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REGIONAL NEUROPATHOLOGY FOLLOWING KAINIC ACID INTOXICATION IN C57BL/6J MICE.

S.A. Benkovic*, J.P. O'Callaghan, and D.B. Miller, Chronic Stress Laboratory, CDC-NIOSH, Morgantown, WV 26505

We have evaluated regional neuropathological changes in young (4 month) and aged (20 month) male C57BL/6J mice treated systemically with kainic acid. Young animals received a single i.p. injection of kainate (35mg/kg), while aged animals received a lower dose of KA (20 mg/kg) to prevent excessive mortality. Seizures were scored according to the Racine scale and were grouped into two categories: animals which seized severely and died, and animals which generally seized at Stage 1 (mouth and facial movements). Following various recovery times from 12 hours to seven days post-treatment, animals were sacrificed and prepared for histological evaluation using the cupric-silver neurodegeneration stain. Kainate-induced argyrophilic neurons were observed in most major brain regions including cortex, hippocampus, thalamus, amygdala, and septum, and the extent of argyrophilia was exacerbated with age. Silver stained neurons were quantified using a four-point non-parametric scale which revealed significant neuropathological profiles in most brain regions examined. Neurotoxicity of kainate was considerably underestimated by Nissl and Fluoro-Jade B stains. Concomitant with neuropathology, we observed robust reactive gliosis (activation of astrocytes and microglia). Our data indicate kainic acid causes widespread neuropathology in C57BL/6J mice following limited seizure activity, which is exacerbated with age. Evaluation of potentially neurotoxic compounds should incorporate sensitive indicators of histological damage and a thorough time-course of analysis.

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