

trial 4 was performed one week following probe trial 3 (d). Regardless of injury, adolescent mice do not show a preference for the target quadrant, indicating a lack of long-term spatial memory. In the adult cohort, both sham and TBI mice show long-term memory retention, with a strong preference for the target quadrant (*post-hoc*; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$; $n = 10/\text{group}$).

Supplementary Figure 1: Anxiety measures were typically comparable between injury groups, while general locomotion and exploration was age-dependent. Time spent in the center of the open field arena (a) was similar in sham and TBI mice in the adolescent cohort (t-test, $t_{1,18} = 1.703$, $p = 0.1057$). At adulthood, however, TBI mice showed a decrease in time spent in the center compared to sham mice ($t_{1,17} = 2.138$, $p = 0.0473$), suggesting an injury-induced increase in anxiety. In more specific measures of anxiety, the elevated plus and elevated zero mazes (b, c), sham and TBI mice spent a comparable time in the open areas at both adolescence and adulthood (t-tests, n.s). When comparing locomotion across the different-aged cohorts, an age-dependent effect was evident in all three tasks, with adult animals traveling a greater distance compared to mice at adolescence (2-way ANOVA, effect of age, *** $p < 0.0001$). This was independent of any effect of injury.

Supplementary Figure 2: Probe trials, in which the target platform is removed, were performed to assess spatial memory retention after frontal TBI. Time spent in the target (black bar), opposite (white bar) or adjacent quadrants (striped bar) were compared within each group (1-way ANOVA). In probe trial 1 (a), all groups spent a similar amount of time in all quadrants of the pool. By probe trial 2 (b), adolescent sham mice and both sham and TBI mice at adulthood show a preference for the target quadrant compared to the opposite quadrant (*post-hoc*; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$), indicating memory retention. Probe trials 3 and 4 are illustrated in Figure 8.

REFERENCES

- 1 Langlois JA: Traumatic Brain Injury in the United States: Assessing outcomes in children. Atlanta, GA, National Center for Injury Prevention and Control, 2000, pp http://www.cdc.gov/traumaticbraininjury/pdf/TBI_assessing.pdf.
- 2 Claus CP, Tsuru-Aoyagi K, Adwanikar H, Walker B, Manvelyan H, Whetstone W, Noble-Haesslein LJ: Age is a determinant of leukocyte infiltration and loss of cortical volume after traumatic brain injury. *Dev Neurosci* 2010;32:454-465.
- 3 Potts MB, Koh SE, Whetstone WD, Walker BA, Yoneyama T, Claus CP, Manvelyan HM, Noble-Haesslein LJ: Traumatic injury to the immature brain: inflammation, oxidative injury, and iron-mediated damage as potential therapeutic targets. *NeuroReport* 2006;3:143-153.

Supplementary Figure 1: Anxiety measures were typically comparable between injury groups, while general locomotion and exploration was age-dependent. Time spent in the center of the open field arena (a) was similar in sham and TBI mice in the adolescent cohort (t-test, $t_{1,18} = 1.703$, $p = 0.1057$). At adulthood, however, TBI mice showed a decrease in time spent in the center compared to sham mice ($t_{1,17} = 2.138$, $p = 0.0473$), suggesting an injury-induced increase in anxiety. In more specific measures of anxiety, the elevated plus and elevated zero mazes (b, c), sham and TBI mice spent a comparable time in the open areas at both adolescence and adulthood (t-tests, n.s). When comparing locomotion across the different-aged cohorts, an age-dependent effect was evident in all three tasks, with adult animals traveling a greater distance compared to mice at adolescence (2-way ANOVA, effect of age, $***p < 0.0001$). This was independent of any effect of injury.

Supplementary Figure 2: Probe trials, in which the target platform is removed, were performed to assess spatial memory retention after frontal TBI. Time spent in the target (black bar), opposite (white bar) or adjacent quadrants (striped bar) were compared within each group (1-way ANOVA). In probe trial 1 (a), all groups spent a similar amount of time in all quadrants of the pool. By probe trial 2 (b), adolescent sham mice and both sham and TBI mice at adulthood show a preference for the target quadrant compared to the opposite quadrant (*post-hoc*; $*p < 0.05$, $**p < 0.01$, $***p < 0.0001$), indicating memory retention. Probe trials 3 and 4 are illustrated in Figure 8.



