

THE COX-2 INHIBITOR MELOXICAM AMELIORATES SHORT TERM MEMORY DYSFUNCTION AND MODULATES MICROGLIA ACTIVATION AFTER SPLENECTOMY IN ADULT MICE

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Introduction: Surgery induced neuro-inflammation is implicated in cognitive disorders. We tested whether the NSAID meloxicam (MEL) 24h after splenectomy could suppress microglia activation and prevent short-term memory (STM) impairment in adult mice. Splenectomy causes neuro-inflammation and cognitive dysfunction (1).

Methods: After IACUC approval 63 Swiss-Webster mice (35-45gm, 6-8 wks) randomized: 1) splenectomy, test on day 1; 2) splenectomy, test d5; 3) splenectomy, test d9; 4) splenectomy, test d14; 5) splenectomy then i.p. MEL at 24h, test od5; 6) splenectomy, MEL 24h, test d9. Splenectomy under isoflurane, 1 cm incision, ligation with 6-0 silk, closure with 4-0 silk. The object recognition test (ORT) was used to test STM. On d5 training, mouse placed in arena with identical objects for 15mins. For 3 mins testing 1h later a novel object replaced familiar one. STM scores were defined as the ratio of time spent exploring the novel object to time spent exploring both objects. Statistics used Wilcoxon and Kruskal Wallis rank tests. 3 additional mice per group had histology and histochemistry (Tomato lectinstaining) to visualize activated microglia.

Results: Hippocampal photomicrographs show microglia activation shown by staining and morphology changes: normal on d1 (A1, A2), inflammation on d5 (B1, B2) and d9 (C1, C2), resolved d14 (D1, D2). On d5 (B3, B4) and d9 (C3, C4), MEL significantly reduced activation.

References:

- (1) Newman et al. Postoperative cognitive dysfunction after noncardiac surgery: a systematic review. *Anesthesiology* 2007;106(3):572-90.
- (2) Allan et al. Cytokines and acute neurodegeneration. *Nat Rev Neurosci* 2001;2(10):734-44.
- (3) Steinman. Modulation of postoperative cognitive decline via blockade of inflammatory cytokines outside the brain. *PNAS* Nov30, 2010 vol. 107 no. 48.

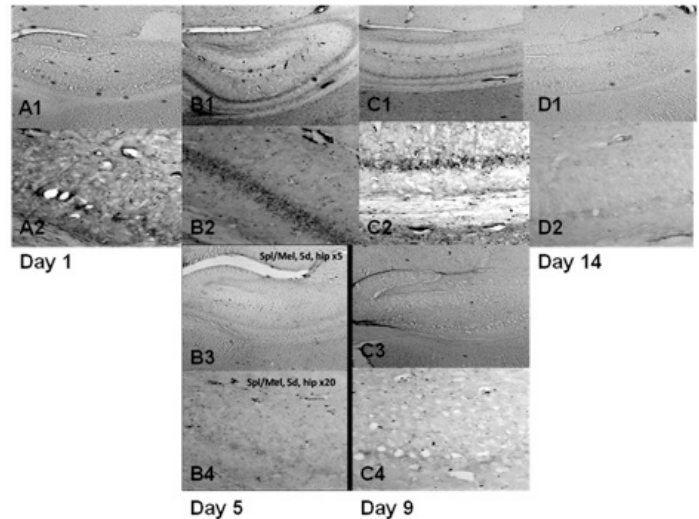


Figure 1

STM was normal on d1, dysfunctional d5 through d9 and resolved by d14. MEL restored STM on d5 & d9.

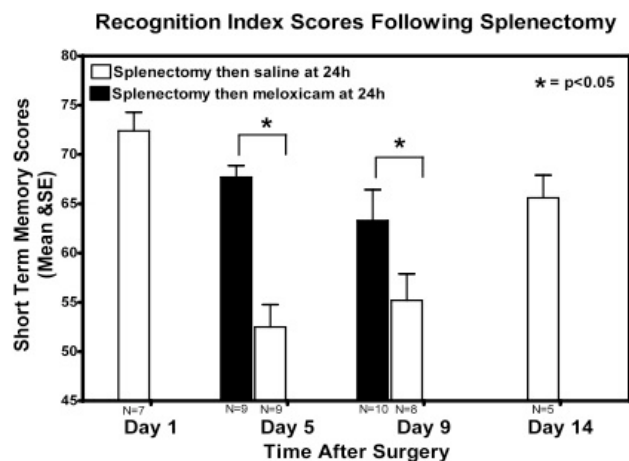


Figure 2