5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 16

Traumatic Brain Injury, stroke and subarachnoid haemorrhage – How to Make an Impact in neurocritical care management and research (Level 2)

Neuroimaging, CSF and plasma biomarkers in TBI

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Neuroimaging, CSF and plasma biomarkers in TBI

Virginia Newcombe

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Consultant in Neurointensive Care and Emergency Medicine
RCEM Associate Professor

FDA

WHAT IS A BIOMARKER?

A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions.

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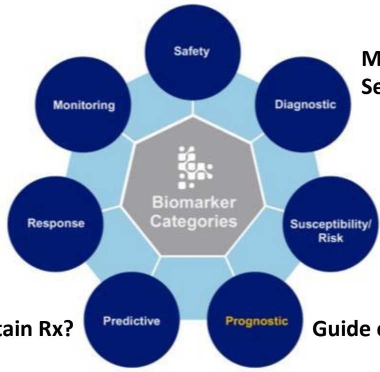

Mild TBI – replace CT?
Secondary injury in ICU

Return to sport?

Guide early decision making?

Clinical Trials

Who may benefit from certain Rx?

Potential biomarkers in TBI (in the ICU setting)

- Intracranial dynamics (ICP, CPP, PrX, PbtO2)
- Microdialysis markers (glucose, lactate, pyruvate, glycerol, glutamate, tau).
- MRI
- PET (Regional cerebral metabolic rate of glucose (CMRglc) or oxygen (CMRO2), activated microglia (PK 11195)
- Blood and (CSF) (proteomics, metabolomics)

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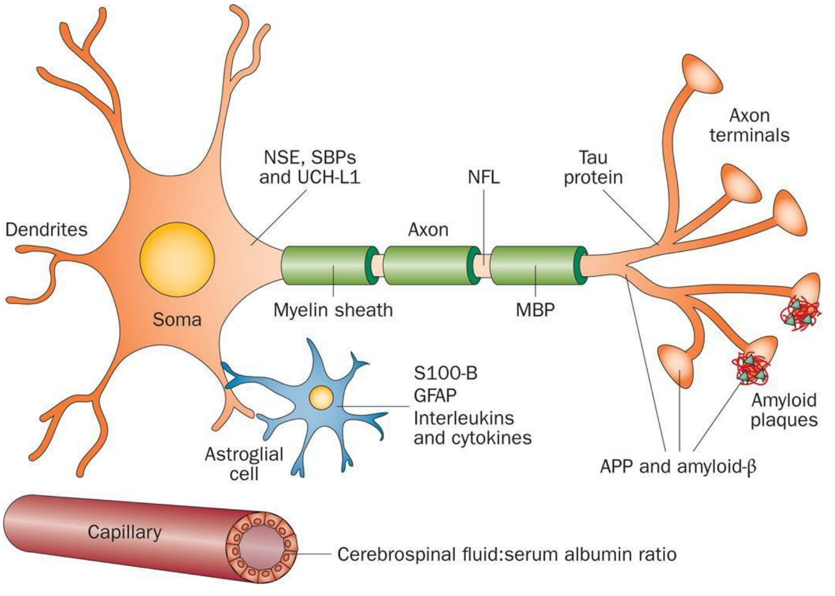
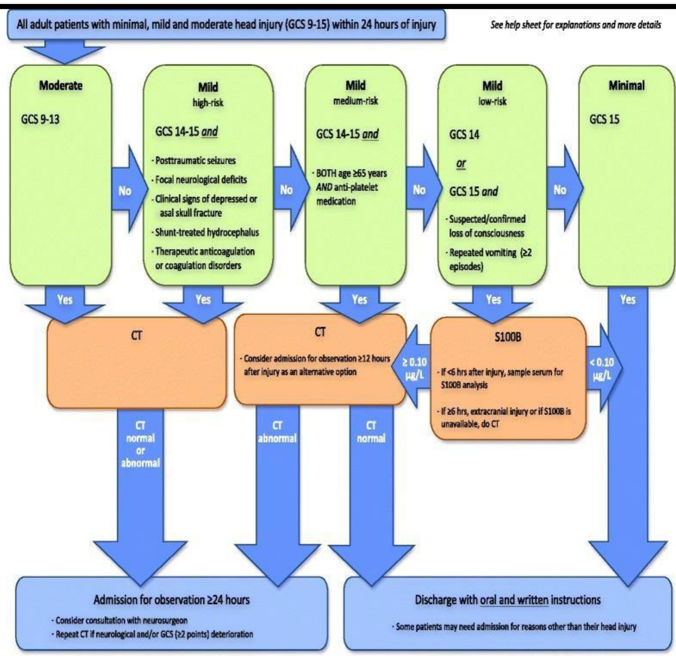
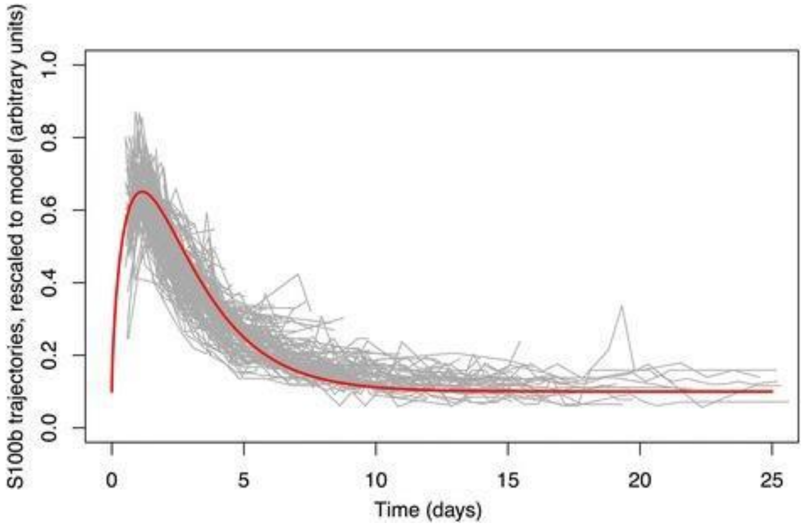


nature REVIEWS NEUROLOGY **Zetterberg et al, 2013:9;201-2010**



Scandinavian Neurotrauma Committee Guidelines 2013

s100b in severe TBI

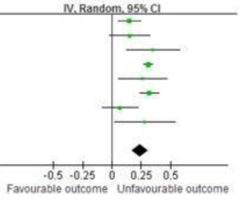


Ercole et al, BMC Neurol, 2016;16:93

Neuron Specific Enolase (NSE)

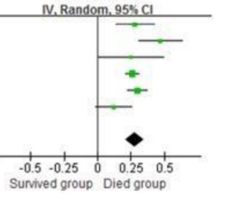
Study or Subgroup	Unfavourable outcome Mean	SD	Total	Favourable outcome Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Woertgen 1997	1.58	0.18	30	1.43	0.21	30	16.5%	0.15 [0.05, 0.25]	1997
Raabe 1998	1.26	0.37	20	1.11	0.15	24	10.0%	0.15 [-0.02, 0.32]	1998
Raabe 1999	1.43	0.48	33	1.08	0.57	49	6.9%	0.35 [0.12, 0.58]	1999
Guan 2003	1.82	0.06	11	1.51	0.05	30	22.6%	0.31 [0.27, 0.35]	2003
Vos 2004	1.57	0.6	38	1.31	0.25	40	8.0%	0.26 [0.05, 0.47]	2004
Li 2004	1.56	0.12	18	1.24	0.13	22	18.8%	0.32 [0.24, 0.40]	2004
Gradisek 2012	1.29	0.36	36	1.22	0.35	48	11.4%	0.07 [-0.08, 0.22]	2012
Stein 2012	1.32	0.36	8	1.04	0.11	16	5.9%	0.28 [0.02, 0.54]	2012
Total (95% CI)			194			259	100.0%	0.24 [0.17, 0.31]	

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 19.58$, df = 7 (P = 0.007); $I^2 = 64\%$
Test for overall effect: Z = 6.61 (P < 0.00001)



Study or Subgroup	Died group Mean	SD	Total	Survived group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Dauberschmidt 1983	0.96	0.17	6	0.68	0.04	3	13.8%	0.28 [0.14, 0.42]	1983
Yamazaki 1995	1.71	0.16	7	1.24	0.18	10	11.7%	0.47 [0.31, 0.63]	1995
Vos 2004	1.59	0.59	26	1.34	0.35	52	6.3%	0.25 [0.00, 0.50]	2004
Baker 2009	1.59	0.08	10	1.33	0.06	54	29.0%	0.26 [0.21, 0.31]	2009
Sogut 2010	2.32	0.15	27	2.02	0.21	73	24.7%	0.30 [0.23, 0.37]	2010
Gradisek 2012	1.36	0.31	26	1.24	0.27	58	14.4%	0.12 [-0.02, 0.26]	2012
Total (95% CI)			102			250	100.0%	0.28 [0.21, 0.34]	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 11.14$, df = 5 (P = 0.05); $I^2 = 55\%$
Test for overall effect: Z = 7.91 (P < 0.00001)



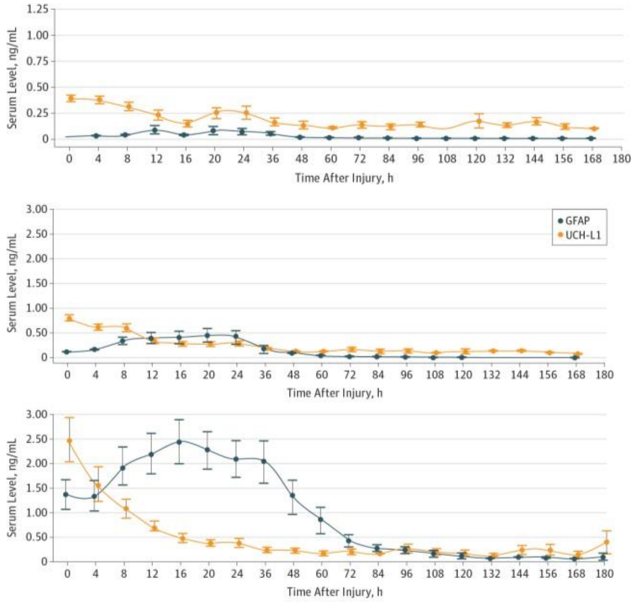
Cheng et al, Plos One, 2014;9(9)e106680

GFAP and UCH-L1 in mild TBI

Trauma Controls

mTBI
No lesions

mTBI
Lesion positive



Pappa et al, JAMA Neurol, 2016;73(5):551-560

Serum GFAP and UCH-L1 for prediction of absence of intracranial injuries on head CT (ALERT-TBI): a multicentre observational study

