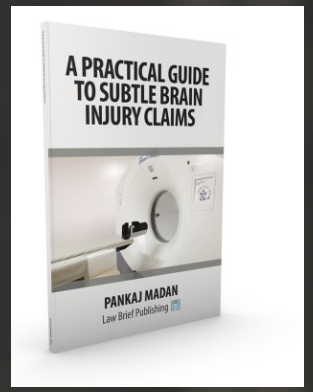
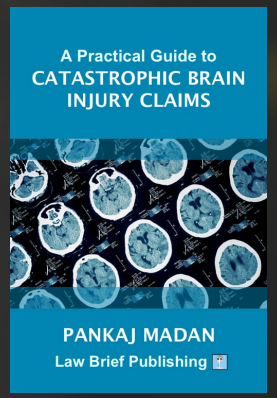
12
King's Bench Walk

Advancements in detecting Traumatic Brain Injury





Pankaj Madan

Barrister

12 King's Bench Walk & Exchange Chambers

" He has the ability to challenge the unusual in cases"

Legal 500 2017/18

"....Combative with charm. Knows exactly what he is doing.

Has a real touch for big PI claims".

The Legal 500 2021

Summary

- Advancements in detection
- Not just imaging

What do you mean by a subtle traumatic brain injury? Are they always mild?

- Mild and subtle traumatic brain injury are not necessarily the same?
- Known many moderately-severe traumatic brain injuries in practice which could be described as subtle.
- Subtle tbi's are cases where the main effects are not transparent and **physical but** where the main effects are **cognitive and emotional** and therefore upon casual observation or acquaintance may well be missed.
- They may however be very serious and indeed approaching catastrophic values
- Some tbi's are sadly obvious and catastrophic, inability to walk or feed.
- Others- lack of capacity is obvious and plain
- All others would regard as a subtle TBI.

How can imaging help us with a diagnosis of TBI?

- The differential diagnosis is normally between psychiatric disorder and TBI or sometimes even malingering may be alleged
- Imaging will detect gross heamorrhages and may detect microheammorhages
- Imaging is important in the A & E setting to exclude a major bleed which may cause raised intra-cranial pressure and death
- Imaging of choice because it is available and convenient is CT scanning.
- CT scanning however is not sensitive to microheamorhages and cannot image white fibre tracts.
- Detection of microheamorrhages is important because they frequently accompany Diffuse axonal injury.
- White matter in the brain consists of axons which leave the main cell body, neuron and travel and form interconnections with other neurons
- Vessels are much tougher and more fibrous and larger than axons.
- If forces have therefore ruptured, torn or sheared vessels then we know that it is almost certain that axons have also been damaged.
- Even Regular MRI scanning at T2 level will not be able to image even bundles of white matter
- Some imaging now is able to detect large bundles of axons or tracts which have been damaged although not individual axons of course

MRI vs CT

Prevalence of MR Evidence of Diffuse Axonal Injury in Patients with Mild Head Injury and Normal Head CT Findings

Robert L. Mittl, Jr, Robert I. Grossman, John F. Hiehle, Jr, Robert W. Hurst, Donald R. Kauder, Thomas A. Gennarelli, and George W. Alburger

PURPOSE: To assess the prevalence of MR evidence for diffuse axonal injury at 1.5 T in patients with normal head CT findings after mild head injury. **METHODS:** Twenty consecutive patients with mild head injury (Glasgow Coma Scale, 13 to 15; no subsequent deterioration, loss of consciousness < 20 minutes) and normal head CT findings were examined with MR at 1.5 T. Pulse sequences included a conventional T2-weighted spin-echo sequence (2500–3000/30,80/1[repetition time/echo time/excitations]) and a T2*-weighted gradient-echo sequence (750/40/2, 10° flip angle). Each sequence was read independently by two blinded readers. **RESULTS:** The readers agreed that abnormalities compatible with diffuse axonal injury were present in the white matter of 6 (30%) of 20 patients (95% confidence interval, 12% to 54%). Both readers agreed that foci of high signal intensity were present on the T2-weighted spin-echo sequence in 3 (15%) of the 20 cases (95% confidence interval, 3% to 38%) and that foci of hypointensity compatible with hemorrhagic shear injury were present on the T2*-weighted sequence in 4 (20%) of the 20 patients (95% confidence interval, 6% to 44%). Both types of abnormality were noted by the readers in one patient. **CONCLUSIONS:** MR shows evidence of diffuse axonal injury in some patients with normal head CT findings after mild head injury. These lesions may represent the pathologic substrate underlying the postconcussion syndrome that occurs in many patients with moderate to severe head injury.

