Changes in Cortical Thickness After Mild TBI

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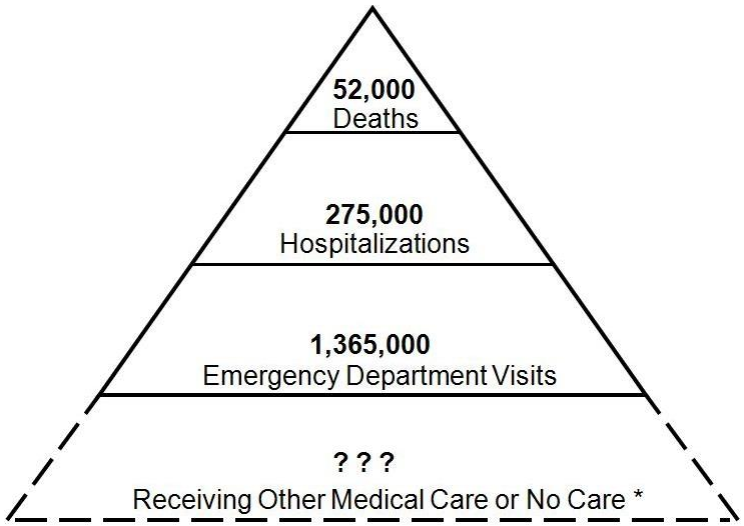
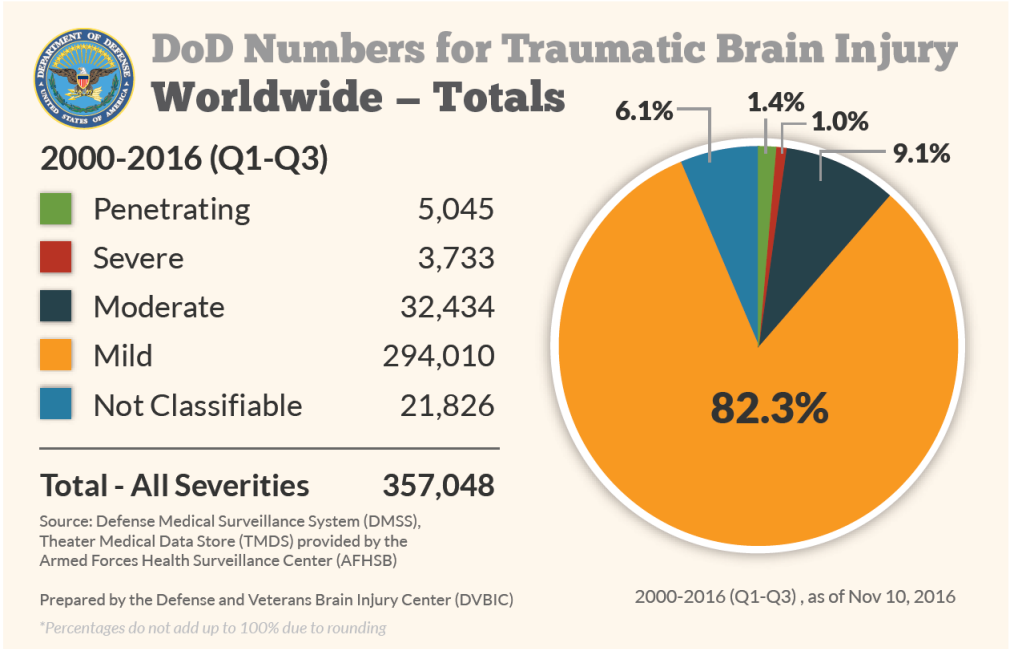
Speakers Disclosure

- **No competing financial interest to disclose**
- **No use of unlabeled and unapproved drug uses**
- **This project is part of a larger study on mTBI supported by the Department of Defense (DoD).**

Background

- **Mild traumatic brain injury (mTBI) is a major public health concern among civilians and military personnel; diagnosis and outcome assessment relies on self-report of symptoms which are subjective.**





From CDC

Background (contd)

- Magnetic resonance imaging (MRI) is one of the most widely used noninvasive neuroimaging modality to investigate neurological injury
- Conventional MRI is of limited value in the diagnosis of mTBI.
- MRI-based diffusion tensor imaging (DTI) is shown to have potential in the diagnosis of mTBI.
- However, DTI requires specialized acquisition that may or may not be available at all MRI centers.
- Cortical atrophy has attracted considerable attention as a possible diagnostic and prognostic marker
- Animal studies reported cortical atrophy following mTBI (Weber 2007)
- In humans cortical atrophy was reported in blast mTBI (Lindemer 2013; Tate 2014; Corbo 2014; Keightley 2014; Wang2015)
- In this longitudinal study we investigated the potential role of cortical thickness as a measure of cortical atrophy using conventional T1-weighted MRI in mTBI patients recruited ≈24 hours after injury.

