, CCL2 and OSM) at 6 hrs. post dosing. These effects were markedly enhanced by the prior exposure to CORT and broadened to include another cytokine (IL-1β). These findings suggest that stressors experienced by pesticide applicators and other workers exposed to CPF will contribute to a neuroinflammatory response of yet to be characterized duration or severity. (supported by intramural funds from CDC-NIOSH)

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