The Challenge of Managing Patients Suffering from Traumatic Brain Injury and the Utility of Multi-Parametric Magnetic Resonance Imaging: A Case Series

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Introduction

- Traumatic Brain Injury (TBI) is a complex phenomenon affecting multiple areas of the brain in multiple ways caused by motor vehicle accidents (MVA), military blast injury, blunt object trauma, falls, and repetitive sports-associated concussion.
- Mechanical forces of brain injury disrupt and dismantle brain circuitry. Endogenous reparative processes attempt to rebuild the circuits, are confounded by ongoing pathology lack of a coordinated repair strategy.
- As a result, it has been difficult to develop therapeutic strategies.
- TBI patients suffer with physical and cognitive symptoms, including problems with memory, attention, balance, and most commonly, post-traumatic headaches.
- Structural (standard) imaging studies are frequently negative or grossly underestimate the severity of TBI. These false negative conclusions of “no significant abnormality” may exacerbate and prolong patient suffering.
- Neuropathological associated injury that is below the threshold of the standard structural imaging can be detected by including specialized MRI techniques including MRI spectroscopy (MRS), arterial spin labeling perfusion (ASL), susceptibility weighted imaging (SWI), diffusion tensor imaging (DTI), functional MRI (fMRI) and artificial intelligence (AI) assisted volumetric measurements such as NeuroQuant.

Objectives

To analyze the demographics, medical history, and clinical presentation of two individuals with severe traumatic brain injury who completed mpMRI using T2, FLAIR, DWI and T1 sequences, and specialized sequences including susceptibility weighted (SWAN/SWI), 3D FLAIR, single voxel MRI spectroscopy (MRS), diffusion tensor imaging (DTI), arterial spin labeling perfusion (ASL) and volumetric MRI (NeuroQuant).

Methodology

- Retrospective analysis of two cases of traumatic brain injury who underwent mpMRI using T2, FLAIR, DWI and T1 sequences, and specialized sequences including susceptibility weighted (SWAN/SWI), 3D FLAIR, single voxel MRI spectroscopy (MRS), diffusion tensor imaging (DTI), arterial spin labeling perfusion (ASL), and volumetric MRI (NeuroQuant).
- All MRI studies were performed on GE 1.5 Tesla MRI machines.
- Multi-Parametric MRI (mpMRI) Technique:
- Standard Sequences
- DWI, T2w FSE, FLAIR, SWAN or GRE T2*w, T1w.
- Specialized Sequences
- SWAN/SWI: extremely sensitive to microhemorrhages (superior to GRE) and reveals a high number in severe to moderate TBI, but relatively few in mild TBI.
- MRI Spectroscopy: TBI adversely affects cerebral metabolism and a number of research groups have successfully used this technique as a biomarker of injury and/or outcome in both pediatric and adult TBI populations. Abnormal metabolism is part of the pathophysiologic cascade following traumatic brain injury (TBI). ^{1}H-MRS has been utilized to identify metabolite changes in regions of injury, to define the extent of pathology, and as a biomarker of outcome.
- ASL: Used to noninvasively assess cerebral blood flow by magnetically labeling inflowing blood, using arterial blood as a contrast agent.
- NeuroQuant: The technique initially focused on medial temporal lobe anatomy and has been used to demonstrate brain atrophy in association with dementia and TBI since 2009. Now automated and semi-automated methods are utilized to accurately measure brain volume.

Conclusions

- Multiparametric MRI (mpMRI) brain includes NeuroQuant, DTI, ASL, MRS, SWI ,3D-FLAIR, post-contrast 3D-FLAIR and MRS.
- Markedly improves detection of brain abnormalities after TBI.
- Protocol can be performed in most imaging centers and hospitals.
- Small investment in hardware, software and time.
- Provides snapshot of functional, anatomical and metabolic data of the brain.
- reveals the multifaceted nature of brain injury.
- Can serve as biomarkers of TBI pathologies to assist stratification of patients.
- Finally, the objective diagnosis of a brain abnormality caused by TBI can have a major effect on the patient, the family, the caregivers and insurance companies by establishing that a real injury has occurred, that the patient is not malingering, and that the patient is worthy of compassion, care and in some situations, compensation.