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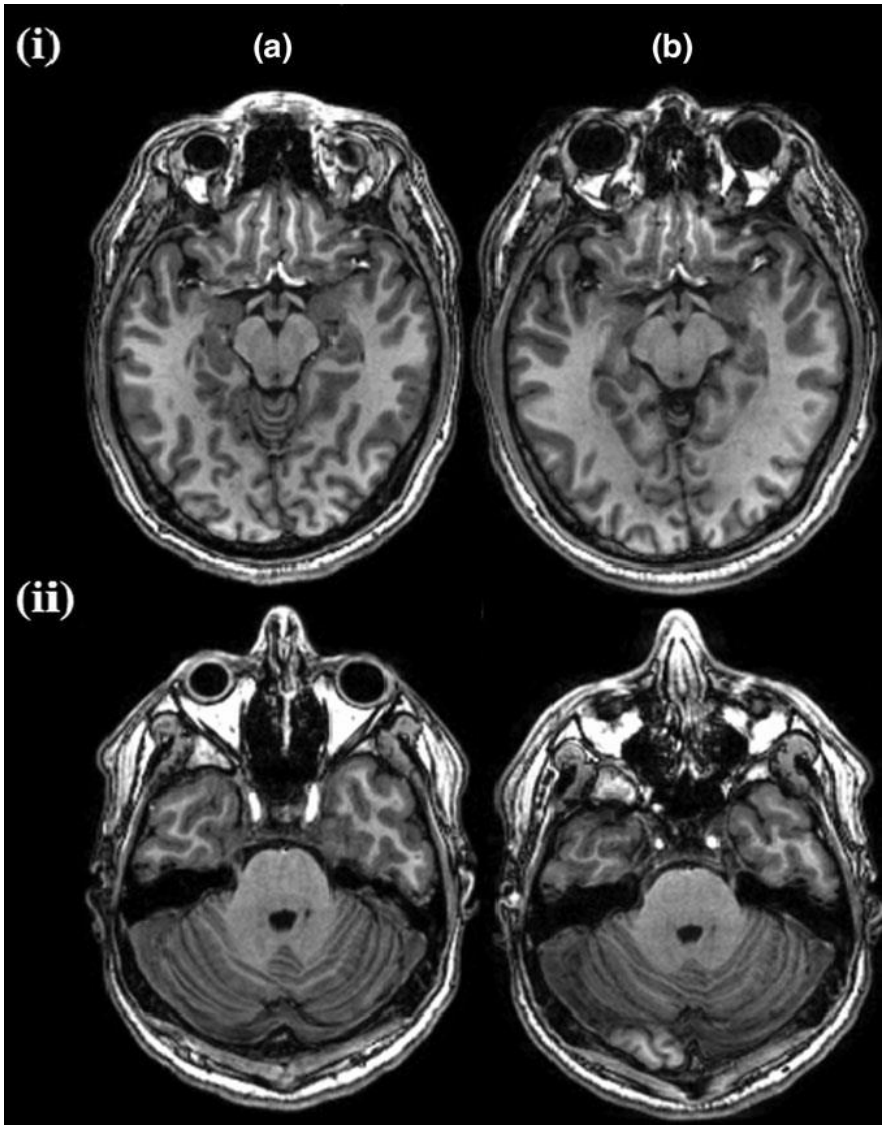
Background (Continued)

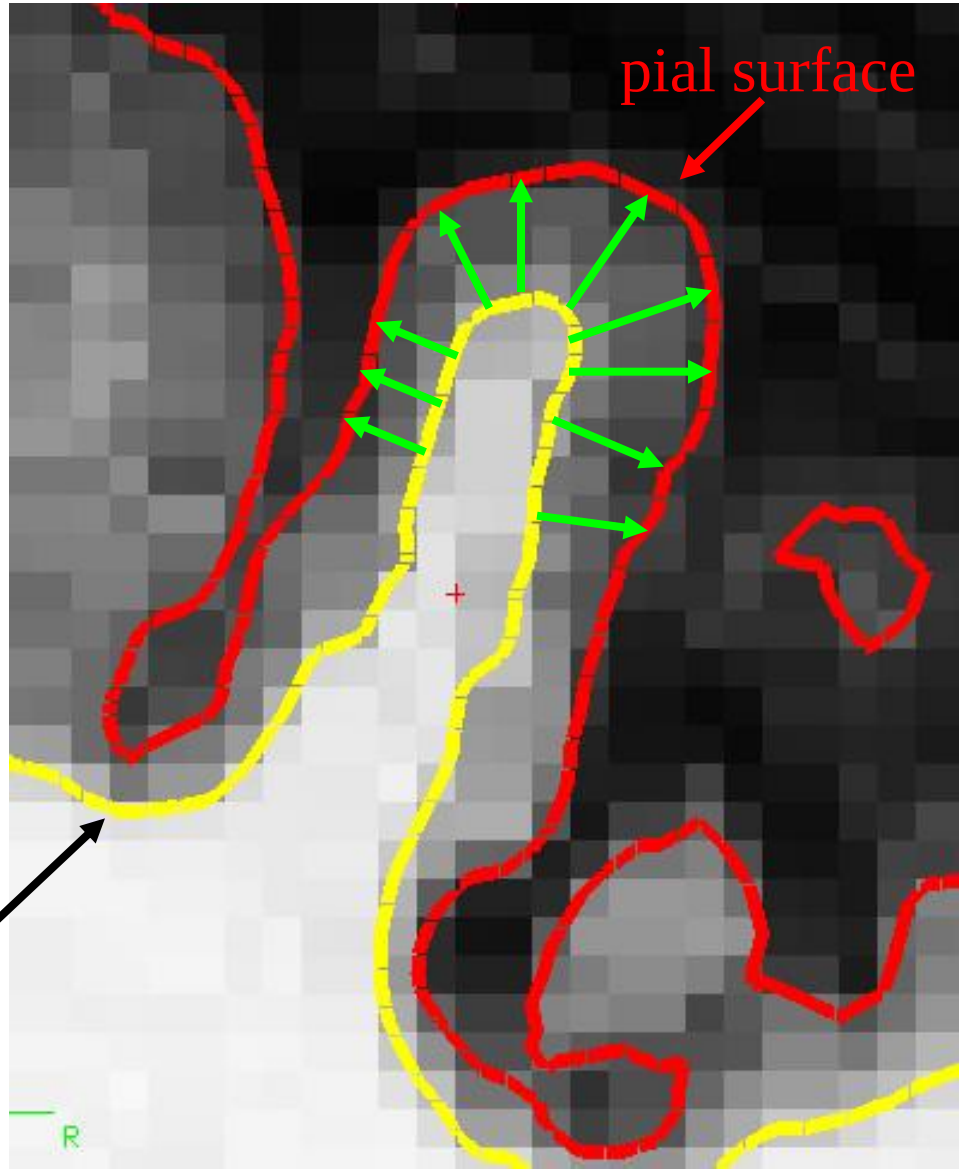
- **Software packages such as FreeSurfer enable automatic measurement of cortical thickness (Fischl 1999; Dale 1999)**
- **The main objective of this study was to evaluate the effect of mTBI on cortical thickness on a relatively large and well-characterized cohort on whom data were acquired in the acute phase (around 24 h post-injury) and in the recovery phase (around 3 months)**
- **Cortical thickness measurements were based on three-dimensional T1- weighted magnetic resonance imaging (MRI) scans. (Govindarajan 2015)**

Typical T1-weighted MRI



Axial T1-weighted magnetic resonance images at the levels of orbitofrontal cortex (i) and temporal poles (ii) of one subject at baseline (a) and follow-up (b). The voxel size is 1mm X 1mm X 1 mm.

