Objective: Traumatic Brain Injury (TBI) is a complex injury with a broad spectrum of symptoms and disabilities and is a major cause of morbidity and death in military and civilian populations. TBI costs the world more than $76 billion a year in US and more than 1.7 million people are affected by it every year.1 There is a pressing demand to understand the effects (structural, biochemical, physical, psychological etc) of TBI on the people. The decrease in hippocampus volume due to neurodegeneration in TBI subjects is reported in Jorge et al.2 In our study, we developed a non-invasive fluid percussion injury (FPI) technique on a rodent model to replicate the broad categories of injury severity: mild, moderate and severe TBI to explore the biochemical, cognitive and structural changes in the rat brain. Our study aims at exploring the longitudinal changes in the hippocampus volume (ipsilateral and contralateral) and cognitive assessment in different injury models.

Materials and Methods: Adult male Sprague Dawley rats (280 – 300g) were subjected to focal brain injury using the lateral fluid percussion device. Animals were subjected to either 1) Sham (4mm-diameter hole, in the skull), 2) Mild (22.75 ± 0.75 psi) or 3) Severe (64.04 ± 1.49 psi) injury at 2mm lateral and 3.8mm posterior to bregma. The study set had three shams, 6 mild and 6 severe rats. A 3D MPRAGE images of the rat brain were acquired on 7T Bruker Clinscan, along the transverse direction with TR/TE= 2000 ms/1.5 ms, IR = 800 ms, base resolution of 512 x 416 x 52, and voxel dimensions of 0.06836 x 0.06836 x 0.5 mm3. MR imaging was performed on baseline (BL), day-1, 3, 7, 14 and 28 to study the ipsi- and contra- lateral hippocampus volume changes. Cognitive assessments were done at the same time points on a separate batch of rats with similar injury models. Animals were tested on the Rotarod (0 – 24 rpm in 60s) to assess the motor skills. The segmentation of hippocampus and volume calculation was done semi-automatically using the ITK Snap.3 Amyloid precursor protein and Fluoro-jade staining were done to check the protein deposition and degeneration of neurons in the ipsilateral hippocampus.

Results and Discussions: Fig.1 shows the three planes based segmentation tool used for hippocampus segmentation and volume quantification. The ipsilateral hippocampal volume decreased due to neuronal degeneration in all the injury models from day – 1 to day 3, increased from day-3 to day – 14, and reached the baseline volume by day 28. The contralateral hippocampal volume increased due to neurogenesis in severe than in the mild and sham conforming the results of MR imaging. Our study demonstrated good correlation of results obtained by MR image based analysis of hippocampal volume, histopathology and cognitive assessment. Our study results suggests both the rate of change and total volume of hippocampus due to neuro-degeneration (immediately after the injury) and the neurogenesis (during the recovery phase), depend on the type of injury. The changes in volume indicate reorganization of neurons could be taking place in the hippocampus after the acute phase of injury and during the recovery phase. Reduction of hippocampus volume due to TBI suggests psychological and behavioral changes in the animal.2, 4 Cognitive assessments also showed an improvement in motor coordination during the recovery phase (day-7 to day-14).

Conclusions: Our study demonstrated good correlation of results obtained by MR image based analysis of hippocampal volume, histopathology and cognitive assessment. Our study results suggests both the rate of change and total volume of hippocampus due to neuro-degeneration (immediately after the injury) and the neurogenesis (during the recovery phase), depend on the type of injury. The changes in volume indicate reorganization of neurons could be taking place in the hippocampus after the acute phase of injury and during the recovery phase. Reduction of hippocampus volume due to TBI suggests psychological and behavioral changes in the animal.2, 4 Cognitive assessments also showed an improvement in motor coordination during the recovery phase (day-7 to day-14).