Funding

No funding was used for this case series.

Results

Patient #1:

- A 43-year-old previously healthy, honorably discharged and gainfully employed. former US Marine suffered a severe TBI from a motorcycle accident 8 years ago.
- Following TBI he experienced a major depressive disorder, occasional seizure and intermittent explosive episodes including severe anger, agitation and irritability.
- He demonstrated physical public aggressiveness with minimal provocation.
- He denies thought disorder, mania, demoralization and apathy and shows no cognitive deficits since his TBI.
- He has developed hypothyroidism, sleep apnea and diarrhea (not due to medication).
- Recently revaluated for medication modification and subsequently underwent multiparametric MRI as part of his re-evaluation.
  - Medications prescribed and used as a result of re-evaluation include escitalopram oxalate, aripiprazole, lamotrigine.
- mpMRI shows:
  - bifrontal encephalomalacia, dural thickening, dural enhancement
  - MRS abnormal reduced NAA, elevated Cho and mI
  - SWI bifrontal microbleeds, meningeal hemosiderosis
  - ASL hypoperfusion right frontal, left frontal, left temporal hypoperfusion
  - DTI abnormal decreased FA and tract disruption multiple areas including corpus callosum and right cingulum
  - NeuroQuant multiple areas of atrophy, right hemisphere most affected including right cingulum, bilateral orbitofrontal and middle frontal gyri, right middle temporal gyrus

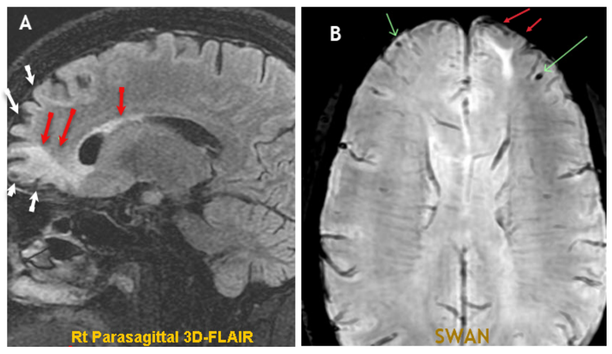

Figure 1 *(A) Encephalomalacia areas (red arrows), cortical atrophy (white arrows). (B) Parenchymal microbleeds (green arrows) and meningeal hemosiderosis (red arrows).*

Structure	Total Volume (cm³)	Percentile
Intracranial Volume	1511	-
Whole Brain	1163	7
Forebrain Parenchyma	996	4

Total Volumes	Percentiles		
	Left	Right	Total
Cerebral White Matter	18	12	15
Cortical Gray Matter	25	7	14
Ventricles	94	95	94
Cerebral WM Hypointensities*	97	98	99
Subcortical Structures			
Cerebellar White Matter	83	98	94
Cerebellar Gray Matter	58	87	74
Brainstem	-	-	23
Thalamus	37	34	35
Ventral Diencephalon	41	17	28
Basal Ganglia			
Putamen	6	13	8
Caudate	45	32	38
Nucleus Accumbens	1	5	1
Pallidum	8	18	11
Cingulate	27	2	5
Anterior Cingulate	12	1	1
Posterior Cingulate	32	49	39
Isthmus Cingulate	59	77	68

Cortical Brain Regions	Percentiles		
	Left	Right	Total
Frontal Lobes	28	2	9
Superior Frontal	28	18	20
Middle Frontal	8	1	1
Inferior Frontal	9	5	5
Lateral Orbitofrontal	93	58	83
Medial Orbitofrontal	1	1	1
Paracentral	23	21	19
Primary Motor	83	29	58
Parietal Lobes	15	12	12
Primary Sensory	25	28	24
Medial Parietal	7	15	8
Superior Parietal	17	36	23
Inferior Parietal	55	8	21
Supramarginal	35	35	32
Occipital Lobes	41	61	50
Medial Occipital	56	62	59
Lateral Occipital	34	60	45
Temporal Lobes	34	9	19
Transverse Temporal + Superior Temporal	49	21	33
Posterior Superior Temporal Sulcus	88	97	96
Middle Temporal	43	4	15
Inferior Temporal	15	11	10
Fusiform	47	22	32
Parahippocampal	99	89	97
Entorhinal Cortex	63	93	85
Temporal Pole	56	36	44
Amygdala	9	37	19
Hippocampus	7	14	9

