Supplementary Material

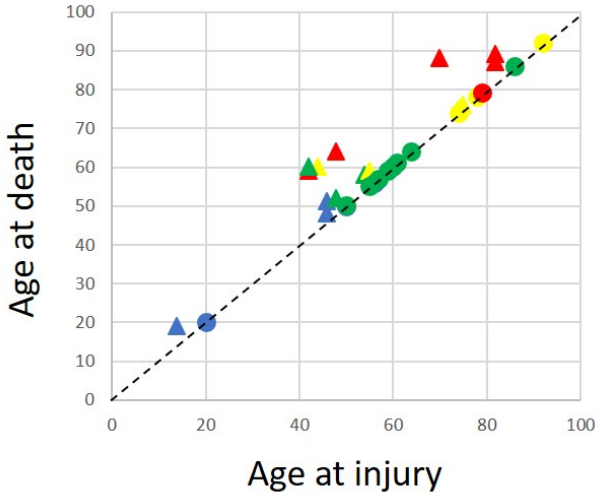
Supplementary Table

	TBI (n=15)	Controls (n=15)
Median age (range)	60 years (19-89)	60 years (20-92)
Males	12	11
Median TBI survival (range)	5 years (1-18)	NA
Mean pm delay (range)	52 hours (19 h – 5 days)	39 hours (12 h – 6 days)
Cause of TBI		NA
Road traffic accident	5	
Fall	5	
Assault	3	
Not known	2	
Cause of death		
Respiratory	6	8
Cardiovascular disease	4	1
Gastrointestinal disease	2	2
Trauma	2	0
Seizure	1	0
Malignancy	0	2
Sepsis	0	2

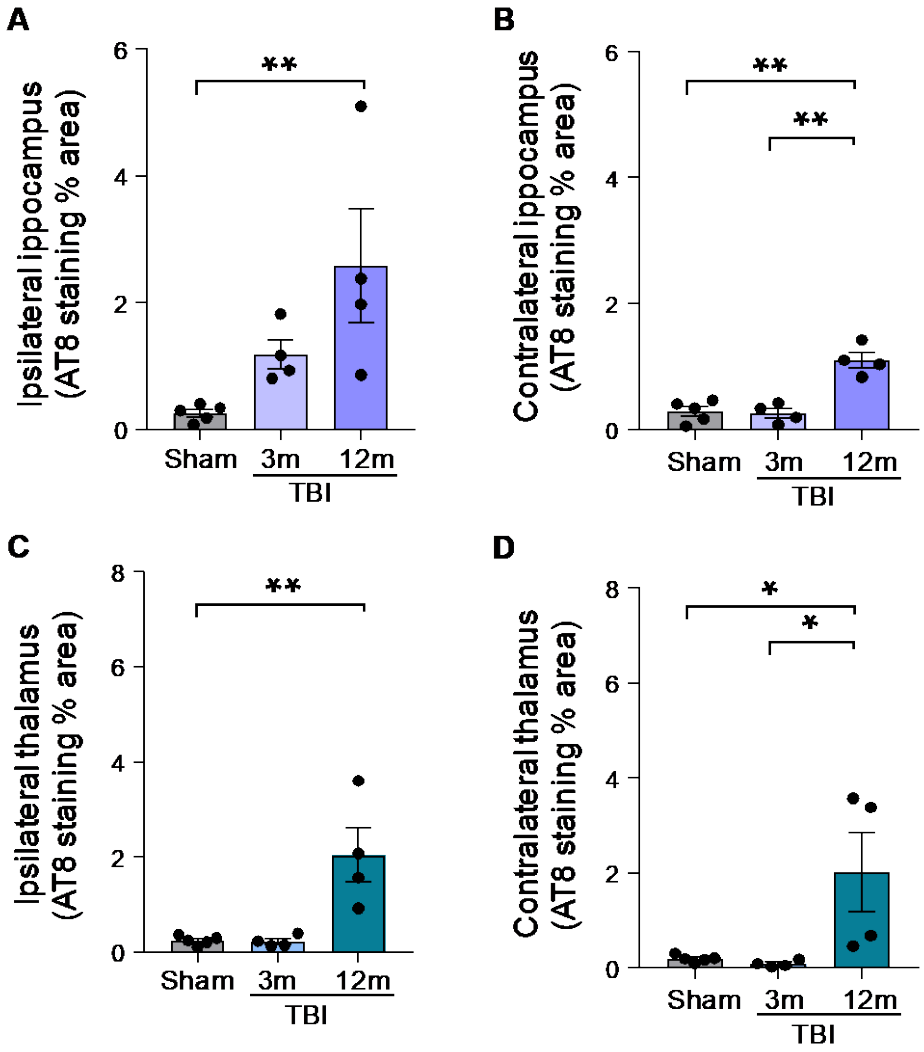
Supplementary Table 1. Demographic and clinical data for TBI and control subjects.

