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Endoplasmic reticulum (ER) stress is implicated as a significant contributor to neurodegeneration and cognitive dysfunction. Recently, we reported that repeated exposure to deltamethrin (3 mg/kg every 3 days for 30 or 60 days) causes hippocampal ER-stress, apoptotic cell death, and deficits in learning and memory in adult mice (Hossain et al., 2015). Here, we investigated whether ER-stress and apoptotic cell death in the brain occurs following oral administration of a single dose of deltamethrin. We found that deltamethrin exposure (6 mg/kg) caused ER stress as the levels of C/EBP-homologous protein (CHOP) and glucose-regulated protein 78 (GRP-78) significantly increased in both the hippocampus and cortex. The levels of CHOP were increased by 148% in the hippocampus at 24 to 48 h. In the frontal cortex, CHOP was increased by 146% at 48 h after deltamethrin exposure. Similarly, the level of GRP-78 was increased by 314% and 262% in the hippocampus at 24 and 48 h. The levels of GRP-78 increased to 178% at 24 h and remained 139% increased at 48 h in the frontal cortex. These were accompanied by increased levels of activated caspase-12 both in the cortex and hippocampus. To determine whether these effects resulted in apoptosis, activated caspase-3 was evaluated in both brain regions. We found that deltamethrin-treated animals resulted in a 249% increase of caspase-3 in the hippocampus compared to 171% in the cortex at 48 h after deltamethrin exposure. Collectively, these results demonstrate that single exposure to deltamethrin leads to ER stress and causes apoptotic cell death in the cortex and hippocampus, with the hippocampus displaying an earlier and more robust response. Together, these data suggest hippocampal-mediated behaviors may be more affected following deltamethrin exposure. *Supported in part by R01ES015991 and U01NS079249*.