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ORGANOPHOSPHATE-INDUCED BRAIN DAMAGE: NECROSIS, APOPTOSIS AND GFAP EXPRESSION

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The distribution of necrotic and apoptotic neural cells, and expression of astrocytic glial fibrillary acidic protein (GFAP) in the brain of rats poisoned intraperitoneally with diisopropylfluorophosphate were investigated. Pyridostigmine bromide (0.1 mg/kg) and atropine methylnitrate (20 mg/kg), which are centrally inactive, were treated intramuscularly 30 min and 10 min, respectively, before diisopropylfluorophosphate (4 - 10 mg/kg) poisoning to reduce the mortality. Diisopropylfluorophosphate induced severe limbic seizures, and early necrotic and delayed apoptotic neural injuries, and rapid astrocytic responses. The necrosis, which was closely related to seizure intensity, was observed as early as 1 hr predominently in hippocampal pyramidal cells, cerebellar Purkinje cells and neurons in pyriform/entorhinal cortices, showing malacia of neurophils. In contrast, typical TUNEL-positive apoptosis started to appear 12 hr after poisoning in neurons in thalamus, amygdala and neocortex, and ephendymal cells surrounding the 4th ventricle. Marked apoptotic changes were induced in rats exhibiting relatively-low seizure intensity. Thus, the degree of necrotic and apoptotic injuries was shifted to each type according to the seizure intensity. The distribution of activated astrocytes, observed within 1 hr along the limbic system, was not in parallel with those of necrotic and apoptotic injuries, implying that the astrocytic responses resulted from seizure activity rather than neural injuries. In addition, astrocytes as well as neurons in malacic tissues disappeared during the severe limbic seizures. Therefore, it would be one of the cautionary notes on the GFAP expression in astrocytes as a biochemical marker of brain injuries following acute exposure to organophosphates.