Index terms: Head, injuries; Brain, injuries; Brain, magnetic resonance; Nerve cells

AJNR Am J Neuroradiol 15:1583–1589, Sep 1994

So what is the problem?

- Even advanced neuroimaging techniques have shown the potential for evalulating subtle tbi
- However, there is a relatively poor correlation in the literature between actual symptoms of TBI and imaging
- Iverson et all were putting people through DTI scanners in the US for many years. When they uncovered the blind, many of those with symptoms had nothing show up on even advanced imaging. Some of those with positive imaging had no symptoms.
- It’s a little like having degenerative changes in the spine on an x-ray doesn’t mean you will have symptoms or that if you have symptoms the pain is coming from those degenerative changes.
- That’s not to say that imaging is not very helpful. It can be but it is open to challenge and interpretation

Post-concussion like symptoms are non-specific

Applied Neuropsychology
2003, Vol. 10, No. 3, 137–144

Examination of "Postconcussion-Like" Symptoms in a Healthy Sample

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Rael T. Lange
University of British Columbia,Vancouver, British Columbia, Canada

The post-concussion syndrome (PCS) is relatively common following mild traumatic brain injury (MTBI). However, the factors that cause and maintain this syndrome continue to be debated. The purpose of this investigation was to examine the prevalence of postconcussion-like symptoms in a sample of healthy individuals. Participants (N = 104) completed the British Columbia Postconcussion Symptom Inventory-Short Form (BC-PSI-Sf), a test designed to measure both the frequency and intensity of ICD-10 criteria for PCS, and the Beck Depression Inventory (2nd ed.). Specific endorsement rates of postconcussion-like symptoms ranged from 35.9% to 75.7% for any experience of the symptoms in the past 2 weeks, and from 2.9% to 15.5% for the experience of more severe symptoms. Symptoms reported on the BC-PSI-Sf also showed a moderately high correlation with self-reported depressive symptoms [r (102) = .76, p < .01]. This study illustrates that the presence of postconcussion-like symptoms: (a) are not unique to mild head injury and are commonly found in healthy individuals, and (b) are highly correlated with depressive symptoms.

Key words: post-concussion syndrome, mild traumatic brain injury, base rates

Depression can give rise to cognitive complaints

process. This is especially true if a person is experiencing both depression and chronic pain. In a recent study of 275 consecutive pain patients with no history of head injury, 54% reported at least one cognitive complaint (McCracken & Iverson, 2001). Based on multiple regression analyses, depression was the single greatest predictor of cognitive complaints in this sample.

What are the more advanced types of imaging we can use?

- First let me tell you about structural types
- SWI- susceptibility weighted imaging- looks for heammorhages. The effect causes microheammorhages to become more conspicuous relative to other pulse sequences- 3 to 6 times more sensitive than conventional T2 sequences.
- Quantitive susceptibility mapping (QSM)- looks more closely at the isotropes left behind by bleeds and quantifies them in more detail reflecting the spatial extent of lesions.

What is the other type?