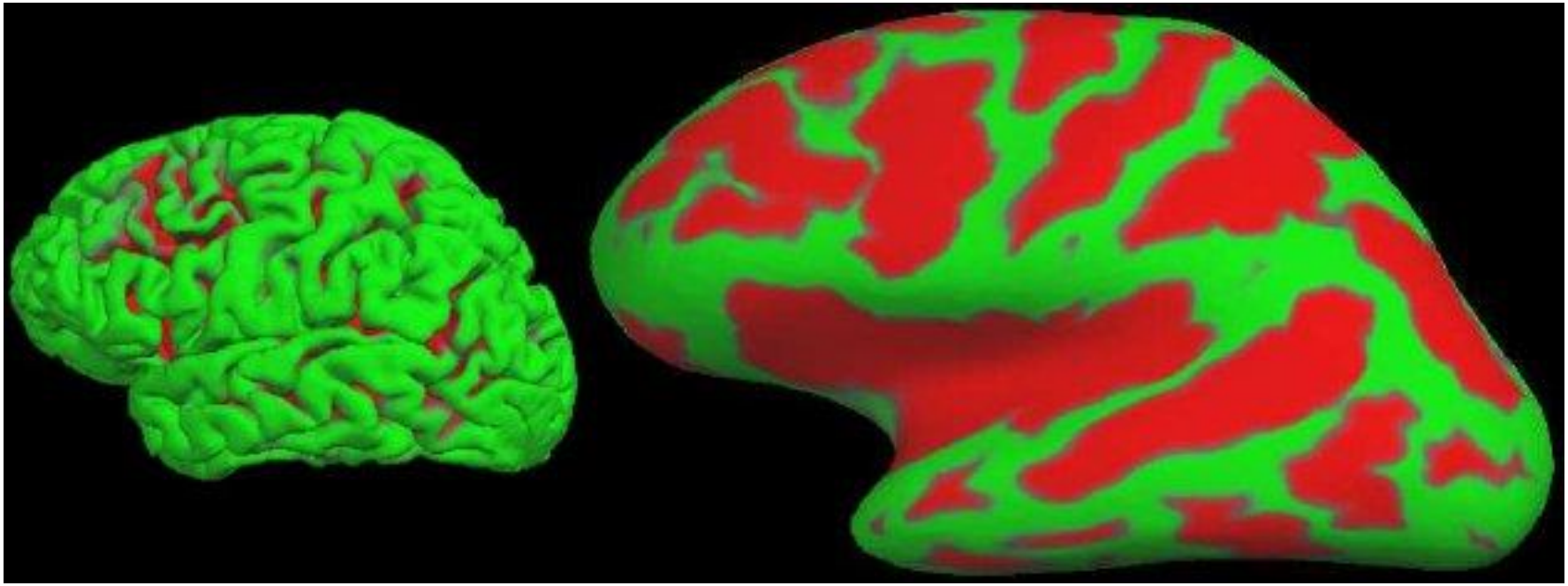
Cortical Thickness



Distance between white and pial surfaces

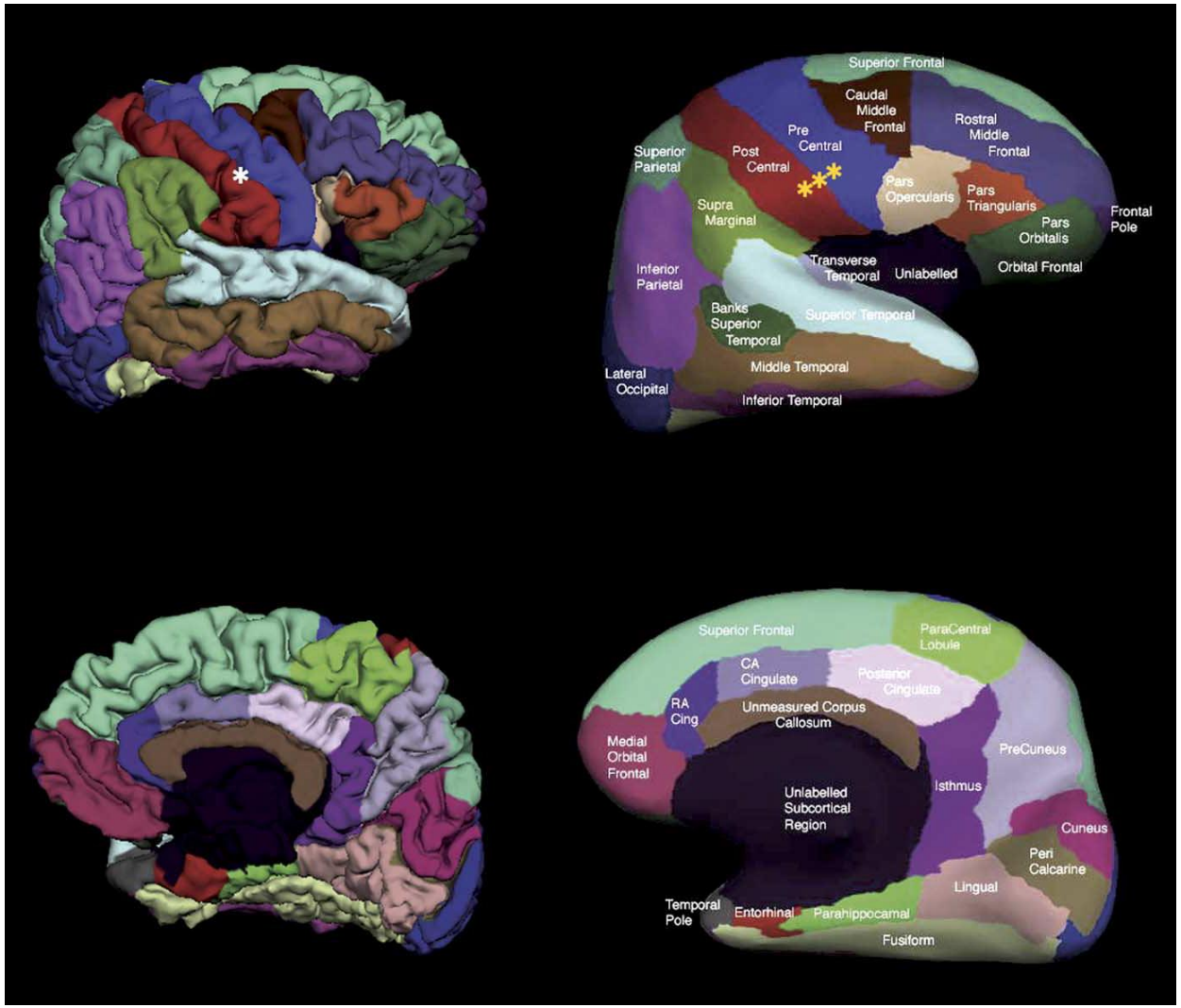
white/gray surface

Inflated Brain Surface



Green : Gyrus. Red : Sulcus

Surface Labeling



The white asterisk on the pial surface (left) indicates the cortex around the perimeter of the central sulcus that is buried within the gyri and thus not visible. The yellow asterisks on the inflated surface (right) indicate the cortex around the perimeter of the central sulcus that has been inflated and is now visible

Subjects