Legend: PM = post mortem; NA = not applicable. Controls had no known history of TBI.

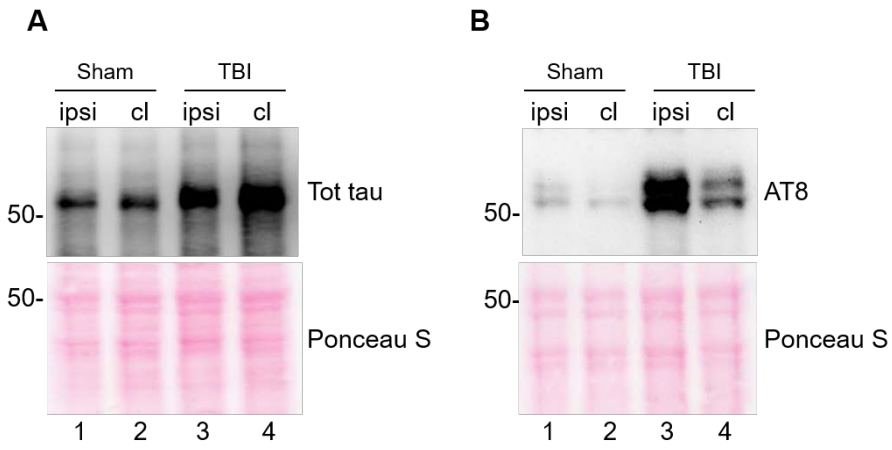
Supplementary Figures



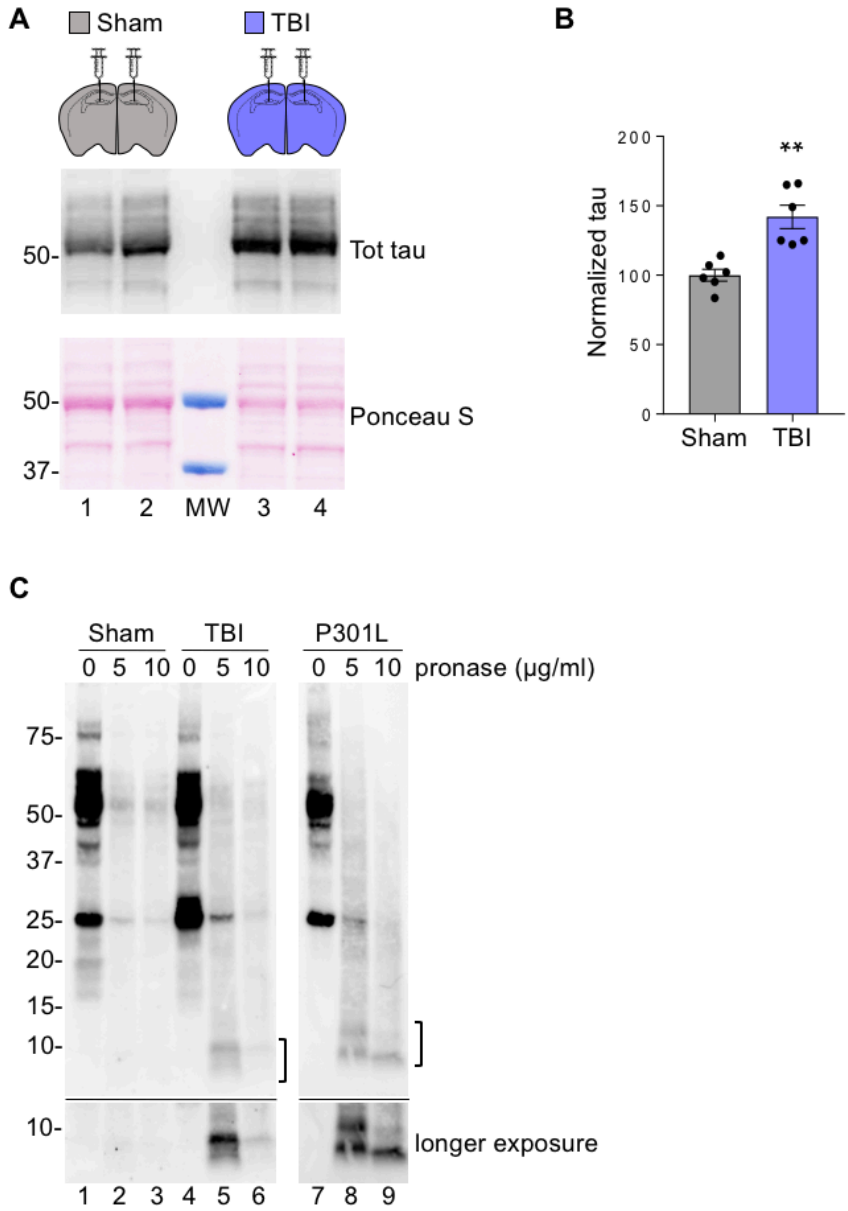
Supplementary Figure 1: Extent of tau pathology against age and survival interval in late TBI cases and controls. *(Key to plot: circles, controls; triangles, late TBI cases; blue, tau score 0; green, tau score 1; yellow, tau score 2; red, tau score 3).* Higher score tau pathology (score 2 or 3) was broadly associated with older age in both controls and in late TBI patients, though with this level of pathology present from a younger age in TBI survivors (59 and above) compared to controls (74 and older). No clear association between survival interval and extent of tau pathology was present. The x-axis represents the age at injury, the y-axis age at death. For controls these figures are the same, with this intersection marked by the dotted line. Vertical deviations from that line in late TBI cases are equivalent to survival interval.



Supplementary Figure 2. Evidence of tau pathology in hippocampus and thalamus in TBI mice. Quantification of the AT8-positive area in the ipsilateral and contralateral hippocampus (**A, B**) and thalamus (**C, D**) of sham and TBI mice at 3 and 12 months post injury. Data are mean ± SEM; n = 4-5; *p < 0.05; **p < 0.01 by one-way ANOVA, Tukey post-hoc test.