- Scans which look for contusions.
- As MRI hardware and techniques have improved 3D-T2 FLAIR and T” WI.
- Also detect TAI (traumatic Axonal Injury). You’ve heard of “Diffuse” which involves more than 4 tracts.
- Here we are talking about 3 or fewer tracts which are damaged with TAI.
- Here were looking not for heamorhaging but actual damage to large fibre tracts often at grey/white matter junctions (differing density of tissues)
- TAI is now thought to be much more common. Whereas before we were blaming DAI. TAI is not limited to catastrophic TBI’s. Linked to mild and moderate too
- Commonly occurred in the lobar white matter frontal and temporal lobes the corpus callosum (22% of lesions).
- CT by the way has extremely poor sensitivity for TAI, and virtually no sensitivity for non- Heamorrhagic TAI and limited sensitivity for heamorrhagic TAI.
- DWI (diffusion weighted imaging) is sensitive in the early to acute stage of injury. Looks at the microscopic motion of water molecules in brain tissue and is a complement to T2 scanning and SWI. Highly sensitive to TAI. Problem is that can show constitutional white matter lesions as well especially ischeamic disease, common after middle age.

What is DTI?

- A very advanced technique, Diffusion Tensor Imaging
- Based on DWI but has enhanced ability to track the direction of the water molecules in 3D space.
- So in normal white matter tracts with parallel fibre bundles, water diffuses more felly along the direction of the white matter fibres than transverse to the fibres.
- Normal undamaged white fibre tracts exhibit highly directional diffusion whereas damaged white matter tracts are thought to demonstrate more isotropic diffusion perhaps because of the lack of longditudinality say in the microstructural elements of the fibre tracts
- So DTI is a marker for white matter pathology including traumatic brain injury.
- Quantifies the diffusion. A common parameter is FA or fractional anisotropy

