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Endoplasmic reticulum (ER) stress and neuroinflammation are implicated as significant contributors to neurodegeneration and cognitive dysfunction in a variety of neurodegenerative diseases. Recently, we reported that exposure to deltamethrin, the pyrethroid insecticide, causes hippocampal ER-stress, apoptotic cell death cognitive deficits in adult mice (Hossain et al., 2015). Here, we investigated the mechanistic links between ER-stress and neuroinflammation following exposure to deltamethrin**.** We found that single oral exposure to very low dose of deltamethrin (1 mg/kg) caused neuroinflammation as mice exhibited with microglial activation and increased protein levels of TNF-α, gp91phox, and iNOS in the hippocampus. These changes were accompanied by induction of ER stress as the protein levels of C/EBP-homologous protein (CHOP) and glucose-regulated protein 78 (GRP-78) were significantly increased in hippocampus following exposure to deltamethrin. To determine whether induction of ER Stress triggers the inflammatory response, mice were treated with two intraperitoneal (i.p.) injections of 1 mg/kg salubrinal (ER stress inhibitor) 24 h and 30 min before the administration of deltamethrin. Inhibition of ER stress with salubrinal prevented deltamethrin-induced TNF-α, gp91phox and iNOS activation. For further confirmation of these results, we performed an additional experiment with BV2 cell lines. We found that inhibition of ER stress with salubrinal significantly attenuated the levels of TNF-α, gp91phox, and iNOS in BV-2 cells. Collectively, these results demonstrate that exposure to deltamethrin leads to ER stress mediated neuroinflammation, which may contribute to neurodegeneration and neuronal dysfunction in mice. *Supported in part by* 1R01ES027481-01A1.