Is It Appropriate to Use Fear Conditioning to Assess Behavior Impairment in Fracture Rat Models?

To the Editor:
We have read with interest the article of Susana Vacas et al.1 The authors demonstrated the effect of preoperative abrogation of high-mobility group box 1 protein in preventing postsurgical neuroinflammation and cognitive impairment. They have done excellent work in attempting to find the mechanisms and resolution of surgery-induced memory decline. However, we have two concerns about this study.

The first concern is about the cognitive test used in the experiments. The authors applied fear conditioning to assess the postoperative cognitive dysfunction, following tibia fracture in rats. The primary outcome used to assess the cognitive decline was the percentage of freezing time during the context session, observed in each group. As the other investigators point out, motor impairments may affect the behavior of freezing responses in rats.2 Moreover, traumatic tibia fracture with an intramedullary fixation may alter the nociception of hind paws, which may also influence the responsiveness to foot shock stimulation. As the control group was not exposed to tibia fracture, the differences of freezing time in the surgery group may have been overstated.

Therefore, we think that to use the trace-fear conditioning test for cognitive or memory evaluation in this tibia fracture model is inappropriate, and may overstate the effect of neurodevelopment impairment and cognitive decline.

The second concern regards the healing of the tibia fracture after the neutralization of high-mobility group box 1 protein and the depletion of bone marrow-derived macrophages, as the activation of the immune system and the inflammatory response is essential for tissue repair cascade, following any injury. We are wondering whether the authors have observed the fracture healing process in their experiment.

Competing Interests
The authors declare no competing interests.

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Accepted for publication August 15, 2014.