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Title: Addition of Ketamine to Standard-of-Care Countermeasures for Acute Organophosphate Poisoning Improves Neurobiological Outcomes

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ACCEPTED MANUSCRIPT

Addition of Ketamine to Standard-of-Care Countermeasures for Acute Organophosphate

Poisoning Improves Neurobiological Outcomes.

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Highlights:

- 1. Rodents exposed to Sarin show a substantial degree of neurobiological compromise (as indexed by EEG, mnemonic behavior, and histology), even when treated with standard-of-care (SOC) countermeasures consisting of atropine and 2PAM, within one minute of exposure, and Midazolam at 50 minutes post-exposure. Although animals improve over the days and weeks post-exposure, a significant degree of compromise persists for at least one month post-exposure.
- 2. When the Midazolam-SOC is augmented by addition of high-dose Ketamine, the neurobiological burden is markedly reduced. As early as hours 13-24 post-sarin, the group with both high-dose Ketamine and the Midazolam-SOC shows better EEG than the group with just the Midazolam-SOC (p<0.005, Mood's Median Test). At 29 days post-sarin exposure, 90% of the animals that received

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