Jeffrey J Bazarian*, Peter Biberthaler*, Robert D Welch, Lawrence M Lewis, Pal Barzo, Viktoria Bogner-Flatz, P Gunnar Brolinson, Andras Büki, James Y Chen, Robert H Christenson, Dallas Hack, J Stephen Huff, Sandeep Johar, J Dedrick Jordan, Bernd A Leidel, Tobias Lindner, Elizabeth Ludington, David O Okonkwo, Joseph Ornato, W Frank Peacock, Kara Schmidt, Joseph A Tyndall, Arastoo Vossough, Andy S Jagoda

Design
- Prospective, multicentre observational trial

Patients
- 1959 patients

Inclusion
- TBI with GCS 9 to 15, needed CT Head, bloods collected within 12 hours of injury

Intervention
- Measurement UCH-L1 and GFAP

Outcome
- Sensitivity and negative predictive value for lesion detected on CT

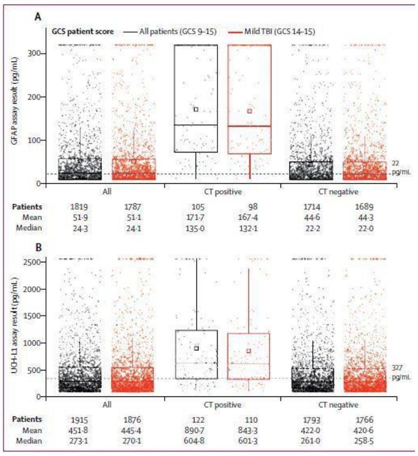
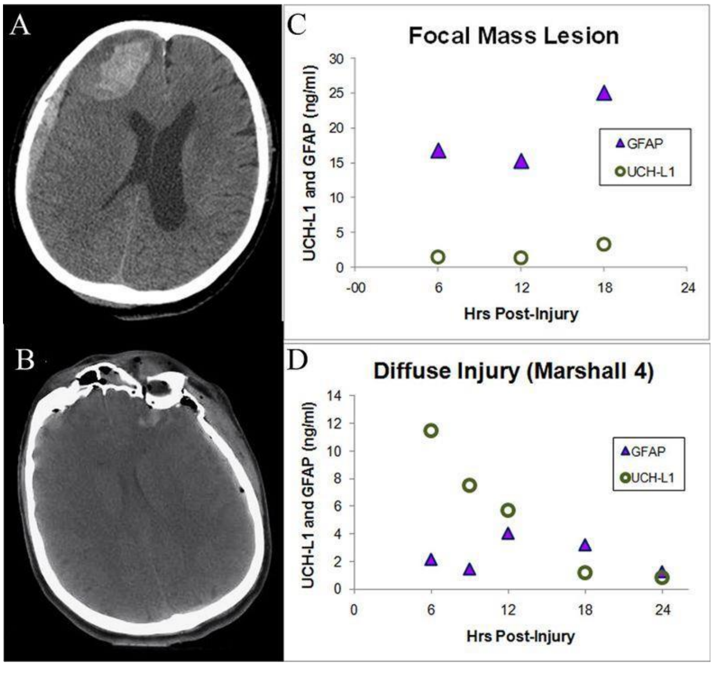


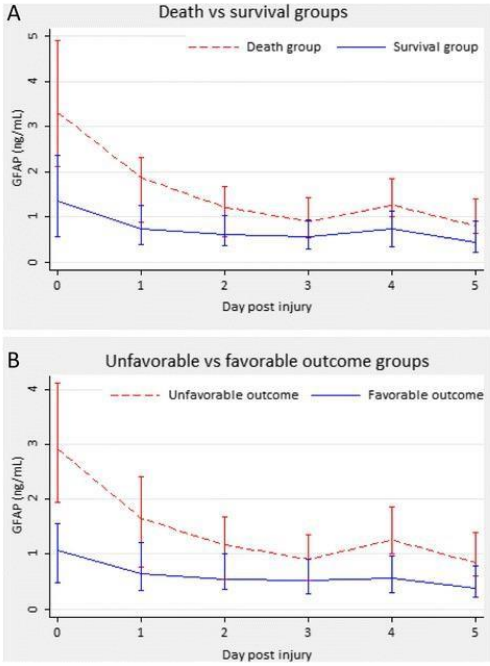
***Figure 2:* (A) Serum GFAP and (B) UCH-L1 levels by head CT result**
The upper and lower bounds of each box indicate the 75th and 25th percentiles, respectively. Within each box, the square marker symbol indicates the mean and the horizontal line indicates the median. Whiskers extend up to 1·5 x IQR (bounded by observed minimum and maximum). Small circles indicate actual datapoints, staggered by patient. Dotted horizontal lines represent prespecified cutoff value. UCH-L1=ubiquitin C-terminal hydrolase-L1. GFAP=glial fibrillary acidic protein. GCS=Glasgow Coma Scale.

ALERT-TBI



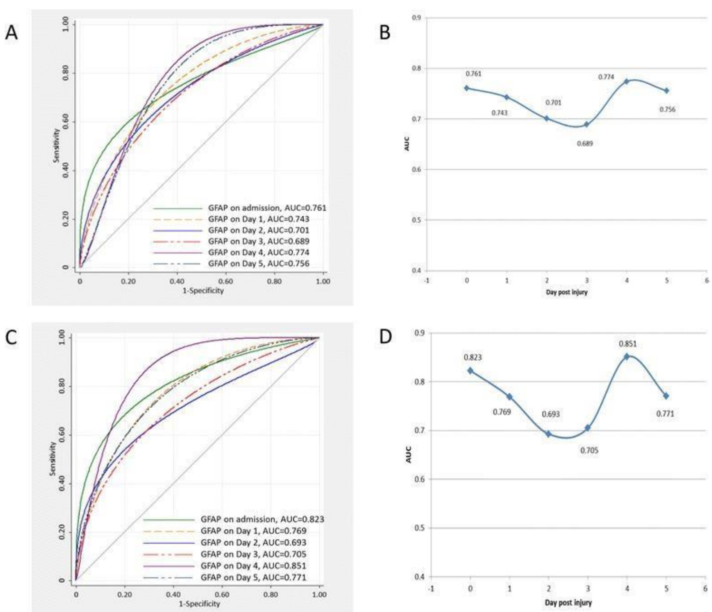
Mondello et al, Crititical Care 2011;15:R156