- **Patients were categorized into either mTBI or orthopedic injury group based on the guidelines by the Department of Defense and the American Congress of Rehabilitation Medicine.**

- **Patients, irrespective of race, gender and ethnicity were recruited by healthcare professionals (RN, MD, and EMT-P) with prior clinical experience with brain injury patients.**

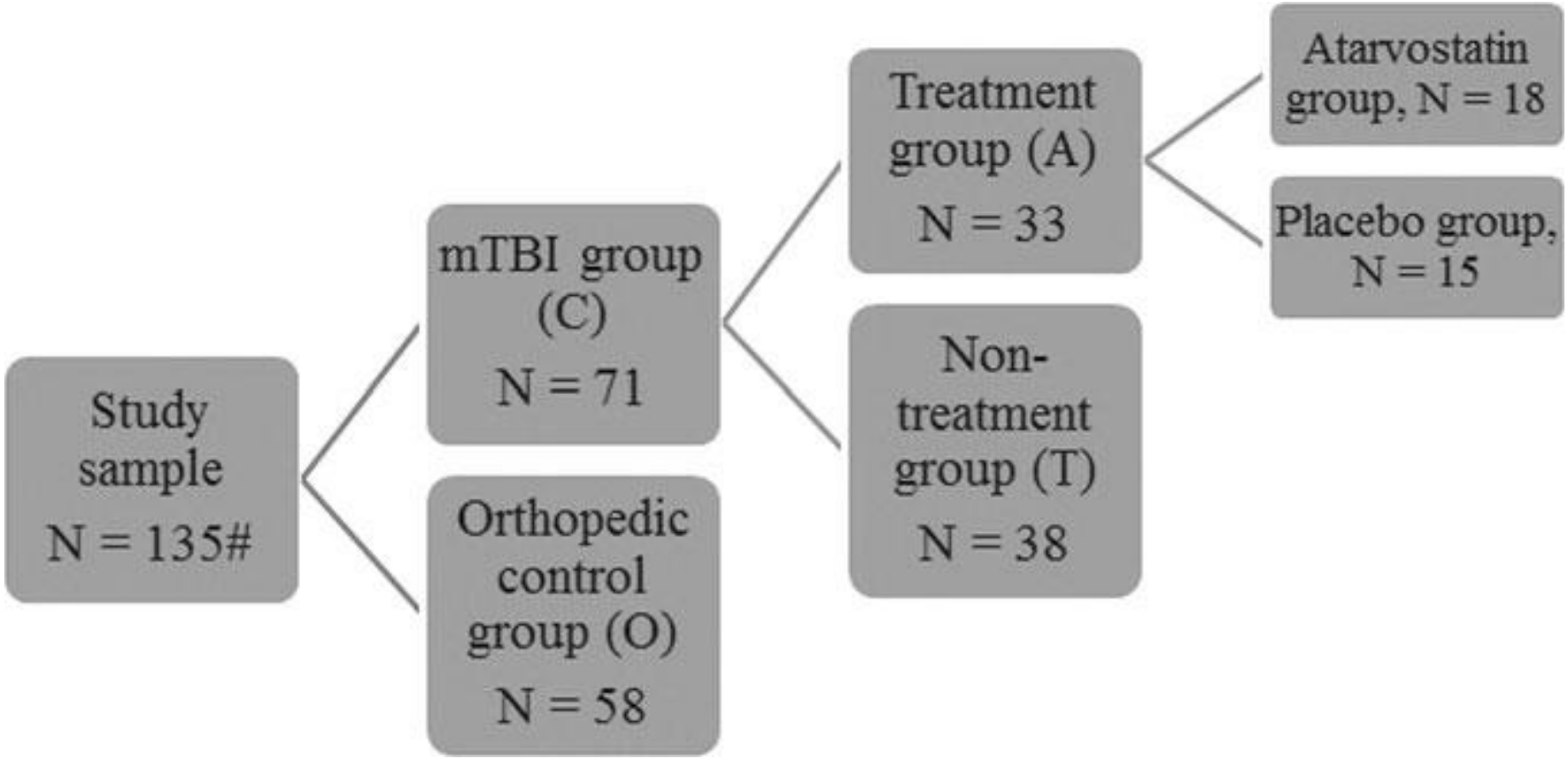
- **Screening process comprised of a review of electronic healthcare system data, consultation with emergency staff, and patient interviews. Patients were categorized into either mTBI or orthopedic injury group based on the guidelines by the Department of Defense and the American Congress of Rehabilitation Medicine.**