T1 vs SWI

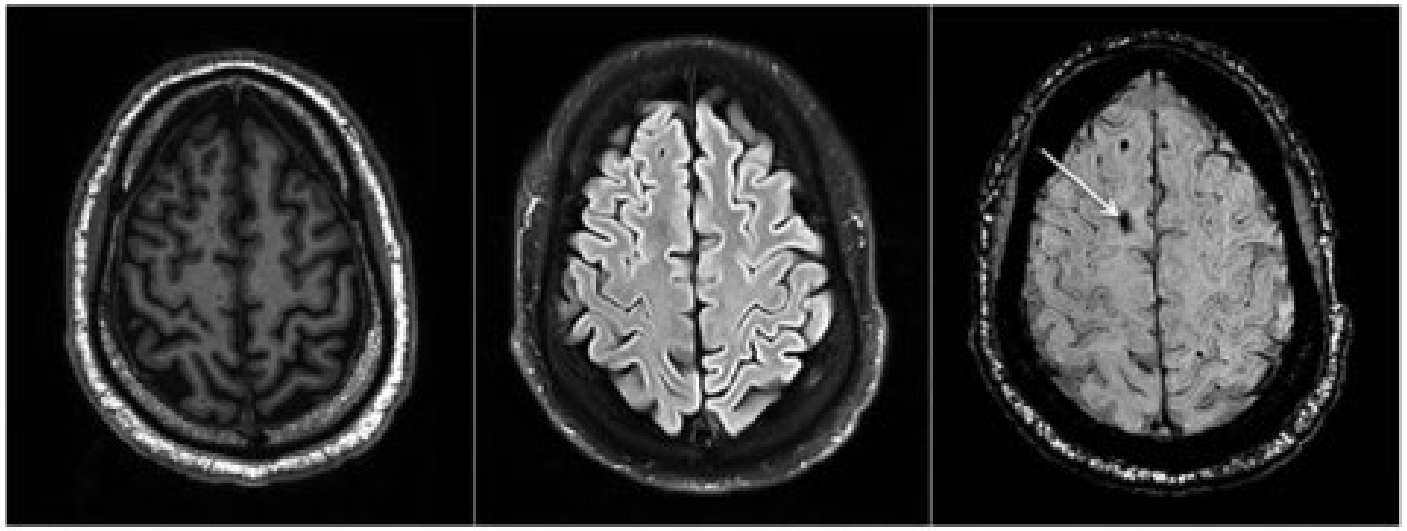
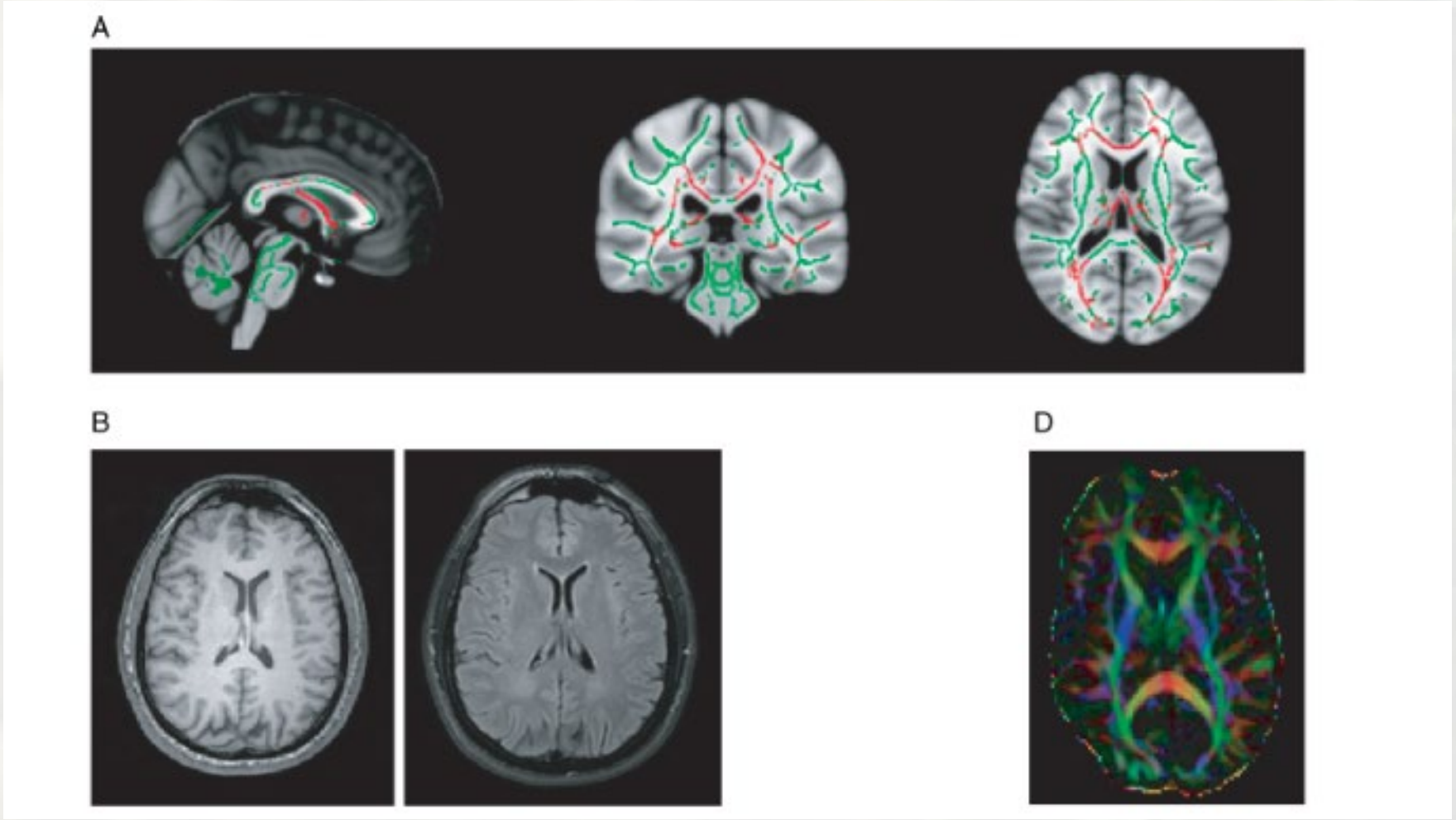


Figure 6 A microbleed is clearly identified on susceptibility weighted MRI (marked with white arrow) but not clearly visible on standard T1 weighted nor fluid-attenuated inversion recovery MRI.

DTI (Credit: Concussion is confusing us all- David Sharp et al)



Are there any problems with DTI in medico-legal use?

