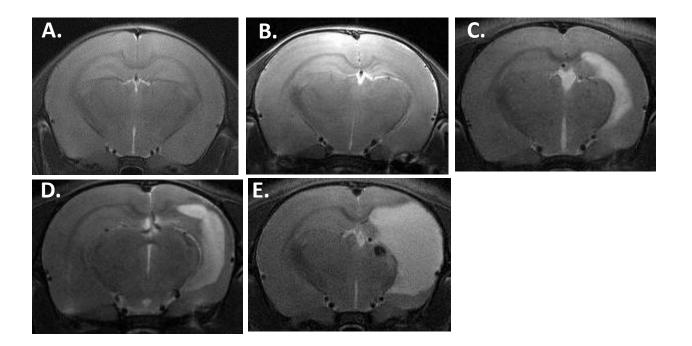
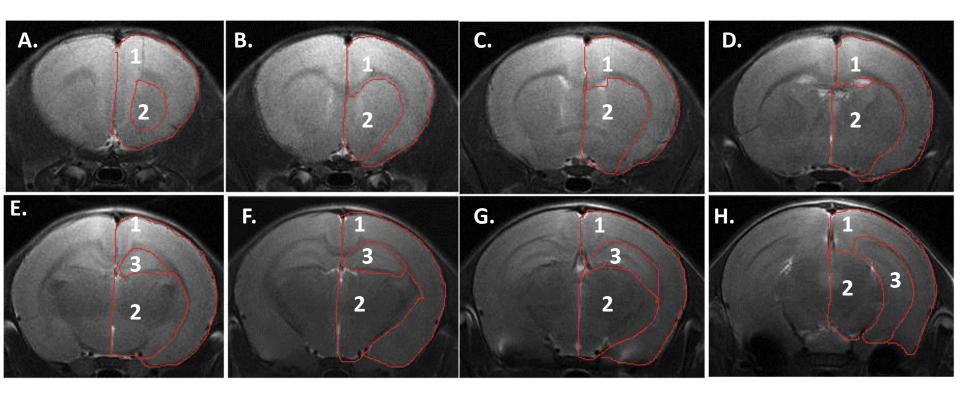


Supplemental Figure 1 (online): **Average rectal temperatures during hypothermia and damage scores at 2 weeks.** The target rectal temperature for hypothermia was 32°C; rectal temperatures were monitored in each pup hourly. Analysis of damage at 2 weeks post-HI with T₂ MRI in initial experiments (n=33) demonstrated that all pups that achieved a temperature of 33°C or less had moderate to no damage compared with pups that were greater than 33°C and had mild to severe damage, p<0.01, unpaired t-test.

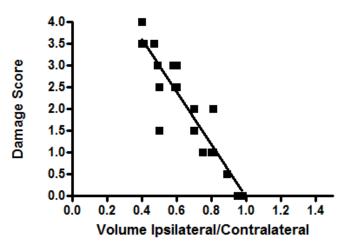


Supplemental Figure 2A, online: **Damage Score (DS) and Volume determinations from MRI.** 8 MRI images, 1 mm apart, from Bregma 2.52 to -5.40 were assigned a gross damage score based on an ordinal scale of 0-4, and the 8 scores were averaged to obtain the overall score for the brain. Shown are representative images from Bregma - 3.3. DS is assigned as: 0 = no damage; 1 = mild atrophy only; 2 = increased atrophy with ventriculomegaly; 3 = 1-25% infarct; 4 = 25-100% infarct.