- **Galveston Orientation and Amnesia Test (GOAT) was administered prior to informed consent. Subjects needed to score 75 or higher in the test in order to provide informed consent and if not, a legally authorized representative had to provide consent. All subjects in this study had a GOAT score above 75.**
- **.**

Inclusion/Exclusion Criteria

- **Inclusion criteria**
  - **mTBI-group: Presence of a head injury, Glasgow Coma Scale (GCS) score in the range of 13-15, a negative CT scan, post-traumatic amnesia under 24 hours and loss of consciousness for under 30 minutes.**
  - **Orthopedic injury control group: Confirmed that they had not hit their head during the injury to the best of their recollection. Neither had visible signs of injury nor had undergone any loss of consciousness or amnestic event**
- **Exclusion criteria**
  - **Subjects with pre-existing, psychiatric disorders, PTSD, substance-abuse and alcohol dependence were excluded as were subjects with previous head injuries or left-handedness.**
- .

Sample distribution



Injury Mechanisms

Injury mechanism	mTBI group (%)	Orthopedic control group (%)
Motor vehicle crash	39.5	11.4
Assault	18.3	1.2
Blow to head	11.3	0
Lacerations	0	44.7
Fall	18.4	20.9
Auto-pedestrian collision	8.3	0
Other	4.2	21.8

Demographic Data

Parameter	Group O (Controls)	mTBI	p
Number of participants	60	75	
Age; Mean ±SD, Range, Median	28.95±8.8, 20-50, 26.5	29.1±9.9, 18-49, 25	0.69 (t-test)
Gender (M/F)	43/15	21/12	0.71 (χ^2)
Education Level	13.33 ± 2.59 years (range 6 to 19 years)	13.21 ± 2.43 years (range 6 to 19 years	0.793 (t-test)
Socioeconomic Index	0.07 ± 0.96 (range -1.72 to 2.84)	0.04 ± 1.06 (range -1.69 to 2.39)	0.86 (t-test)

Clinical and Other Data

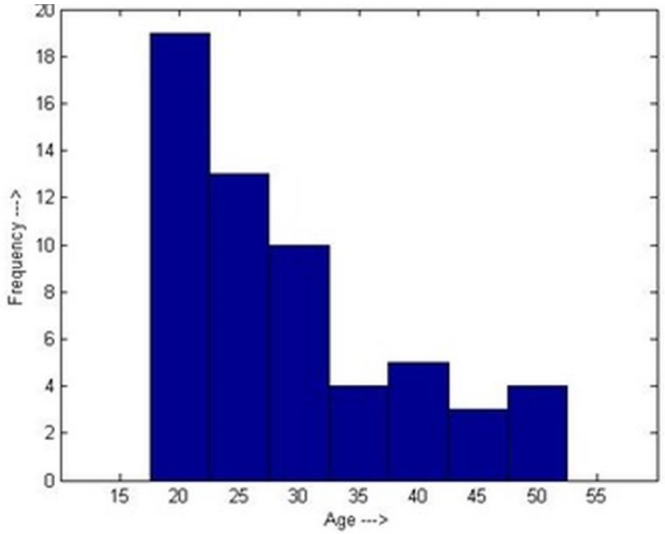
- **Two subjects in the mTBI group had Glasgow Coma Scale scores of 14 and the rest of the group had a score of 15**

- **Average duration of loss of consciousness in the mTBI group was 3.95 ± 5 min (range: 1-20 min)**

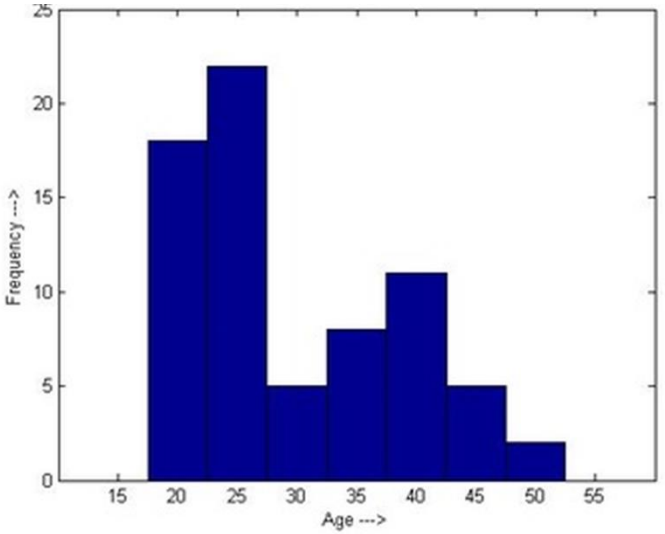
- **Mean time from injury to first MRI was 25.5 ± 12.26 hours (range: 5.8 – 46 hours) for the mTBI group and 27.1 ± 13.7 hours (range: 0.3 – 56 hours) for orthopedic injury group.**
- **For the follow-up MRI, mean times from injury were 97.9 ± 17.57 days (range: 83.3 – 202 days) for the mTBI and 96.7 ± 9.26 days (range: 82.9 – 126.9 days) for orthopedic injury groups.**

Age distribution

Controls



mTBI patients



Methods

- **Data acquired at 2 time points – acute phase (~24 hours post injury) and recovery phase (~ 3 months post injury).**
- **All 135 subjects were scanned at both time points**
- **3D T1-weighted images with 1x1x1 mm^3 isotropic voxel size acquired on a 3T Philips scanner.**
- **Cortical thickness estimated using FreeSurfer (v5.3.0).**
- **Longitudinal unbiased templates created using FreeSurfer's longitudinal pipeline.**