GFAP in severe TBI



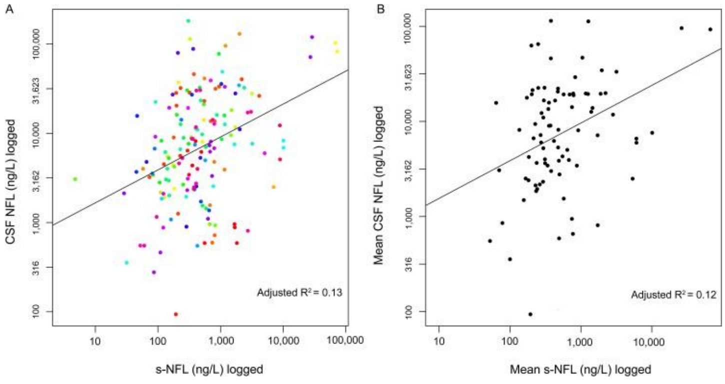
Lei et al, Crit Care, 2015;19:362

GFAP in severe TBI



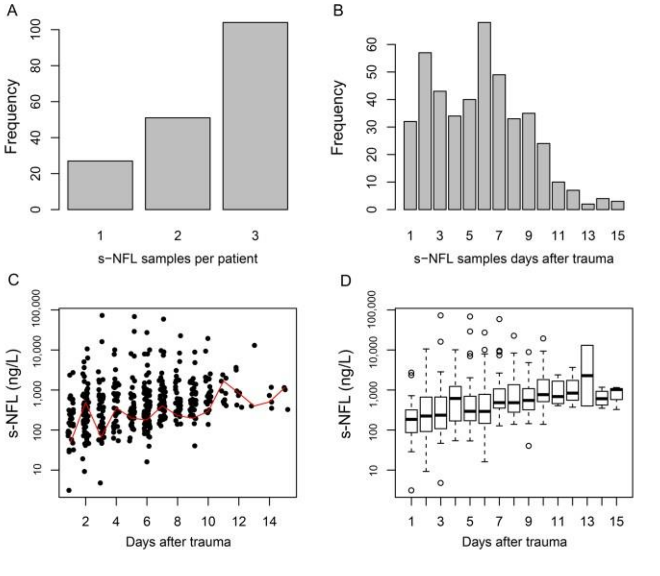
Lei et al, Crit Care, 2015;19:362

Neuro-filament Light in CSF and Plasma



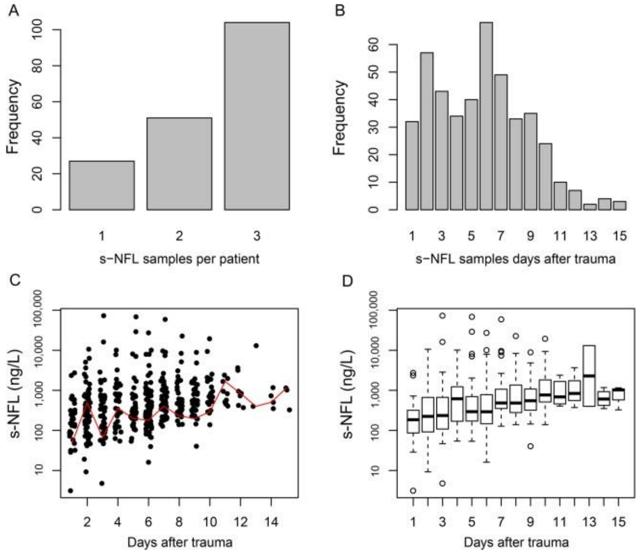
Al Nimer et al, PlosOne 2015

Neuro-filament Light in CSF



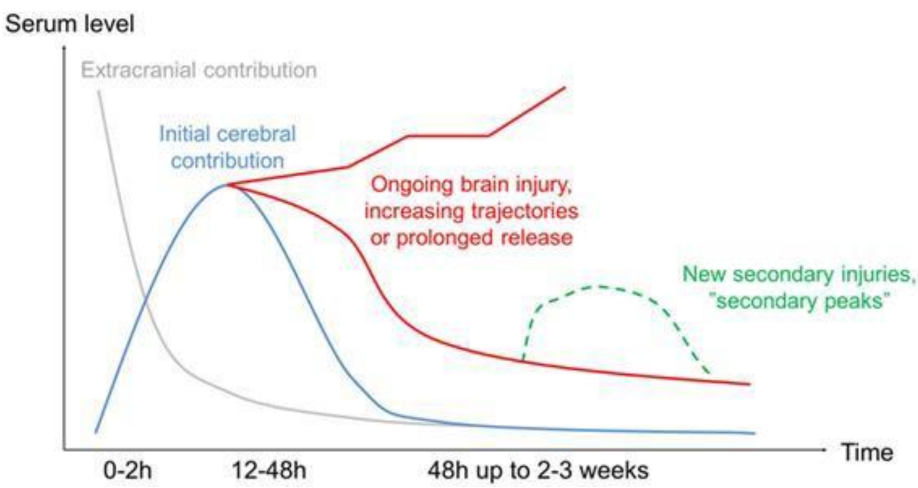
Al Nimer et al, PlosOne 2015

Neuro-filament Light in CSF



No relationship to outcome or imaging findings

Al Nimer et al, PlosOne 2015



Serial Sampling of Serum Protein Biomarkers for Monitoring Human Traumatic Brain Injury Dynamics: A Systematic Review

REVIEW ARTICLE
Front. Neurol., 03 July 2017 |

Thelin et al

Biomarkers	AUC	Cohort	Condition	N	Controls	Reference	Timing	Comment
S100B	0.87	TBI all severity	TBI vs. non-TBI	50	50	(38)	Within 6 h	Non-specific
S100B	0.68	mTBI	Ice hockey vs. pre-season	28	28	(39)	Within 1 h	Poor performance
NSE	0.82	TBI all severity	TBI vs. non-TBI	50	50	(38)	Within 6 h	Non-specific
NSE	0.54	mTBI		28	28	(39)	Within 1 h	Poor performance
NSE	0.64	mTBI	Clinically important injury	25	82	(40)	Day 1	Non-specific
Myelin-basic protein	0.66	TBI all severity	TBI vs. non-TBI	50	50	(38)	Within 6 h	Poor performance
Cleaved Tau	0.74	mTBI	Injury vs. pre-season	28	28	(41)	At 36 h	Late
Total Tau	0.8	mTBI	Ice hockey vs. pre-season	28	28	(39)	Within 1 h	Promising
GFAP	0.84	mild-moderate TBI	Positive CT	209	188	(42)	At 4 h	Limited sensitivity
UCH-L1	0.87	mTBI	GCS 15 vs. controls	86	199	(43)	Within 1 h	Promising
UCH-L1	0.73	TBI	positive CT	N/A	199	(43)	Within 1 h	Promising
Amyloid-β	N/A	sTBI	TBI vs. controls	12	20	(44)	Day 1	poor sensitivity
All-Spectrin break-down	0.76	mTBI	Injury vs. pre-season	25	N/A	(41)	At 36 h	Late
CTS5	N/A	TBI all severity	sTBI vs. orthopedic injury	30	30	(45)	Within 1 h	Promising

New biomarkers (for example microRNA)
Panels rather than individual
Better understanding of individual temporal dynamics
Prevent secondary injury?

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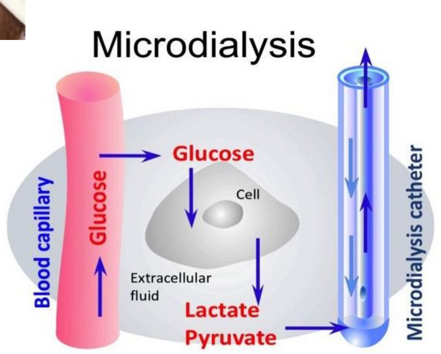
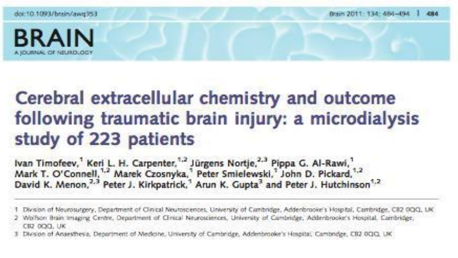


Does brain chemistry monitored by microdialysis relate to clinical outcome?


doi:10.1093/brain/awq353 Brain 2011: 134; 484–494 | 484

BRAIN
A JOURNAL OF NEUROLOGY

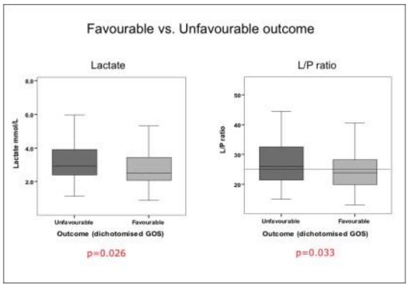
Cerebral extracellular chemistry and outcome following traumatic brain injury: a microdialysis study of 223 patients

Ivan Timofeev,[1] Keri L. H. Carpenter,[1,2] Jürgens Nortje,[2,3] Pippa G. Al-Rawi,[1] Mark T. O'Connell,[1,2] Marek Czosnyka,[1] Peter Smielewski,[1] John D. Pickard,[1,2] David K. Menon,[2,3] Peter J. Kirkpatrick,[1] Arun K. Gupta[3] and Peter J. Hutchinson[1,2]

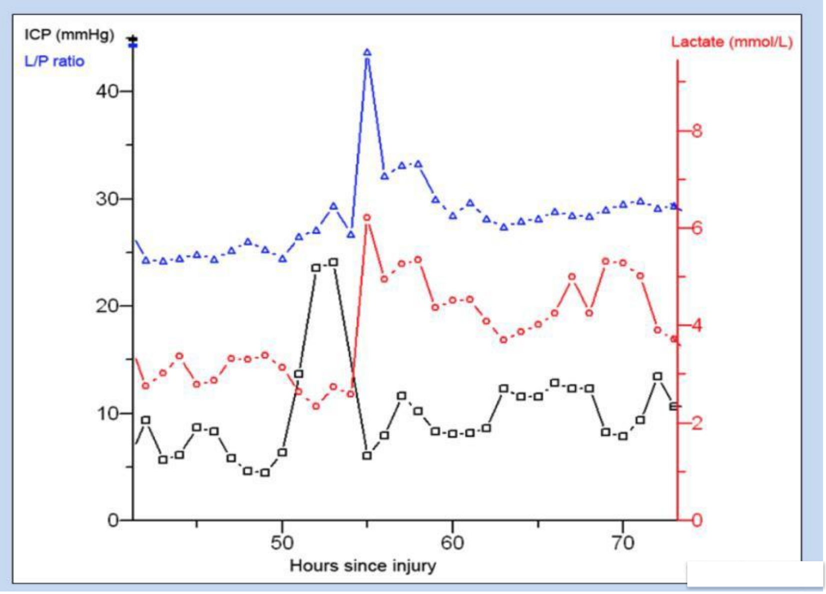
1 Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, CB2 0QQ, UK
2 Wolfson Brain Imaging Centre, Department of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, CB2 0QQ, UK
3 Division of Anaesthesia, Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge, CB2 0QQ, UK

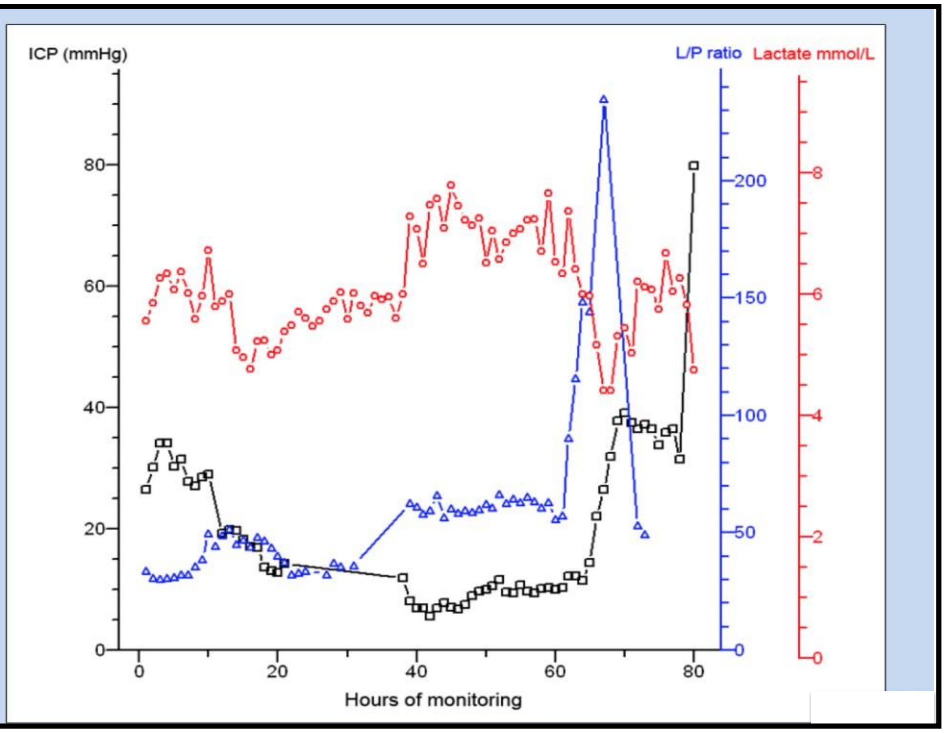
Unfavourable outcome is associated with:

- **High lactate / pyruvate ratio (> 25)**
  - hypoxia or mitochondrial dysfunction
- **High glutamate**
  - excitotoxic cell injury
- **High glycerol**
  - cell membrane breakdown



Interpreting Microdialysis Data



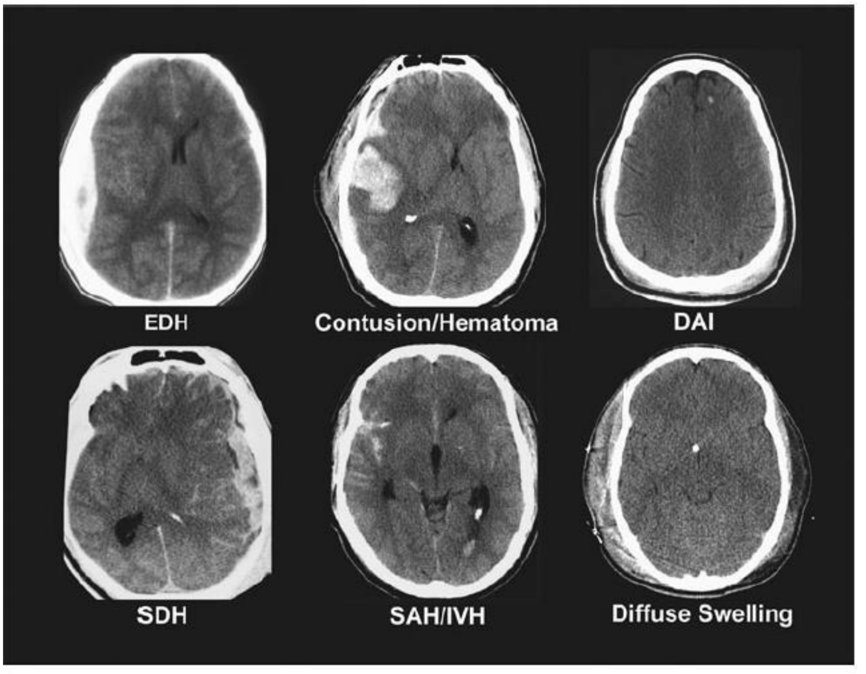


Can brain chemistry be improved with therapeutic interventions?

Intervention	Effect	Reference
Glucose / insulin	Reduction in glucose increase in LP ratio	Vespa 2006, Oddo 2008, Helbok 2010, Rostami 2011, Vespa 2012
Hyperoxia	Increase in brain tissue O_2, variable decrease in LP ratio	Tolias 2004, Nortje 2008, Rockswold 2012, Rockswold 2013
Hyperventilation	Decrease in glucose Increase in LP ratio	Marion 2002, Hutchinson 2002
Mannitol	Decrease in LP ratio	Sakowitz 2007, Helbok 2011
Decompressive craniectomy	Decrease in LP ratio, decrease in glycerol	Ho 2008, Nagel 2009
Hypothermia	Decrease in glucose, decrease in lactate, decrease in glutamate	Soukup 2002, Berger 2002, Stocchetti 2005

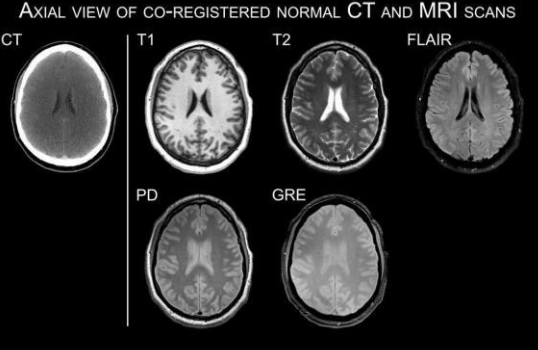
Imaging as a biomarker

- **Diagnostic: Who needs surgery or other urgent therapy?**



Saatman et al, J Neurotrauma, 2008; 25(7):719-38.

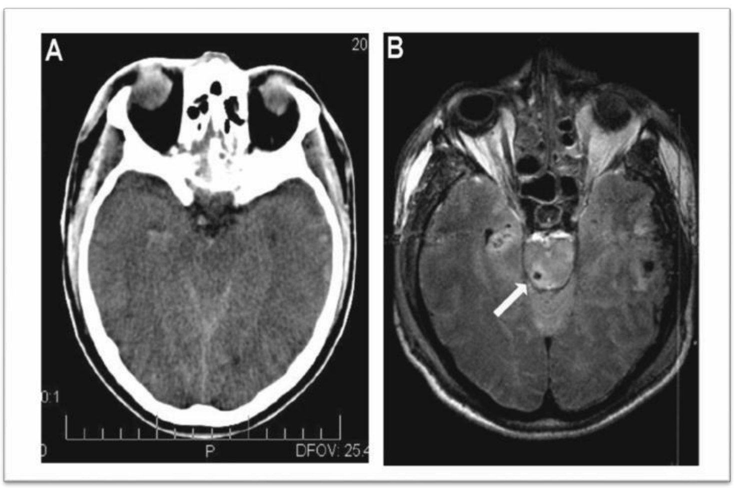
Sequence	Most relevant tissue contrasts for TBI imaging
T1	Normal grey-white contrast
T2	High signal in CSF, vasogenic oedema, gliosis, acute and subacute bleed (may be hypointense signal in hyperacute or chronic bleed)
FLAIR	Like T2, but CSF nulled, so good for superficial lesions
Gradient echo (SWI, SWAN)	Sensitised to blood – very useful for petechial haemorrhages associated with TAI. Most prone to artefacts (air in sinus, probes)
DWI, ADC, DTI	Early cytotoxic oedema, white matter shearing, tractography



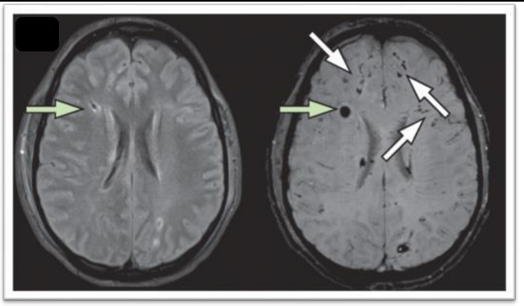
Imaging as a biomarker

- Diagnostic: Who needs surgery or other urgent therapy?
- **Diagnostic: Impact of TBI on the brain**
  - **Lesion detection**
  - **Lesion characterisation**

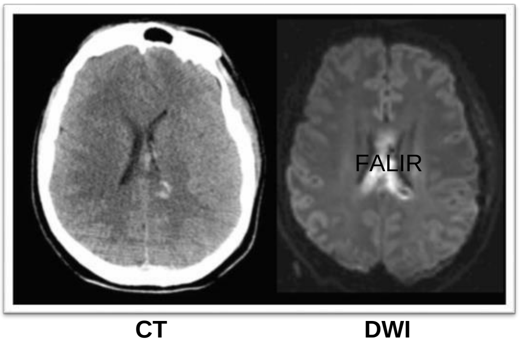
Mechanism-Based MRI Classification of Traumatic Brainstem Injury and Its Relationship to Outcome



Mannion et al, 2007;24(11):128-35



FLAIR **SWI**



CT **DWI**

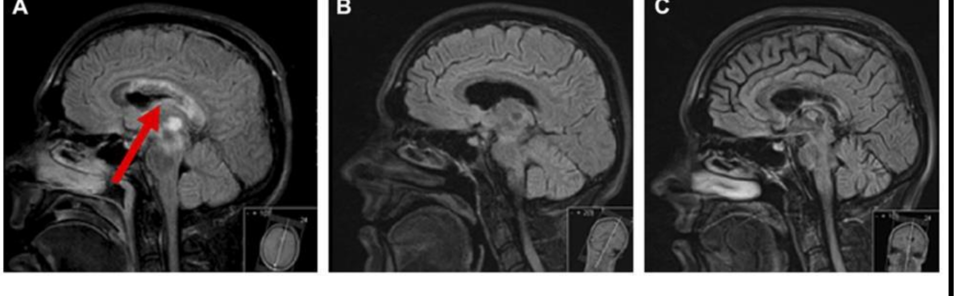
Maas, Menon et al, The Lancet Neurology 2017 16, 987-1048

RESEARCH PAPER

A longitudinal MRI study of traumatic axonal injury in patients with moderate and severe traumatic brain injury

Kent Gøran Moen,[1,2] Toril Skandsen,[1,3] Mari Folvik,[4] Veronika Brezova,[5] Kjell Arne Kvistad,[4,5] Jana Rydland,[4] Geoffrey T Manley,[6] Anne Vik[1,2]