- Getting people to do it.
- Many say it is not ready for medico-legal use
- Reasons are it can be too detailed
- It has been controversial in the USA. Some such as Grant Iverson, suggest that there is a poor correlation between what is shown in these studies and actual deficits. They've been popping people through DTI's for years more than we have.

doi:10.1093/brain/awu095 Brain 2014: 137; 1876–1882 | 1876

BRAIN
A JOURNAL OF NEUROLOGY

REPORT

Acute mild traumatic brain injury is not associated with white matter change on diffusion tensor imaging

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In conclusion, in this large homogeneous, premorbidly healthy sample, acute mild TBI was not associated with obvious DTI abnormalities detectable with TBSS. Clear differences in DTI findings were associated with age, even in healthy subjects in their 40s. Therefore, age should always be considered a potential confounder in DTI studies.

What about MR spectroscopy (MRs)?

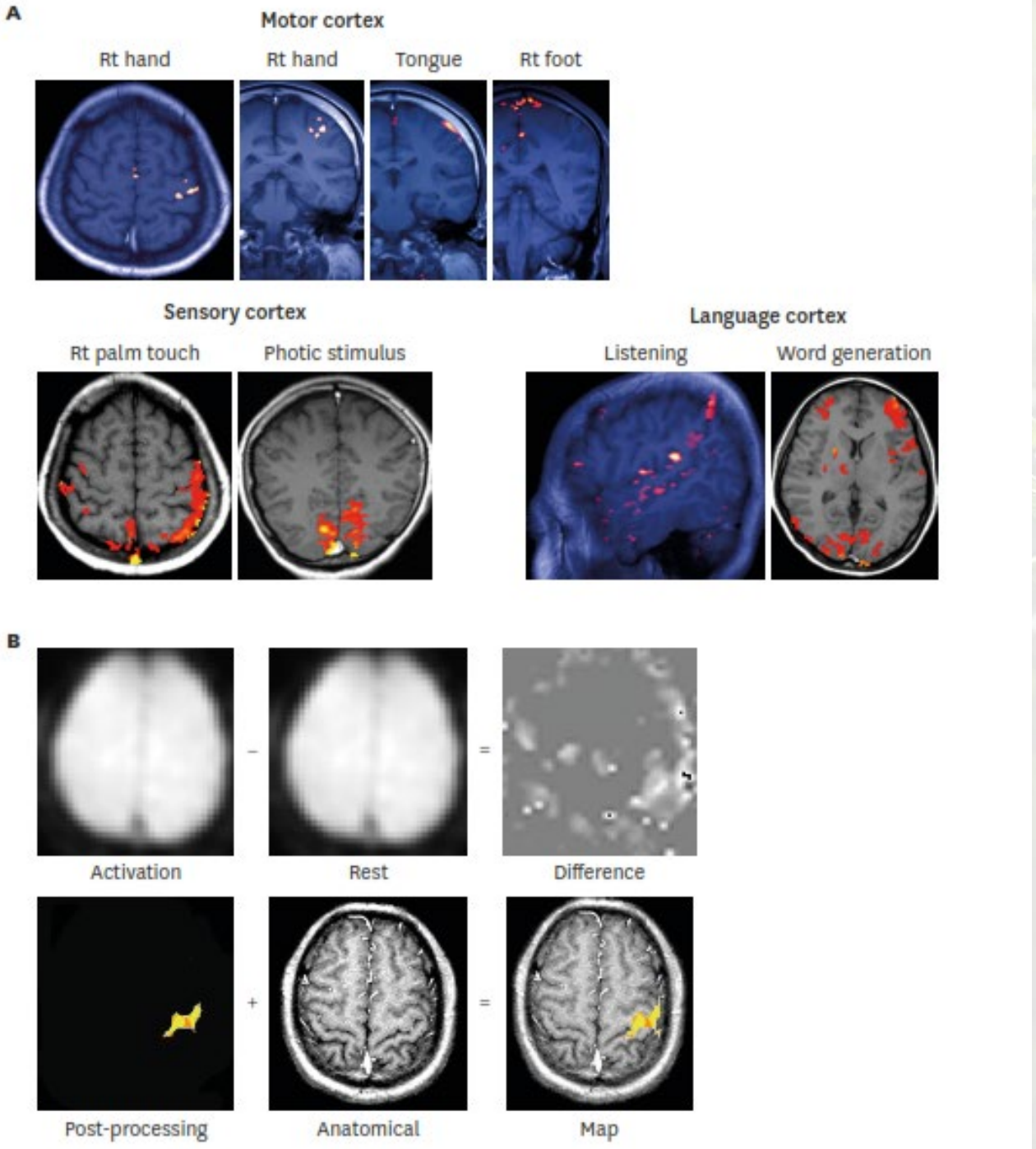
- Similar to MRI but the data is converted to a frequency domain information giving information about brain metabolites.
- Certain markers are released after tbi.
- Certain peaks remain elevated in the chronic stage
- These are being used in studies and not in hospitals
- Not specific to TBI but can have elevations for other brain disorders

