Penetrating traumatic brain injury (PTBI) is common in the USA and worldwide, outcome remains poor in survivors. In the absence of “neuroprotective” therapies, progressive secondary tissue loss after PTBI underlies disability among survivors. This study tests transplantation of human neural stem cells (hNSCs) as a treatment to mitigate lesion in penetrating ballistic-like brain injury (PBBI), a rat PTBI model. One-week post PBBI male Sprague Dawley rats (7-10/group) were randomized to: (1) injured treated with vehicle (media, no cells), (2) uninjured (sham+hNSCs), two PBBI groups (PBBI+hNSC) either (3) into surrounding (peri) or (4) within lesion core(intra), one million cells were stereotactically microinjected into brains of immunosuppressed group 2-4. Motor function was assessed on grid walk prior to euthanasia at 12 weeks post-transplantation. Lesion size, axonal injury was quantitated with Matlab based scripts of brain sections stained with histochemical stains. Lesion size and remote secondary axotomy were significantly reduced in transplant groups. Engraftment or neuronal differentiation did not differ between groups 3 and 4, despite being higher than in sham. On the grid walk test, sham animals had fewer foot faults than vehicle group as expected. Compared to vehicle, groups 3 and 4 had significantly reduced foot faults but still significantly higher than control.

A two-way ANOVA of the rat brain cortical tissue quantity between +3.72 mm and -0.28 mm bregma (rat motor cortex) there was significant interaction between bregma levels and treatment. There was reduction in lesion size in both transplant groups (p<0.05). Lesion seize reduction was due to significant increase in tissue sparing in the perilesional transplant group compared to vehicle (p<0.01). One-way ANOVA revealed no statistically significant differences in spared
tissue between two transplant groups but greater sparing of the motor cortex in perilesional transplantation. The concomitant reduction in lesion area and increased cortical tissue sparing suggests that transplantation of hNSCs reduced the progression of PBBI induced cortical atrophy, spared motor cortex reduced secondary axotomy may be associated with improved motor performance in transplant groups. This data provides a rationale for use of hNSC transplants to mitigate PTBI induced secondary tissue loss. Perilesional rather than intralesional transplantation conferred greater neuroprotection.