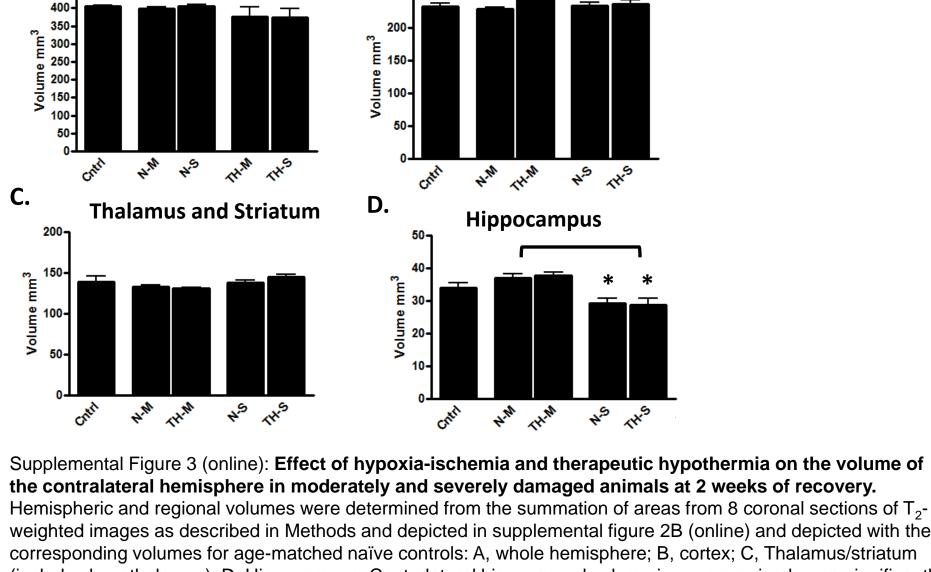


Supplemental Figure 2B. Individual regional areas were measured in the same 8 sequential images, 1 mm apart by tracing regions of interest (ROI) with Image J software (NIH, Bethesda, MD). ROI definitions are: 1) cortex; 2) Thalamus and striatum, including hypothalamus; 3) hippocampus. The volume represented by the areas from each set of 8 sections was calculated as:

Volume = (1 mm) x (Sum of area normal tissue).



Supplemental Figure 2 (online): Damage score (DS) and volume determinations from T_2 -weighted images. C. Comparison of volume measurements and gross damage scores from MRIs of each animal at 2 weeks of recovery, plotted as linear regression of hemispheric volume ratio, Ipsilateral (I)/Contralateral (C) vs DS. N=25, r^2 =0.847.



Cortex

Β.

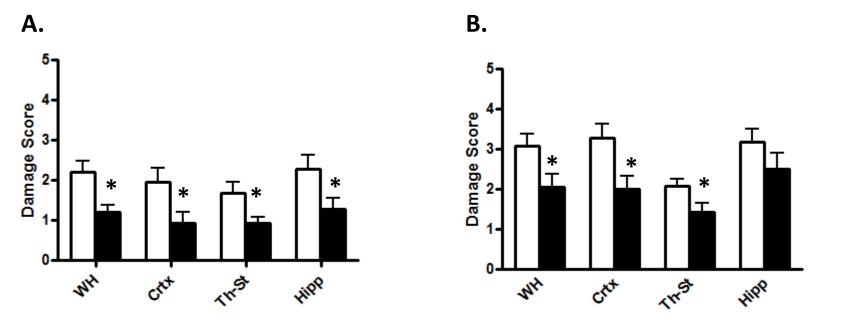
250-

Whole Hemisphere

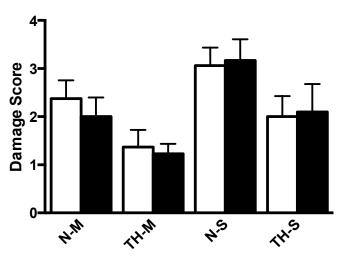
Α.

450-

weighted images as described in Methods and depicted in supplemental figure 2B (online) and depicted with the corresponding volumes for age-matched naïve controls: A, whole hemisphere; B, cortex; C, Thalamus/striatum (includes hypothalamus), D, Hippocampus. Contralateral hippocampal volume in severe animals was significantly less than in corresponding moderate animals, * p<0.001 (unpaired t test). Cntrl, naïve control, n=3; N-M, normothermia-moderate, n=22; TH-M, therapeutic hypothermia-moderate, n=22; N-S, normothermia severe, n=11; TH-S, therapeutic hypothermia-severe, n=11.



Supplemental Figure 4 (Online): Regional DS determined at 2 weeks from T_2 -MRI. Ordinal values for whole hemisphere (WH) and individual regions were determined from 2 week MRIs as detailed in Methods for A: Moderate and B: Severe cohorts. Crtx, Cortex; Th-St, Thalamus +hypothalamus and striatum; Hipp, Hippocampus. For Normothermic (white bars) and Hypothermic (black bars). * p < 0.05, unpaired t-test.



Supplemental Figure 5 (online): Sex does not affect HI-induced damage or protection with hypothermia. Two week damage scores determined from T_2 -weighted MRI images depicted separately for male (white bars) and female (black bars) rats with no significant differences observed by sex (ANOVA). N-M, normothermia-moderate, male, n=12, female, n=9; TH-M, therapeutic hypothermia-moderate, male, n=9, female, n=12; N-S, normothermia-severe, male, n=6, female, 3; TH-S, therapeutic hypothermia-severe, male, n=6, female, n=5.