Figure 2 *Red areas indicate significant atrophy in the forebrain, thalamus, nucleus accumbens, right cingulate gyrus, right frontal lobe and right inferior temporal gyrus. Left amygdala and left hippocampus are between 1.5 -2.0 SD below the mean.*

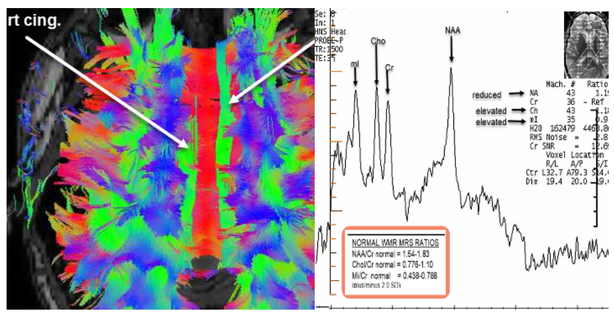

Figure 3 *(A) DTI tractography showing abnormal right cingulum (arrows). (B) MRS showing reduced NAA and elevated Cho and myoinositol.*

Patient #2:

- 48-year-old male retired soldier with 5 concussive military injuries (mild TBI events), including three blast injuries and 2 parachute injuries resulting in up to 45 minutes of unconsciousness.
- Symptoms began after his first injury and worsened after each successive injury.
- Has major depressive disorder, panic disorder, post-traumatic stress disorder, and generalized anxiety disorder.
- Symptoms include nervousness, irritability, anger, emotional lability, amnestic issues, apathy and loss of focus.
- mpMRI shows:
  - scattered white matter lesions frontal lobes
  - MRS elevated myoinositol, normal Cho and NAA
  - SWI left occipital microbleed
  - ASL possible hypoperfusion left prefrontal area
  - DTI abnormal reduced FA in corpus callosum, mild asymmetry in frontal-occipital tractography
  - NeuroQuant shows atrophy of bilateral thalami, nucleus accumbens, right medial orbitofrontal gyrus, left inferior frontal gyrus and mild atrophy cortical gray matter

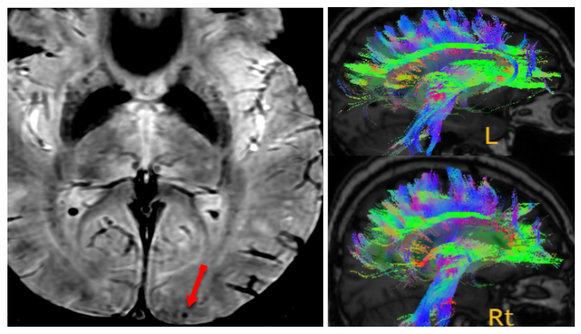

Figure 4 *SWI image (left) shows one microbleed (arrow). DTI (right) shows frontal tract asymmetry.*

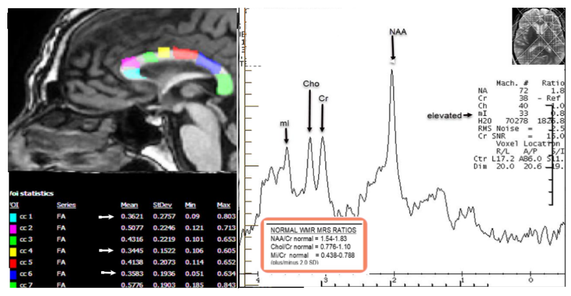

Figure 5
Left. DTI showing abnormal decreased FA values in corpus callosum (arrows). Right. MRS showing elevated myoinositol consistent with increased glial activity. NAA and Cho are normal.

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