What about Perfusion Weighted Imaging studies?

- TBI is associated with impaired cerebro vascaular autoregulation
- Altered blood flow
- Many techniques but DSC imaging (Dynamic Susceptibility Contrast) is the most common.
- Reduced cerebral blood volume in contusional areas was associated with worse clinical outcomes
- Sample sizes and studies are currently limited

Can Functional Mri help?

- This is exciting
- Depends on Blood oxygen level dependent imaging and coupling between CBF and metabolic activity.
- Holds great potential for rehabilitation potential as well as medico-legal use in the future
- Not necessarily going to be determinative in the diagnosis of mild tbi however.
- Likely to be of more use in Catastrophic tbi to show rehab gains.


A
Motor cortex
Rt hand
Rt hand
Tongue
Rt foot
Sensory cortex
Rt palm touch
Photic stimulus
Language cortex
Listening
Word generation
B
Activation
Rest
Difference
Post-processing
Anatomical
Map

What about MEG?

- Magnetoencephacolography essentially combines structural information and electrophysiological information
- Can be used to examine brain activation patterns involved with specific tasks.
- MEG combines functional MRI and EEG
- Huang et al found anatomical and functional correlation between abnormal slow waves and DAI identified with DTI
- Detected abnormal connectivity after TBU even in patients with milder degrees and normal MRI findings
- Ideally can measure such activity whilst giving the Claimant neuropsychometric tests and acquiring data on the working of the brain
- In one study, comparing mild TBI participants with controls, there was a disorganized pattern of activation in the MTBI cohort compated to the healthy controls. Significant differences in regional brain activation and timing of activation. Patients were literally not firing on all cylinders
- MEG is the most promising objective way we may have in the future of identifying subtle brain dysfunction after trauma.

Neurosurgery

OPEN ACCESS

RESEARCH PAPER

Delayed and disorganised brain activation detected with magnetoencephalography after mild traumatic brain injury

Leodante da Costa,[1,2] Amanda Robertson,[3] Allison Bethune,[1] Matt J MacDonald,[3] Pang N Shek,[4] Margot J Taylor,[3,5,6] Elizabeth W Pang[3,7,8]

Innovision, Professor Gary Green
Professor of Neuro-imaging, York University

0.1 Purpose of the report

This report describes the findings of the investigation of brain activity in the referred individual "IPxxxx".

The brain activity was collected by using a magnetoencephalography (MEG) scanner. This device is used to non-invasively record magnetic activity around the head. This magnetic data is then used to calculate the electrical currents generated by neural activity within the brain which are the sources of the recorded magnetic information.

Injured brain tissues in mTBI patients generate abnormally elevated slow-waves (1-4 Hz) that can be measured and localized by resting state MEG. Therefore slow-wave brain activity was compared with data from a control group of individuals from the normal population. Statistical comparisons were made to compare the referred individual's neural activity with the controls' data.

The purpose of the report is to describe whether the brain activity is within the normal range and if not, where in the brain the activity is not within the normal range.

