MRI biomarkers of functional outcome after severe pediatric TBI

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BACKGROUND

Severe pediatric traumatic brain injury (TBI) is a major public health concern, affecting over 30,000 children each year. Mortality is high, and many survivors suffer life-long disabilities. While neuroimaging is a primary diagnostic tool in the clinical assessment of TBI, our understanding of how specific neuroimaging findings relate to outcome remains limited. Identification of imaging biomarkers of long-term neurocognitive outcome will improve clinical prognostication after an injury and help to direct rehabilitation strategies. Additionally, new imaging markers will facilitate future clinical trials of TBI therapies by improving patient stratification and providing surrogate outcome measures.

METHODS

Clinical MRI scans acquired ≤ 30 days post-injury were collected from subjects with severe traumatic brain injury enrolled in the Approaches and Decisions after Pediatric TBI (ADAPT) study (n=356, 24 sites). Forty MRI scans were randomly selected for IRR assessment, by age, sex and site strata observed in the overall cohort. Each MRI scan was reviewed in a blinded fashion by 2 board-certified neuroradiologists and imaging findings were coded to the NIH Common Data Elements for neuroimaging (CDE). Inter-rater reliability (IRR) was determined for CDE lesion presence (Kappa) and lesion quantification (weighted Kappa) in each brain region. Twenty five subjects ≥ 9 years old were recruited for follow-up MRI scanning 1-2 years post-injury. Subjects underwent outcome assessments approximately 1 year post-injury, including the Wechsler Abbreviated Scale of Intelligence (IQ) and the Pediatric Glasgow Outcome Scale-Extended (GOS-E Peds). A typically developing control cohort underwent scanning at the University of Wisconsin. Brain image segmentation was performed on T1-weighted images using Freesurfer. Brain and CSF volumes were used to compute a Ventricle-to-Brain Ratio (VBR) for each subject, and the Corpus Callosum (CC) cross-sectional area was determined in the midline for each subject. Group differences between TBI and control subjects were determined, and volumetric measures were correlated with tests of neurocognitive function.

MRI volumetric measures of Ventricle-to-Brain ratio and corpus callosum cross-sectional area correlate with global functional outcome after severe pediatric TBI.

RESULTS

Figure 1. Ventricle-to-brain ratio (VBR) group comparisons and correlations with the pediatric version of the Glasgow Outcome Scale-Extended (GOS-E Peds).
A) Representative T1-weighted MRI scans showing the prominent ventricles in the TBI subject compared to a control. Freesurfer segmentations of brain tissue and CSF are used to determine VBR, as a measure of cerebral atrophy. **B)** Shown here are the control vs TBI group differences in VBR. * p <.05. **C)** Relationship between brain atrophy and global functional outcome after TBI: After adjusting for age and sex, VBR correlated significantly with GOS-E Peds scores in the TBI group (n=24, p<0.01). No correlation between VBR and IQ was found.

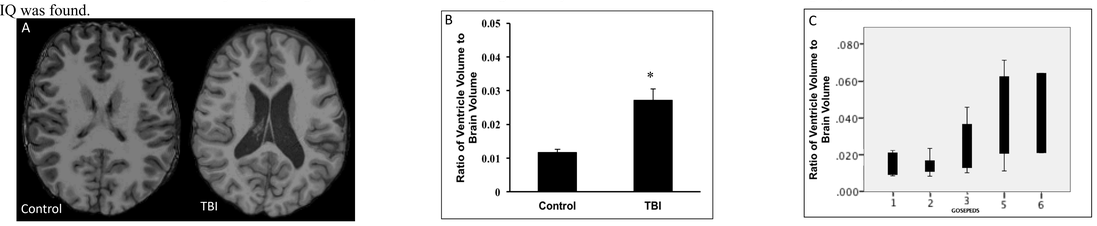
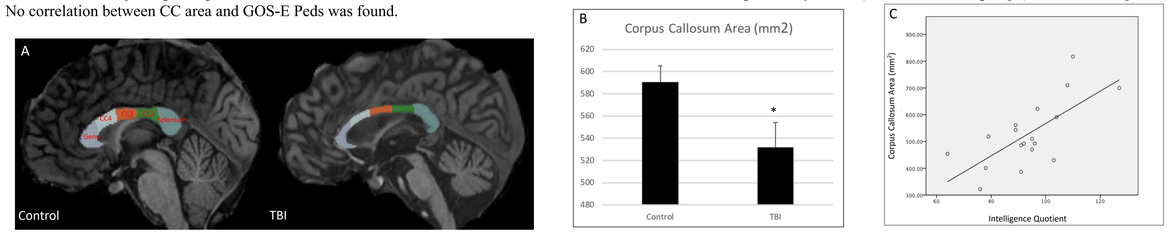


Figure 2. Corpus callosum (CC) group comparisons and correlations with intelligence quotient (IQ).
A) Representative images of a CC segmentation in a healthy control and a severe TBI. Freesurfer segmentation of CC subregions are shown and labelled in red. Volume loss is evident in the CC of the TBI subject when compared to the healthy control. **B)** Group differences in cross-sectional area of the CC. CC area was measured in the midline for each TBI and control subject. A significantly smaller CC area is seen in the TBI cohort compared to the typically developing control subjects. **C)** Relationship between corpus callosum area and IQ after TBI. After adjusting for age, sex, intracranial volume and brain volume, CC cross-sectional area correlated significantly with IQ score in the TBI group (n=18, r=0.699, p<0.02). No correlation between CC area and GOS-E Peds was found.



CONCLUSIONS

- Severe TBI results in significant global brain atrophy and volume loss within the corpus callosum.
- Global brain atrophy on MRI correlates with global functional outcome.
- Corpus Callosum volume loss correlates with impairments in intellectual function.
- DAI, contusion and ischemia are common MRI findings in young children early after injury.
- Abusive head injury is associated with an increase incidence of ischemic lesions on MRI.
- Ongoing analyses will determine early MRI predictors of outcome, and late MRI markers of brain network dysfunction in children recovering from TBI.

ADDITIONAL KEY INFORMATION

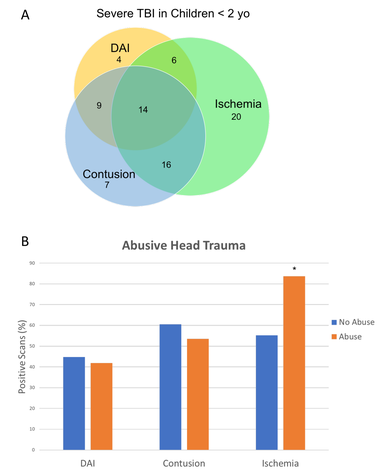


Figure 3. Early MRI findings in children with severe TBI. A) Venn Diagram of the three most common lesions identified on MRI within 30 days of injury: diffuse axonal injury (DAI), cerebral contusion, and cerebral ischemia. Neuroradiologists reviewed clinical MRI scans obtained in 81 children after severe TBI. B) Comparison of imaging findings in children with suspected or confirmed abuse. A significant increase in ischemic lesions were found in children with abusive head injury (* p <.05).

Acknowledgements

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