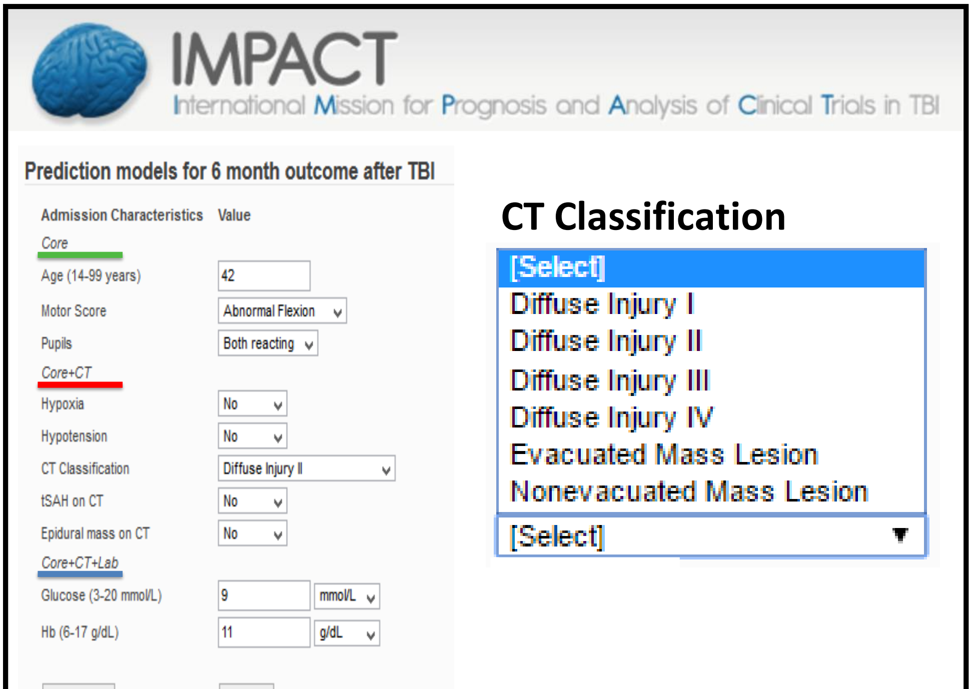
J Neurol Neurosurg Psychiatry 2012;**83**:1193–1200.



4 days **3 months** **12 months**

Imaging as a biomarker

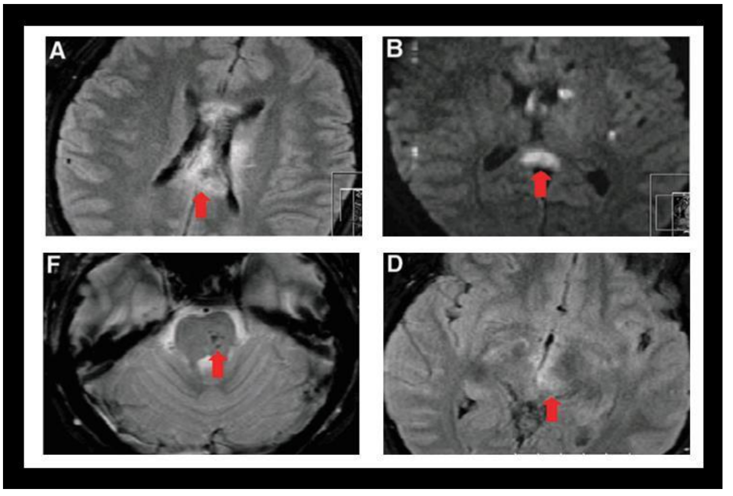
- Diagnostic: Who needs surgery or other urgent therapy?
- Diagnostic: Impact of TBI on the brain
- **Prognostication**



http://www.tbi-impact.org/?p=impact/calc

Traumatic Axonal Injury (Severe TBI)

The Prognostic Value of Lesion Load in Corpus Callosum, Brain Stem, and Thalamus in Different MRI Sequences



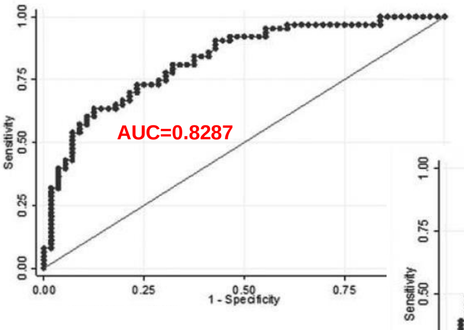
MRI mean of 8 days after injury (within 4 weeks)

Moen et al, J Neurotrauma. 2014;31:1486-1496

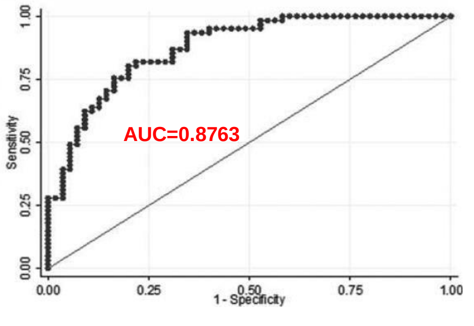
Traumatic Axonal Injury

The Prognostic Value of Lesion Load in Corpus Callosum, Brain Stem, and Thalamus in Different MRI Sequences

Core (IMPACT Model; age, GCS, pupils)



Core+ CT+ All MRI



Moen et al, J Neurotrauma. 2014;31:1486-1496

The Prognostic Value of MRI in Moderate and Severe Traumatic Brain Injury: A Systematic Review and Meta-Analysis

Study or Subgroup	Brainstem Lesions Present Events	Brainstem Lesions Present Total	Brainstem Lesions Absent Events	Brainstem Lesions Absent Total	Weight	Risk Ratio M-H, Random, 95% CI
Bagley et al. 2000	5	5	10	23	9.5%	2.10 [1.25, 3.50]
Carpentier2006	11	11	7	27	8.7%	3.58 [1.92, 6.68]
Chew et al. 2012	10	21	9	15	8.8%	0.79 [0.43, 1.46]
Iwamura et al. 2012	6	10	1	11	2.7%	6.60 [0.95, 45.75]
Lagares et al. 2009	22	33	8	65	8.2%	5.42 [2.71, 10.82]
Mannion et al. 2007	11	13	18	33	10.3%	1.55 [1.05, 2.29]
Moen/Skandsen et al.	15	30	2	75	4.3%	18.75 [4.56, 77.06]
Potapov et al. 2014	58	76	21	86	10.3%	3.13 [2.11, 4.63]
Wedekind et al. 1999	24	29	6	28	8.0%	3.86 [1.86, 8.00]
Wedekind et al. 2002	10	14	7	26	8.1%	2.65 [1.30, 5.42]
Wilberger et al. 1987	5	5	14	19	10.5%	1.26 [0.88, 1.82]
Woischneck et al. 2015	54	66	25	54	10.8%	1.77 [1.30, 2.41]
Total (95% CI)		**313**		**462**	**100.0%**	**2.49 [1.72, 3.58]**
Total events	231		128			

Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 57.84$, df = 11 ($P < 0.00001$); $I^2 = 81\%$
Test for overall effect: $Z = 4.87$ ($P < 0.00001$)

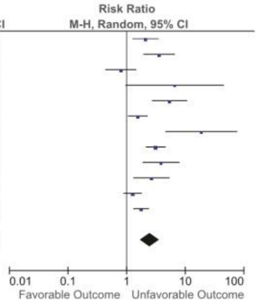


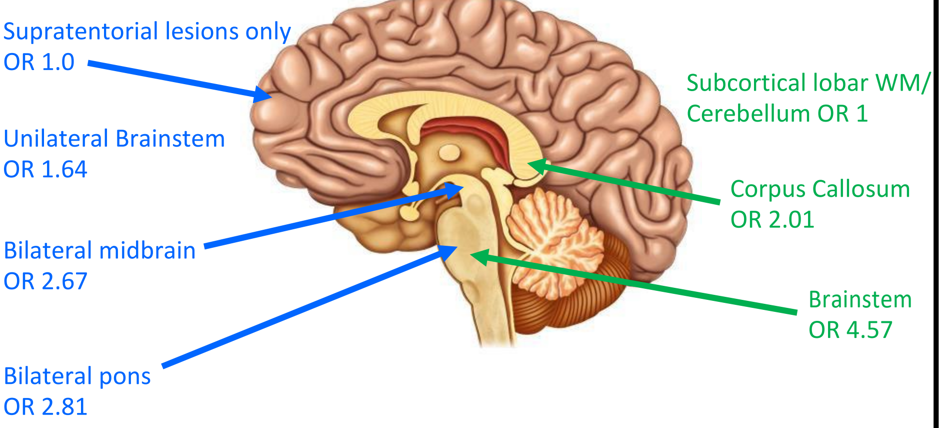
Figure 3. Relative risk of unfavorable Glasgow Outcome Scale in moderate and severe traumatic brain injury with brainstem lesions on acute MRI. M-H = Mantel-Haenszel.

