Quantitative T_2 mapping as a biomarker of neuropathology resulting from acute organophosphate intoxication in a rat model

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Introduction: Acute intoxication with organophosphates (OPs) present in nerve agents and pesticides causes life threatening cholinergic crisis, seizures, and long-term neurologic consequences. T_2 relaxation time (T_2-mapping) from MRI has been used to assess the spatiotemporal progression of these pathologies. However, little data exists to characterize these pathologies beyond the first few days of OP intoxication. The objective of this study was to assess T_2 mapping as a biomarker for characterizing long-term neuronal consequences of OP intoxication and neuroprotective therapies in a rodent model.

Methods: Adult Sprague Dawley rats were imaged at days 3, 7 and 28 post-intoxication with the OP diisopropylfluorophosphate, (DFP, n=32, VEH, n=13) using a spin-echo pulse sequence with 15 echo times (TEs). Three therapies were investigated: midazolam (MDZ, n=29), a neurosteroid allopregnanolone (ALO, n=28), a combination (DUO, n=28). The hippocampus (H) and piriform cortex (PC) were manually delineated given their known significance as targets of OPI. A mono-exponential curve fit was performed with MATLAB using 2 approaches: (1) Voxel-wise quantification: curve fitting the intensity-TE curves for each voxel, providing a voxel-wise map of T_2 values; and (2) Regional quantification: regionally averaging the intensity curves at each TE, performing one curve fit and obtaining a single T_2 value per region.

Results and Conclusion: For both modeling approaches, the DFP group had longest T_2 values compared to treatment groups ($p<0.05$). VEH T_2 values were within the range reported in the literature. T_2 values of OP-intoxicated rats were longest on day 3 and decreased with time. The voxel-wise quantification method showed a larger variation in T_2 values within regions, suggestive of intra-regional heterogeneity of neuronal damage consistent with visible lesions on T_2-weighted images (Figure 1). This study demonstrates the potential of T_2 mapping as a quantifiable biomarker to longitudinally track neuropathology post OP intoxication.

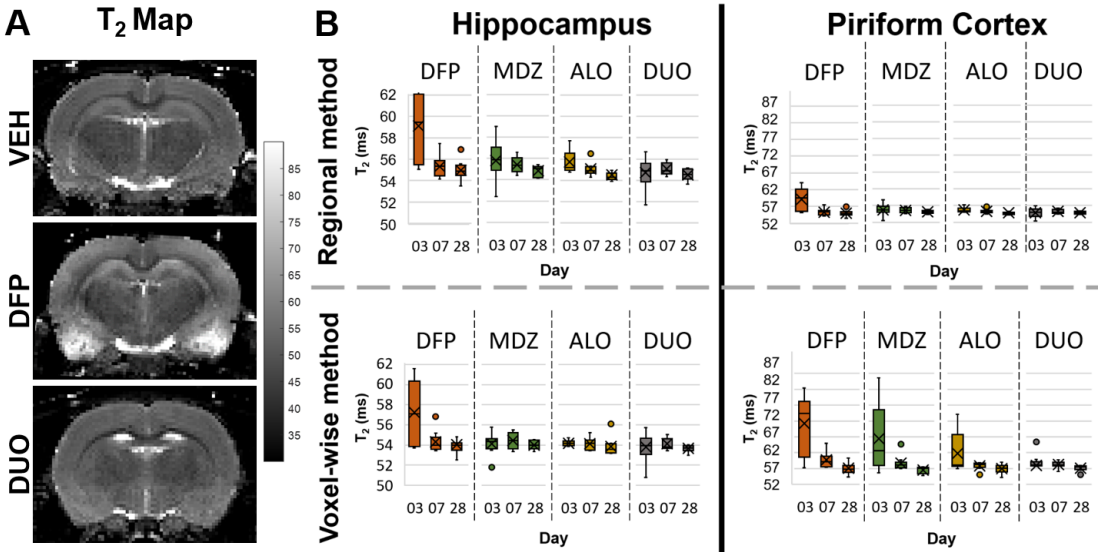

Figure 1) (A) T_2 maps on Day 3 of VEH, DFP, and DUO groups. Color bar shows T_2 values in ms; (B)T_2 value distribution for hippocampus and piriform cortex across groups and with voxel-based (top row) and regional (bottom row) quantification methods.