Methods

- **Between group cross-sectional analysis and within group longitudinal analysis was carried out.**

  FreeSurfer uses Desikan-Killiany atlas for labeling
- **Multiple comparisons analysis was performed using Monte-Carlo simulations with 5000 iterations.**
- **All statistical analysis was carried out at p = 0.01.**

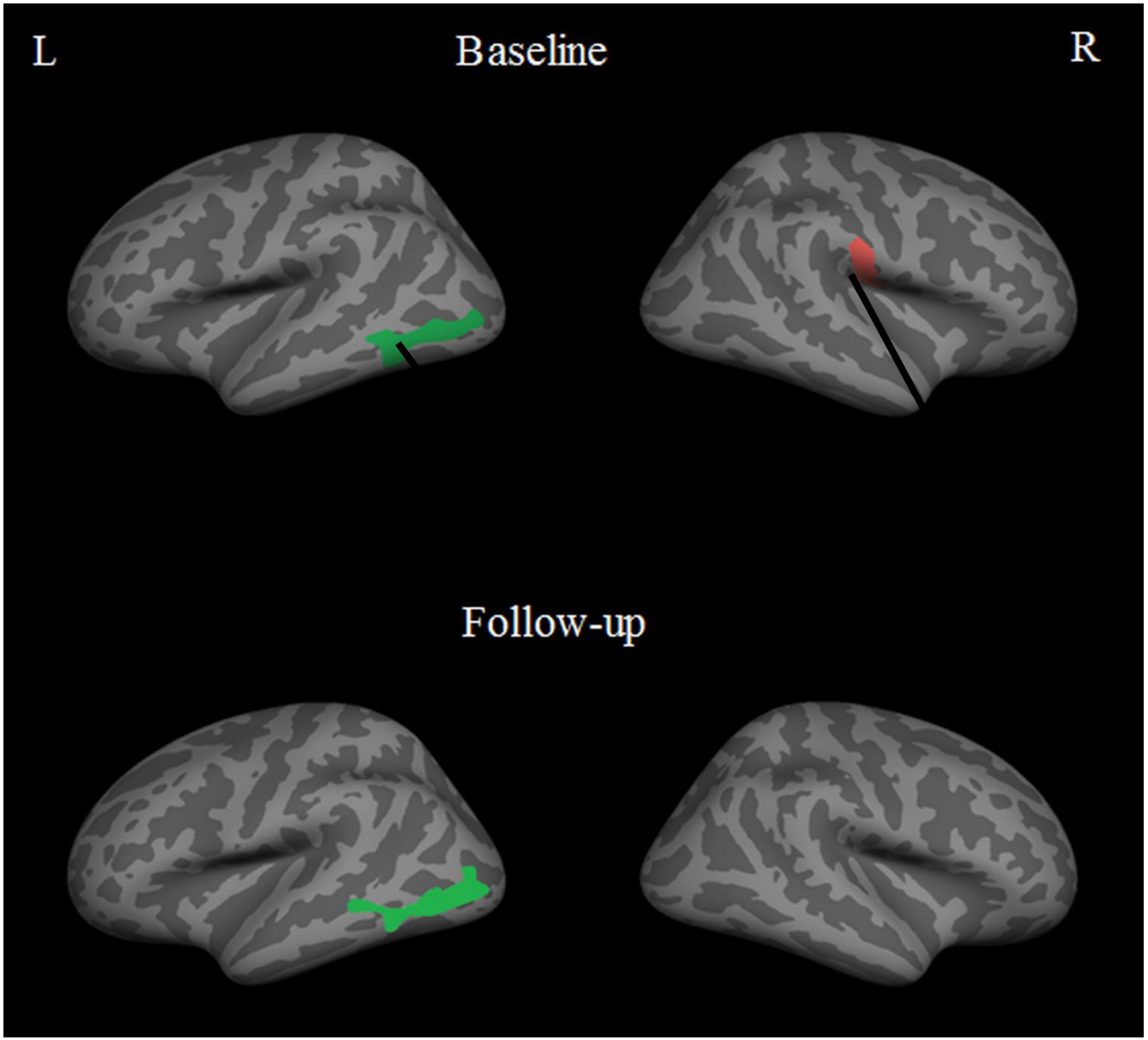
Results

- **On ≈24 hour MRI, significant cortical thinning in mTBI compared to controls in the left middle temporal cortex and right supramarginal cortex.**
- **At follow-up, significant cortical thinning in mTBI compared to controls only in the left middle temporal cortex.**
- **No thickening effects at either time point.**
- **In the longitudinal comparison, no significance in the control group and in the mTBI group, subtle but significant clusters in frontal, temporal and parietal lobes.**
- **With a larger sample size and more serial data points, a comprehensive longitudinal analysis can be performed.**