Haghbayan et al, Critical Care Medicine, 2017(45);12:e1280-1288

The Prognostic Value of MRI in Moderate and Severe Traumatic Brain Injury: A Systematic Review and Meta-Analysis

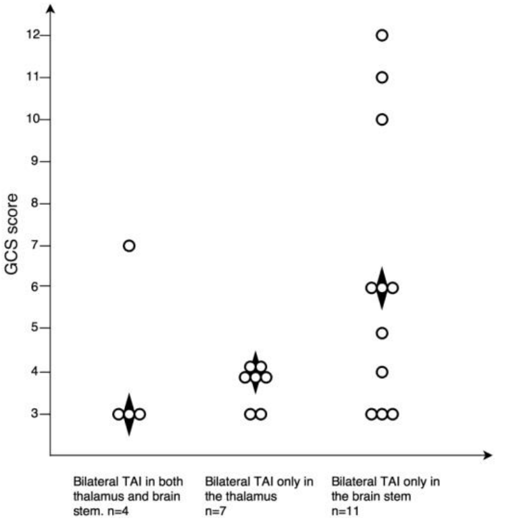
Firsching Score

Adams-Gentry Classification



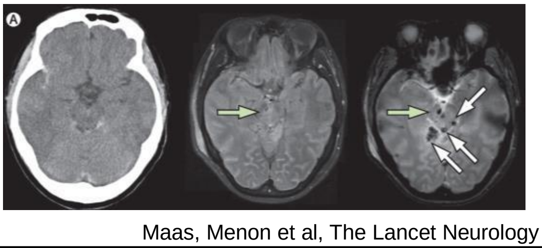
Haghbayan et al, Critical Care Medicine, 2017(45);12:e1280-1288

The Influence of Traumatic Axonal Injury in Thalamus and Brainstem on Level of Consciousness at Scene or Admission: A Clinical Magnetic Resonance Imaging Study



Moe et al, JOURNAL OF NEUROTRAUMA 35:975–984 (April 1, 2018)

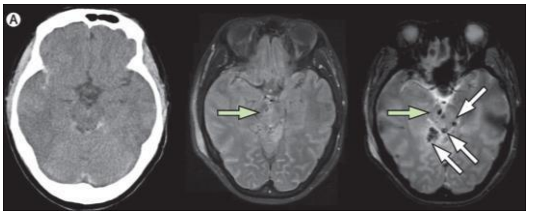
MRI is showing new, <u>prognosis defining</u> pathology



Maas, Menon et al, The Lancet Neurology 2017 16, 987-1048

MRI is showing new, prognosis defining pathology

May not be modified significantly by better ICP control, or decompressive craniectomy



Maas, Menon et al, The Lancet Neurology 2017 16, 987-1048

Neurocritical Care Society Neurocrit Care (2017) 27:199–207
DOI 10.1007/s12028-017-0399-2

ORIGINAL ARTICLE

Revisiting Grade 3 Diffuse Axonal Injury: Not All Brainstem Microbleeds are Prognostically Equal

Saef Izzy[1,2] · Nicole L. Mazwi[4,5] · Sergi Martinez[1] · Camille A. Spencer[1] · Joshua P. Klein[2,3] · Gunjan Parikh[6] · Mel B. Glenn[5] · Steven M. Greenberg[1] · David M. Greer[8] · Ona Wu[7,9] · Brian L. Edlow[1,7]

Prognostic variable	Correlation coefficient [95% confidence interval]	*p*
Ventral brainstem TMBs	0.06 [−0.27, 0.38]	0.72
Dorsal brainstem TMBs	0.37 [0.06, 0.62]	0.02
Corpus callosum TMBs	0.26 [−0.07, 0.54]	0.10
Global brain TMBs	0.10 [−0.23, 0.41]	0.54
AAN nuclei TMB lesion burden	0.36 [0.04, 0.62]	0.02
Age	0.02 [−0.30, 0.35]	0.88
Admission GCS score	−0.22 [−0.51, 0.11]	0.18
Number of lobes with contusions	−0.14 [−0.44, 0.19]	0.40

neurocritical care society Neurocrit Care (2017) 27:199–207
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CrossMark

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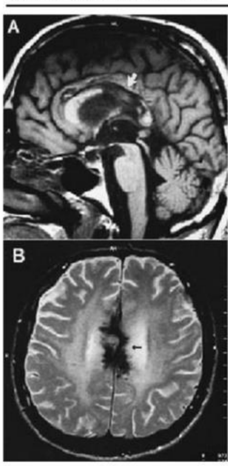
Lancet 1998; **351:** 1763–67 ARTICLES

Prediction of recovery from post-traumatic vegetative state with cerebral magnetic-resonance imaging

Andreas Kampfl, Erich Schmutzhard, Gerhard Franz, Bettina Pfausler, Hans-Peter Haring, Hanno Ulmer, Stefan Felber, Stefan Golaszewski, Franz Aichner



Replicated by recent autopsy case series which suggest pivotal role for diffuse axonal damage, especially in dorsolateral midbrain

Jellinger. Brain Inj 2013; 27:917

Lesion location: Odds for developing PVS

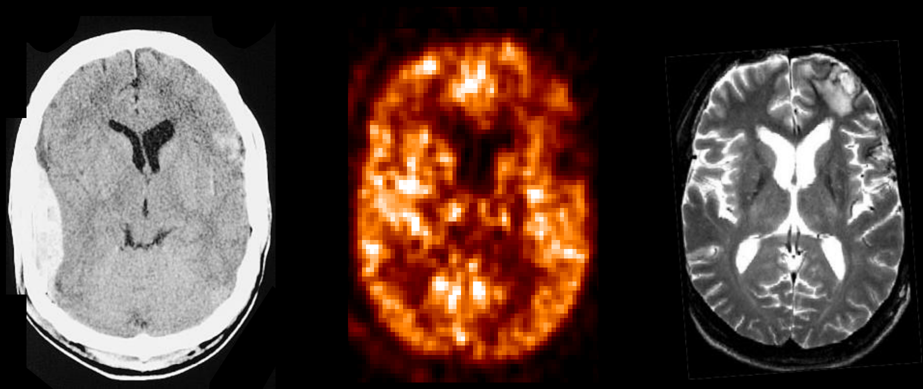
Corpus callosum:	132(16-1100)
Corona radiata:	3.7 (1.5-9.6)
Dorsolateral upper brainstem:	7.9 (2.9-21.4)
Thalamus:	0.6

Imaging as a biomarker

- Diagnostic: Who needs surgery or other urgent therapy?
- Diagnostic: Impact of TBI on the brain
- Prognostication
- **Improved understanding of pathophysiology**

University of Cambridge
Wolfson Brain Imaging Centre

Severe head injury



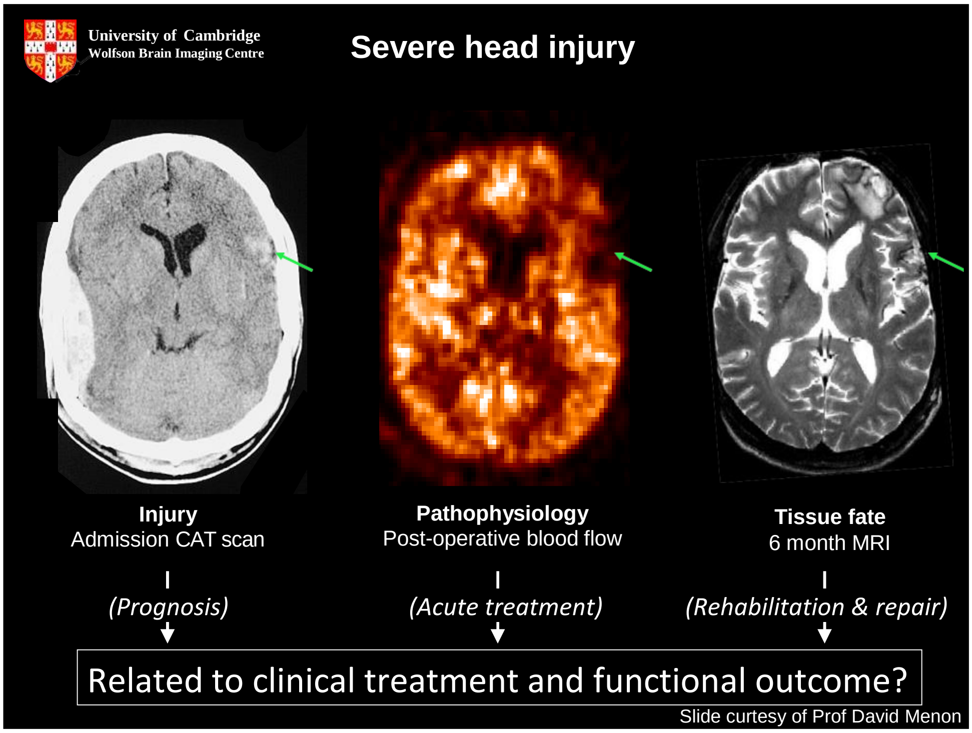
Injury
Admission CAT scan
(Prognosis)

Pathophysiology
Post-operative blood flow
(Acute treatment)

Tissue fate
6 month MRI
(Rehabilitation & repair)

Related to clinical treatment and functional outcome?