The report was compiled on March 5, 2021by Gary Green MA DPhil BM BCh of Innovision-IP Ltd for *A. BBB* of *yyyy* solicitors Ltd concerning participant IPxxxx

1.1 Main Findings

The main findings of the analysis of the brain activity of participant *IPxxxx*, referred by solicitor *yyyyy* are that there are areas of the brain where there is brain activity that is statistically abnormally elevated compared with activity in normal individuals. This increase in slow-wave activity is observed in situations where there is damage to the brain. The findings are therefore compatible with there having been a structural brain injury. We recommend that the imaging findings are correlated to the clinical features of the subject via a clinical neurological opinion taking into account the most affected areas reported here.

- Brain activity was analysed for the presence of oscillations that are known to be found when there has been damage to the brain. These are called slow-waves.
- In an awake normal individual, slow brain waves are very small in amplitude. If brain activity is recorded, the amplitude of slow-waves can be measured every two seconds throughout the recording period. A histogram of the amplitude of the waves can be constructed to show the distribution of normal activity amplitude. Then the participant *IPxxxx*'s activity can be compared with respect to the distribution in the normal population. Statistical tests of the difference in mean activity as well as the overall distribution can be made.
- For participant *IPxxxx* statistically significant elevated than normal slow-wave (delta)[1] brain activity was observed in the following areas. These are the six areas with the most amounts of slow-wave activity when compared to controls.

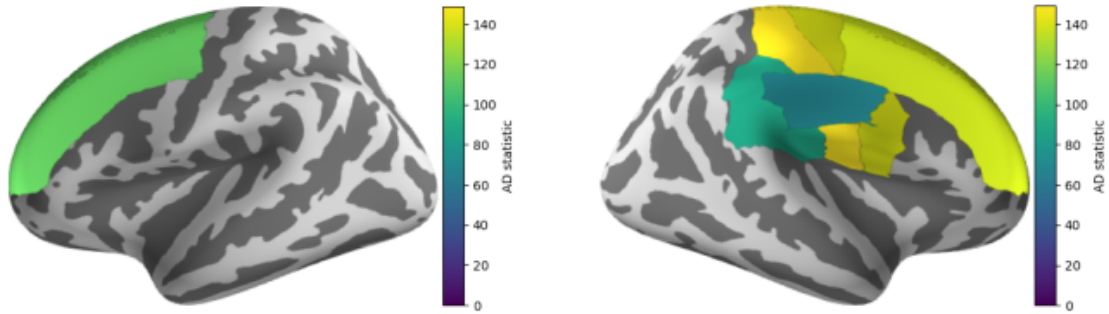


Figure 1: Location of the brain areas with the largest differences in slow-wave brain activity in participant *IPxxxx* compared to normal individuals

  - Right postcentral

[1]Oscillations between 1 and 4Hertz

2 Principal findings

2.1 Brain region Summary

The following brain areas were found to have statistically elevated slow-wave activity. There are listed in descending order of the deviation from normal. That is, the areas that have the lowest probability that the participant's results are from the normal group are listed first ('Left' means Left Hemisphere of the brain and 'Right' means Right Hemisphere). The abnormal activity reported was associated with a probability of less than 1 in a 1000 that this activity was typical of a person from the normal population.

- Right postcentral
- Right precentral
- Right superiorfrontal
- Left superiorfrontal
- Right supramarginal
- Right posteriorcingulate

In each case the histograms of the normal population activity and that recorded from participant *IPxxxx* is then accompanied by a graphic of where that difference was found in the brain.

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Resting-State Magnetoencephalography Reveals Different Patterns of Aberrant Functional Connectivity in Combat-Related Mild Traumatic Brain Injury

Ming-Xiong Huang,[1,2] Deborah L. Harrington,[1,2] Ashley Robb Swan,[1,2] Annemarie Angeles Quinto,[1,2] Sharon Nichols,[3] Angela Drake,[4] Tao Song,[2] Mithun Diwakar,[2] Charles W. Huang,[5] Victoria B. Risbrough,[6,7] Anders Dale,[2] Hauke Bartsch,[2] Scott Matthews,[1,6,8] Jeffrey W. Huang,[9] Roland R. Lee,[1,2] and Dewleen G. Baker,[1,6,7]