Supplementary Figure 3. Example of Western blot analysis of tau in sham and TBI mice. Western blot analysis of the pericontusional (ipsi) and corresponding contralateral (cl) area with anti-total tau (**A**) and AT8 (**B**) antibodies at 12 months post TBI or sham injury. Ponceau S staining of the blots (bottom panels) show similar amounts of total proteins.



Supplementary Figure 4. Detergent-insoluble and protease-resistant tau in mice inoculated with TBI homogenates. Detergent-insoluble tau in dissected thalami of mice inoculated with (**A**) sham or TBI brain homogenates, was analyzed by Western blot using an anti-total tau antibody. The amount of insoluble tau was quantified by densitometric analysis of Western blots, normalized for the total amount of proteins determined by Ponceau S staining of the blot (bottom panel), and expressed as a percentage of the amount in sham-inoculated mice (**B**). Data are mean ± SEM, n = 6. **p < 0.01 by unpaired t-test. (**C**) Triton X-100 lysates of thalami dissected from sham and TBI inoculated mice were incubated with 0-10 µg/mL pronase for 1h at 37°C, and tau was visualized by Western blot using antibody BR135. The bracket indicates the protease-resistant bands, also shown in the longer exposure. Transgenic mice overexpressing mutant tau P301L (Lewis J et al., Nature Genetics 2000), displaying tau seeding activity (de Calignon *et al.*, 2012; Liu *et al.*, 2012) were used as a positive control. Result is representative of three independent experiments.