Slide curtesy of Prof David Menon


University of Cambridge
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Severe head injury
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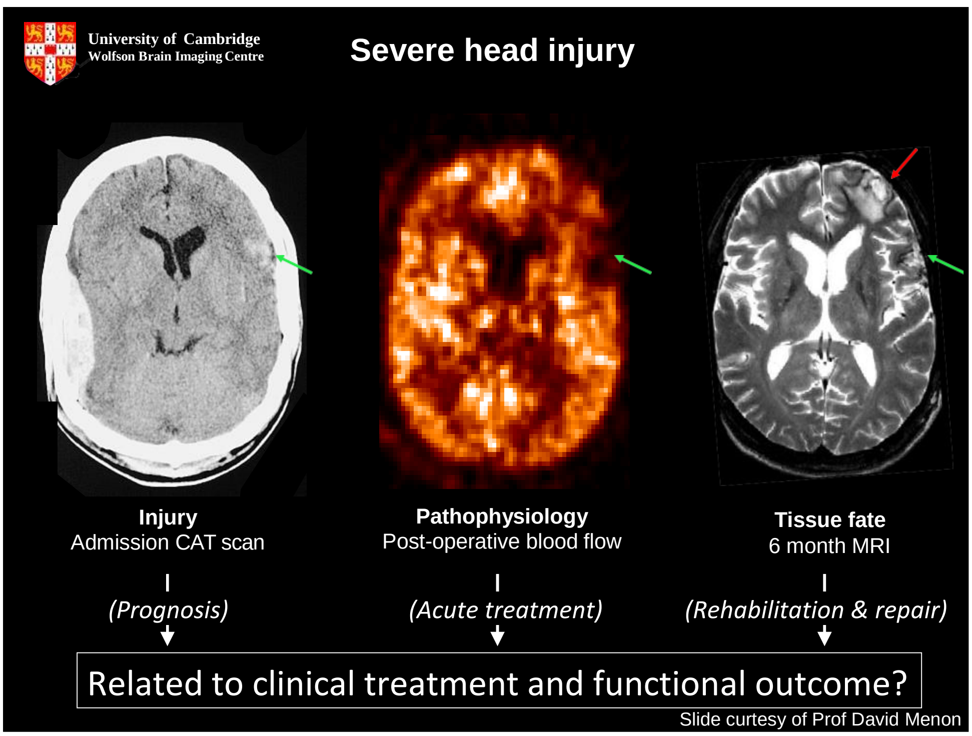
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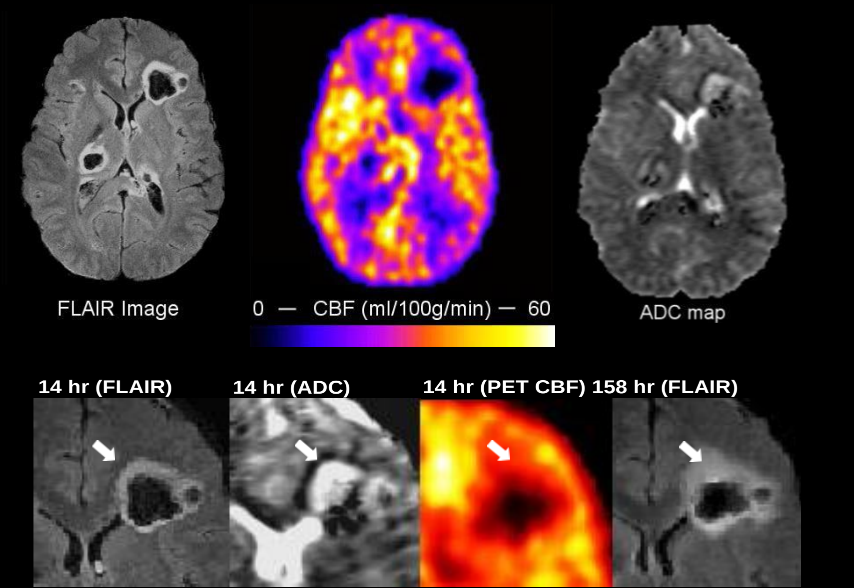
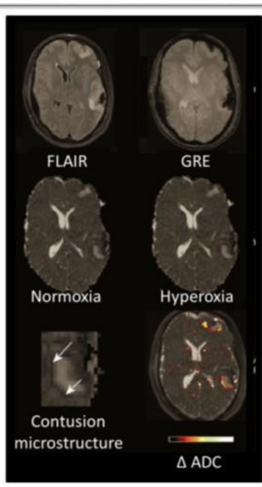
Contusion evolution in TBI

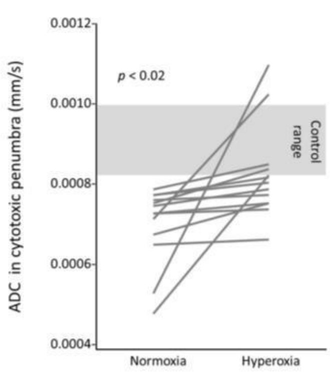


Newcombe et al. J Cereb Blood Flow Metab 2013

Use of diffusion tensor imaging to assess the impact of normobaric hyperoxia within at-risk pericontusional tissue after traumatic brain injury

Tonny V Veenith[1], Eleanor L Carter[1], Julia Grossac[1], Virginia F Newcombe[1], Joanne G Outtrim[1], Sridhar Nallapareddy[1], Victoria Lupson[2], Marta M Correia[2], Marius M Mada[2], Guy B Williams[2], David K Menon[1] and Jonathan P Coles[1]



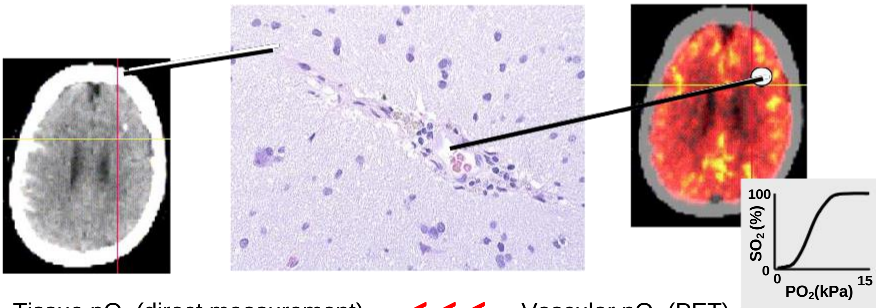


Journal of Cerebral Blood Flow & Metabolism (2014),

Neurologic Critical Care
Crit Care Med 2004;32:1384-90.

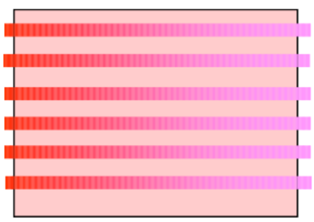
Diffusion limited oxygen delivery following head injury*

David K. Menon, PhD; Jonathan P. Coles, PhD; Arun K. Gupta, FRCA; Tim D. Fryer, PhD; Peter Smielewski, PhD; Doris A. Chatfield, BSc; Franklin Aigbirhio, PhD; Jeremy N. Skepper, PhD; Pawan S. Minhas, FRCS; Peter J. Hutchinson, PhD; T. Adrian Carpenter, PhD; John C. Clark, DSc; John D. Pickard, FRCS

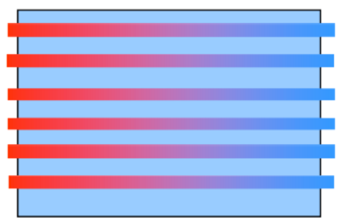


Tissue pO_2 (direct measurement) <<< (TBI) Vascular pO_2 (PET)

Surprising finding: Implies a diffusion gradient for oxygen delivery



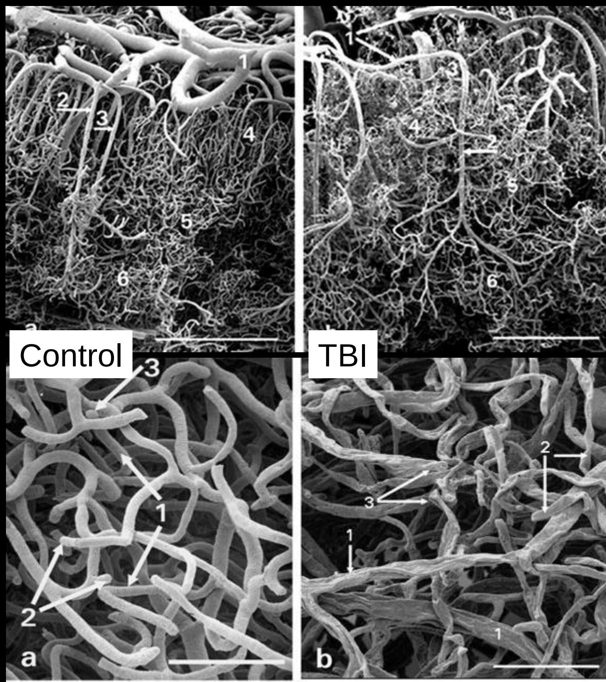
Normal



Simple hypoperfusion:
Macrovascular ischaemia

Microvascular dysfunction:
- Perfusion utilisation mismatch
- Microvascular ischaemia
- Increased O_2 diffusion barriers

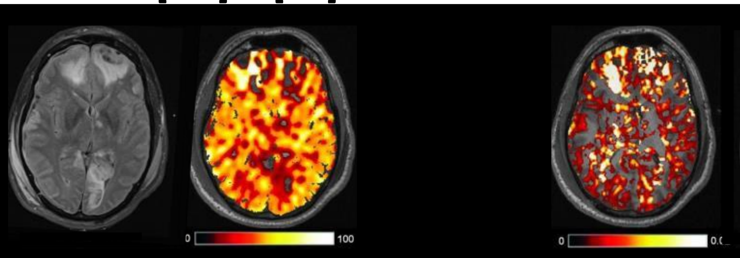
Menon et al. Crit Care Med 2004;32:1384-90.



Microvascular disruption in head injury

Rodriguez-Baeza et al. Anat Rec 2003; 273A: 583-93.

[^{15}O] & [^{18}F]-fluoromisonidazole PET



Severe TBI (GCS 5), sedated for high ICP, 5 days post-injury (ICP 21 mmHg, CPP 74 mmHg)

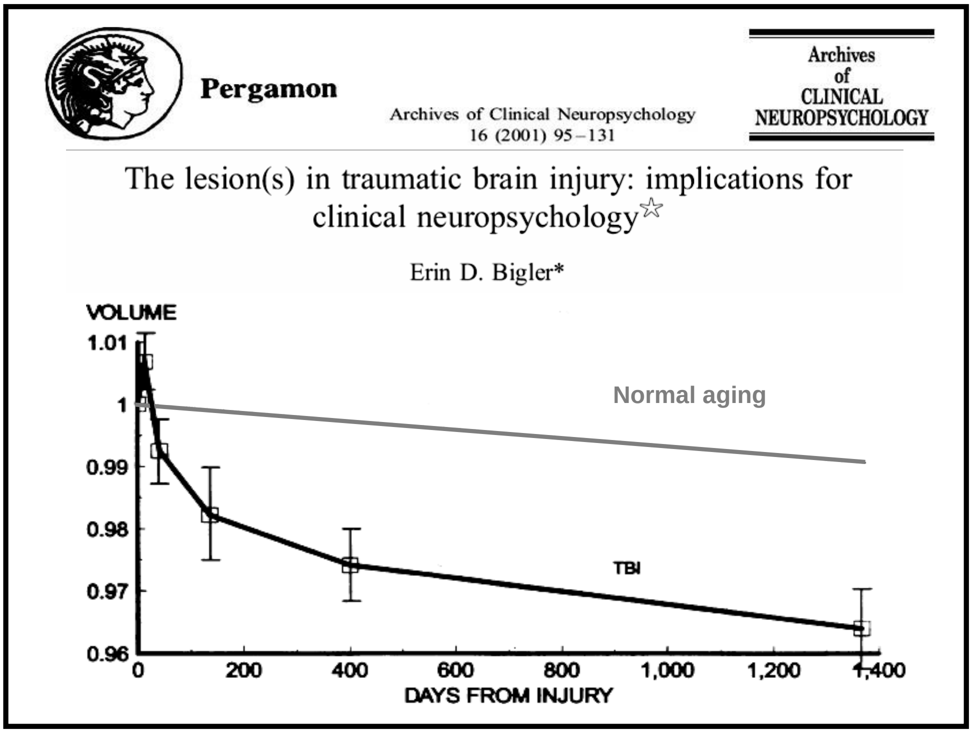
- High signal on FLAIR: Vasogenic oedema
- High OEF = ischaemic brain volume (CvO2 <3.5 ml/dl): Critical ischaemia
- High *k3* for [18F]-FMISO (> 3 SD above control voxel mean): Critical tissue hypoxia