Abstract

Blast mild traumatic brain injury (mTBI) is a leading cause of sustained impairment in military service members and veterans. However, the mechanism of persistent disability is not fully understood. The present study investigated disturbances in brain functioning in mTBI participants using a source-imaging-based approach to analyze functional connectivity (FC) from resting-state magnetoencephalography (rs-MEG). Study participants included 26 active-duty service members or veterans who had blast mTBI with persistent post-concussive symptoms, and 22 healthy control active-duty service members or veterans. The source time courses from regions of interest (ROIs) were used to compute ROI to whole-brain (ROI-global) FC for different frequency bands using two different measures: 1) time-lagged cross-correlation and 2) phase-lock synchrony. Compared with the controls, blast mTBI participants showed increased ROI-global FC in beta, gamma, and low-frequency bands, but not in the alpha band. Sources of abnormally increased FC included the: 1) prefrontal cortex (right ventromedial prefrontal cortex [vmPFC], right rostral anterior cingulate cortex [rACC]), and left ventrolateral and dorsolateral prefrontal cortex; 2) medial temporal lobe (bilateral parahippocampus, hippocampus, and amygdala); and 3) right putamen and cerebellum. In contrast, the blast mTBI group also showed decreased FC of the right frontal pole. Group differences were highly consistent across the two different FC measures. FC of the left ventrolateral prefrontal cortex correlated with executive functioning and processing speed in mTBI participants. Altogether, our findings of increased and decreased regionalpatterns of FC suggest that disturbances in intrinsic brain connectivity may be the result of multiple mechanisms, and are associated with cognitive sequelae of the injury.

Keywords: blast brain injury; excitation; inhibition; FC; MEG; TBI

Brain Imaging and Behavior (2017) 11:591–610
DOI 10.1007/s11682-017-9684-0

REVIEW ARTICLE

Structural imaging of mild traumatic brain injury may not be enough: overview of functional and metabolic imaging of mild traumatic brain injury

Samuel S. Shin[1] · James W. Bales[2] · C. Edward Dixon[3] · Misun Hwang[4]

Published online: 13 February 2017

Magnetoencephalography studies

Magnetoencephalography is a functional imaging technique that detects magnetic fields emitted by activity in the brain. It can be used to detect pathological slow-waves (delta wave: 1-4 Hz frequency band) that indicate axonal injury. Based upon the principle that electrical currents generated by neural elements create weak magnetic fields, MEG is a complimentary analytical technique to EEG that may allow for analysis of larger cumulative effects of cerebral dysfunction.

Prior results of MEG at a chronic timepoint after injury (range: 2–38 months) showed that it can detect abnormal activities in mTBI patients who had no MRI findings (Lewine et al. 1999). Another study using MEG in mTBI patients at a mean time of 8.2 months (range: 4 weeks-3 years) showed that MEG can reveal regions of injury with high detection rates of 87% (Huang et al. 2012). Moreover, detection of slow waves by MEG in prefrontal areas correlated with neurobehavioral changes seen after concussion (Huang et al. 2014). However, there are many directions of research that is needed for the use MEG in mTBI patients. How MEG activity changes over the time course of recovery is unclear. Furthermore, what these alterations acutely mean for long term recovery is yet to be clearly identified. Currently the state of the technology for MEG requires cost similar to that of a high field MRI scanner. A dedicated shielded room is also required since MEG is measured by a superconducting quantum interference device (SQUID) which is a costly equipment to purchase and maintain. This makes MEG an expensive correlate to other imaging and electrophysiological modalities available. Despite the costs and many aspects of the technique that are currently unknown, MEG may have a role in future research for mTBI subjects due to its complimentary function to EEG and unique parameter that is monitored: magnetic field generated by neural activity (Lee and Huang 2014).

CONCLUSION

- MEG scans are now a cost-effective reality
- Costs around £7,000
- Here in the UK
- Very high detection rates over 87%.
- Innovision claim 100% detection rate- no false positives
- Could be used by Claimants or also Defendants or jointly to rule TBI in or out
- Danger,- selective disclosure
- Perception of bias
- Expert neurologists/neuro-radiologists not being aware of or up to date with the technology
- New
- Not suitable for people who cannot lie still or have issues with enclosure

Questions