Results

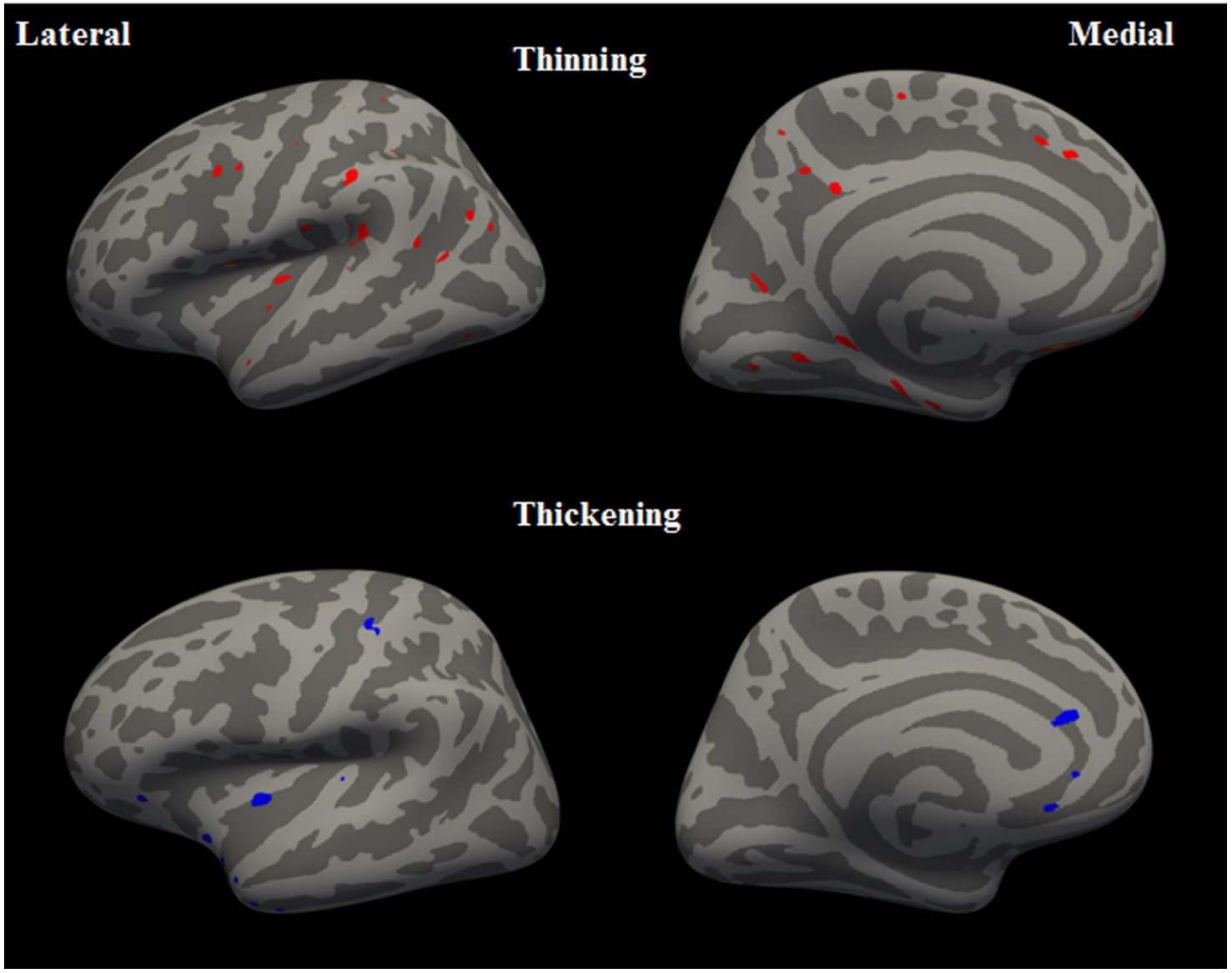
- **Cortical thinning in whole cohort is driven primarily by the non-treatment group, since there were no significant differences between treatment and control groups.**
- **This trend of the nontreatment group being the contributing sample extended into longitudinal analysis also as the orthopedic control and treatment groups did not show any significant changes.**
- **Non-treatment group showed a trend of thinning and thickening in sporadic regions over the frontal, temporal, and parietal lobes.**

Results – cross-sectional



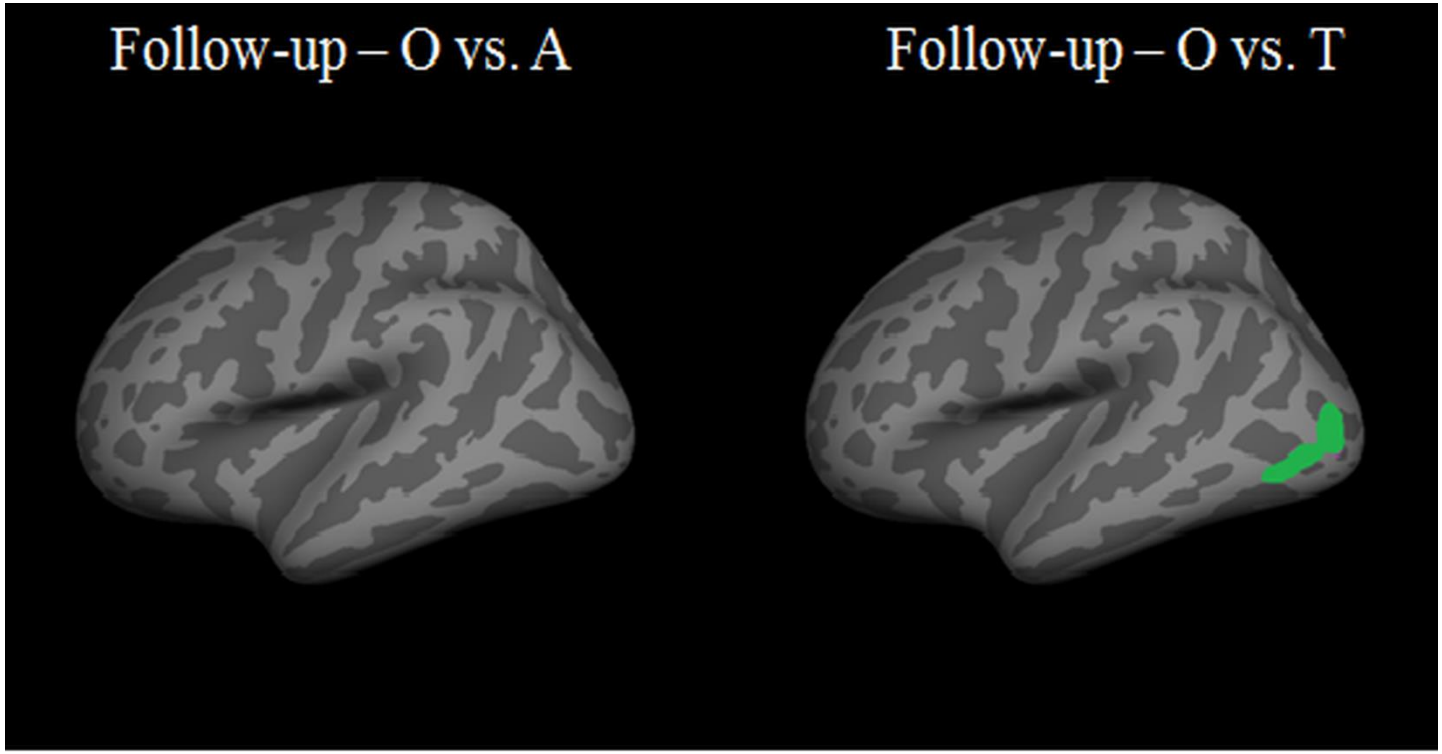
Regions of significant cortical thinning in mTBI patients, compared with OI, at baseline and at 3 months follow-up. Thinning in regions in middle temporal cortex in left hemisphere and inferior parietal cortex in right hemisphere (p = 0.01)