Note pathophysiological heterogeneity

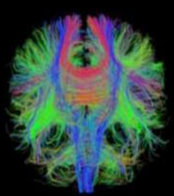
- Matched ischaemia and tissue hypoxia (classical macrovascular ischaemia)
- Mismatched tissue hypoxia (microvascular/diffusion hypoxia)

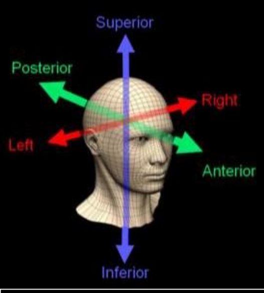
Veenith et al. JAMA Neurology 2016;73(50:542-550

RCTs for PtbO2 guided therapy - BOOST-3 and BONANZA



Control



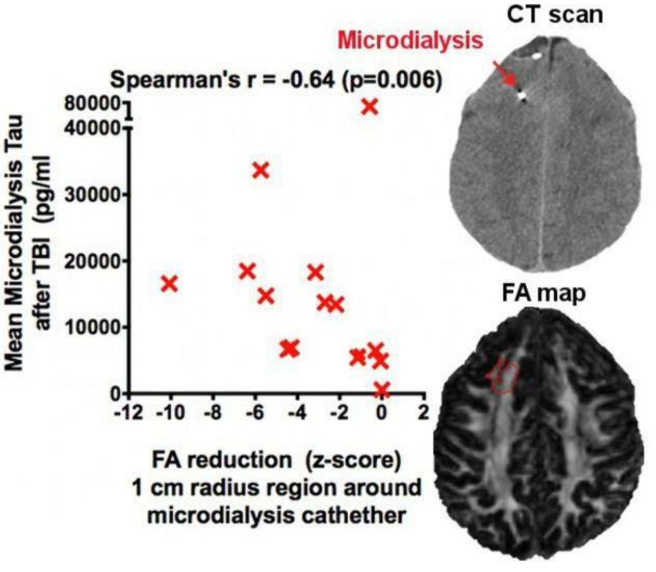


Pattern seen in ~20 to 30% of TBI patients

Correlates with trajectory of functional recovery

Potential new therapy biomarker

Newcombe et al. Neurorehab Neuro Repair 2016;30(1):49-62



BRAIN
A JOURNAL OF NEUROLOGY

Magnoni et al, 2015;138(8): 2263–2277

Head injury as a risk factor for Alzheimer's disease: the evidence 10 years on; a partial replication

S Fleminger, D L Oliver, S Lovestone, S Rabe-Hesketh, A Giora

See Editorial Commentary, p 841

J Neurol Neurosurg Psychiatry 2003;**74**:857–862

	Odds ratio (95% CI)	*p*
All	1.58 (1.21- 2.06)	0.001
♂	**2.29** (1.47-3.58)	<0.001
♀	0.91 (0.56-1.47)	0.69

Overall, the risk of Alzheimer's Disease in later life may be increased up to ~2 fold in individuals who have sustained a significant head injury in the past

This increase in risk possibly scales with severity of head injury

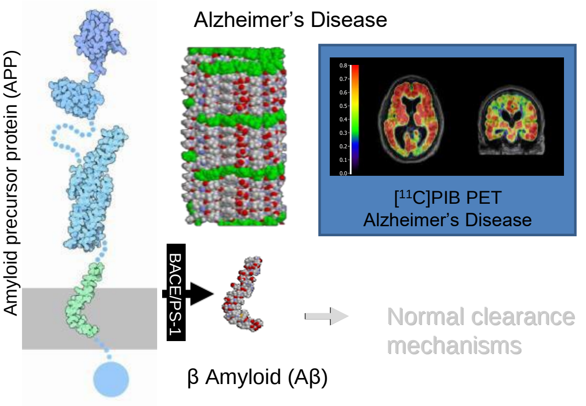
However, when combined with a genetic predisposition to Alzheimer's Disease, the risk may increase up to ~10 fold

OPINION

Traumatic brain injury and amyloid-β pathology: a link to Alzheimer's disease?

Victoria E. Johnson, William Stewart and Douglas H. Smith

30% of patients who die hours - weeks after TBI show Aβ aggregates at postmortem, **even in young patients**

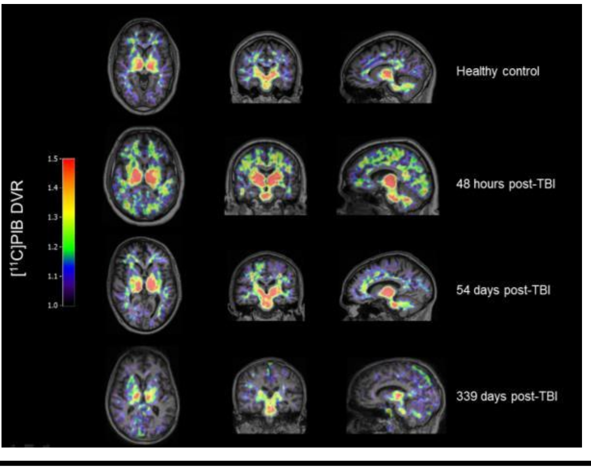


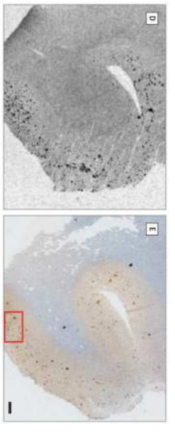
Johnson VE, Stewart W, Smith DH. Widespread tau and amyloid-β pathology many years after a single traumatic brain injury in humans. Brain Pathol 2012; 22(2):142-9

JAMA Neurol. 2014;71(1):23-31.

Amyloid Imaging With Carbon 11–Labeled Pittsburgh Compound B for Traumatic Brain Injury

Young T. Hong, PhD; Tonny Veenith, FRCA; Deborah Dewar, PhD; Joanne G. Outtrim, MSc;
Vaithianadan Mani, FRCA; Claire Williams, FRCA; Sally Pimlott, PhD; Peter J. A. Hutchinson, FRCS, PhD;
Adriana Tavares, PhD; Roberto Canales, PhD; Chester A. Mathis, PhD; William E. Klunk, MD, PhD;
Franklin I. Aigbirhio, DPhil; Jonathan P. Coles, FRCA, PhD; Jean-Claude Baron, ScD, FMedSci;
John D. Pickard, FMedSci; Tim D. Fryer, PhD; William Stewart, FRCPath, PhD; David K. Menon, PhD, FMedSci

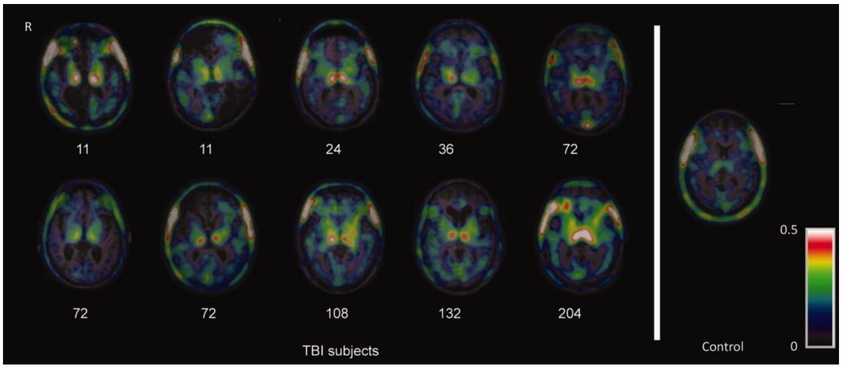




[3H] PIB Autoradiography

Aβ-42 Immunostaining

Inflammation after Trauma: Microglial Activation and Traumatic Brain Injury



Ramlackhansingh et al. Annals of Neurology, Volume: 70, Issue: 3, Pages: 374-383.

Conclusions

Biomarkers may help us to understand:

- Diagnosis and the impact of TBI on the brain
- Improved understanding of pathophysiology and disease progression
- Prognostication
- Treatment effects
  - Biomarker for the effectiveness of treatments
  - Better selection of patients for trials
  - Better selection and monitoring of patients for therapy

Acknowledgements

- David Menon

- Jonathan Coles
- Marta Correia
- Tilak Das
- Enzo Ferrante
- Ben Glocker
- Peter Hutchinson
- Konstantinos Kamnitsas
- Andrew Kane
- Anne Manktelow
- Joanne Outtrim
- Poe Phyu
- Sophie Richter
- Joanna Simpson
- Guy Williams
- Stefan Winzeck
- Lorenz Wernisch

Asterix books contain 704 victims of brain injury, study finds

Most were male, many Roman and more than half were attacked by Asterix and Obelix themselves ... medical academics get their heads around violence in the Asterix comics

Kamp et al, Acta Neurochir (Wien), 2011;153(6):1351-5

The Academy of Medical Sciences

The Health Foundation

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