Results - Longitudinal



mTBI (all mTBI) ≈24 hrs vs 3 months follow-up ($p = 0.01$). Lateral and medial surfaces of the left hemisphere are shown. No significant differences were observed in the right hemisphere.

Longitudinal Changes



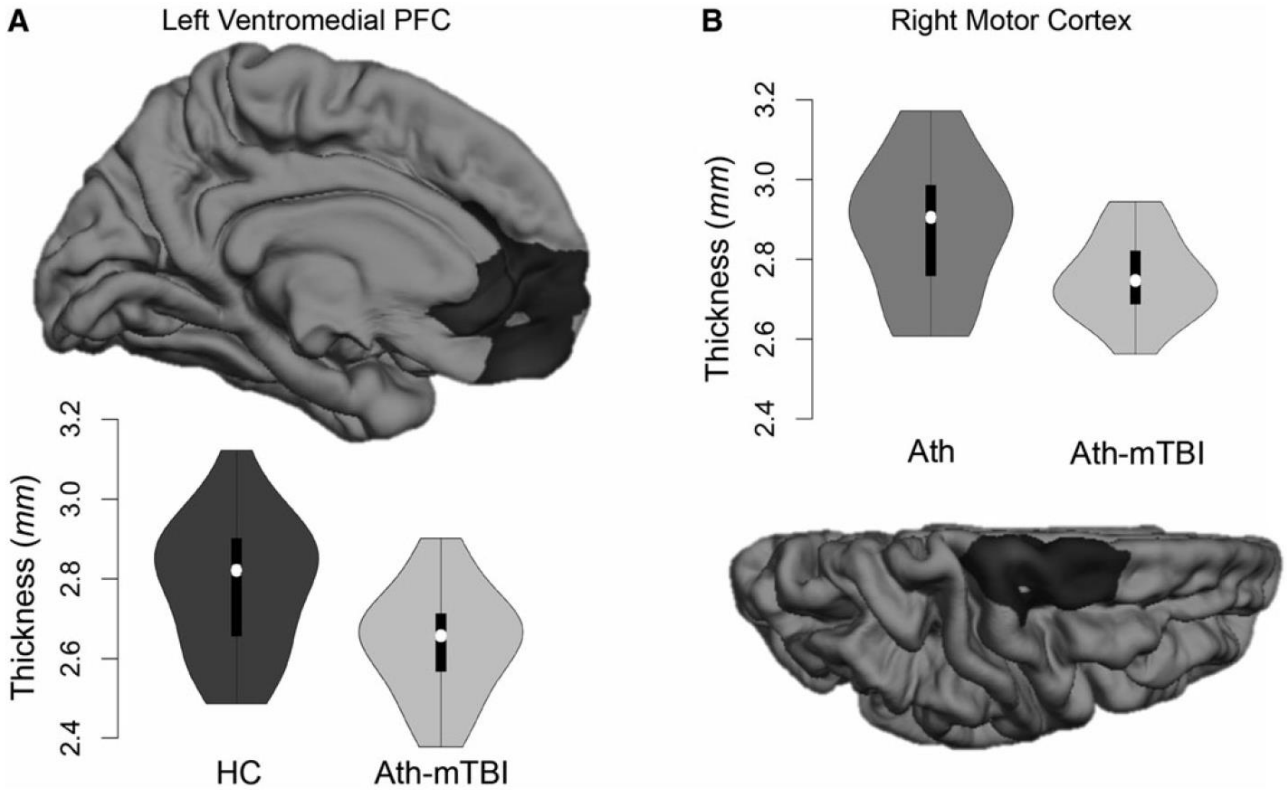
Regions of significant cortical thinning in mTBI patients versus normal controls (O), separated by treatment group (A) and non-treatment group (T) at 3 months follow-up. Regions in the middle temporal cortex in the left hemisphere in the Group O vs. Group T comparison were significant at p = 0.01. No significant differences were observed in the right hemisphere.

Govindarajan 2016

Discussion and Conclusions

- **To our knowledge, this is the first longitudinal mTBI study with a relatively large sample size that investigated cortical thickness changes.**
- **It is interesting to detect cortical thickness change at about 24 hours after injury.**
- **Our results indicate that cortical thickness assessed using conventional MRI could serve as an important measure in identifying subtle pathological changes in mTBI subjects.**
- **A longitudinal design with more time points in the recovery phase and a larger sample size could help establish the potential role of cortical thickness in neurodegeneration after mTBI.**
- **Further investigation in veterans with chronic TBI is timely.**

Thinner Cortex in Collegiate Football Players With, but not Without, Self-Reported History of Concussion



Football athletes with history of concussion (Ath-mTBI) had cortical thinning in left ventromedial prefrontal cortex (PFC) relative to healthy controls (HC; in A) and in right motor cortexrelative to players without history of concussion. Violin plots contain box and whisker and kernal density plots are displayed for each cluster.

Meier J. Neurotrauma, 2016

Thank you

- Question/Answer