THE EXPERIENCE OF MILD TRAUMATIC BRAIN INJURY IN A FRENCH MILITARY HOSPITAL

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BACKGROUND

EPIDEMIOLOGY OF MTBI

- **Traumatic brain injury (TBI) is « *an alteration in brain function, or other evidence of brain pathology, caused by an external force* » (MENON *et al.*, 2010). TBI is the leading cause of death and disability in young people, with an estimated 57 millions people worldwide, hospitalized with one or more TBI (LANGLOIS *et al.*, 2006).**

- **Approximately 2.8 millions TBI occurred in the UNITED STATES in 2013. For the EUROPEAN UNION, it was estimated that 2.5 mille cases of TBI occur, every year (FAUL & CORONADO 2015) and since, at least 90% of these cases of TBI were Mild TBI (MTBI); of all TBI, 75-85% are categorized as MTBI, including concussion, blast injuries and whiplash syndrome.**

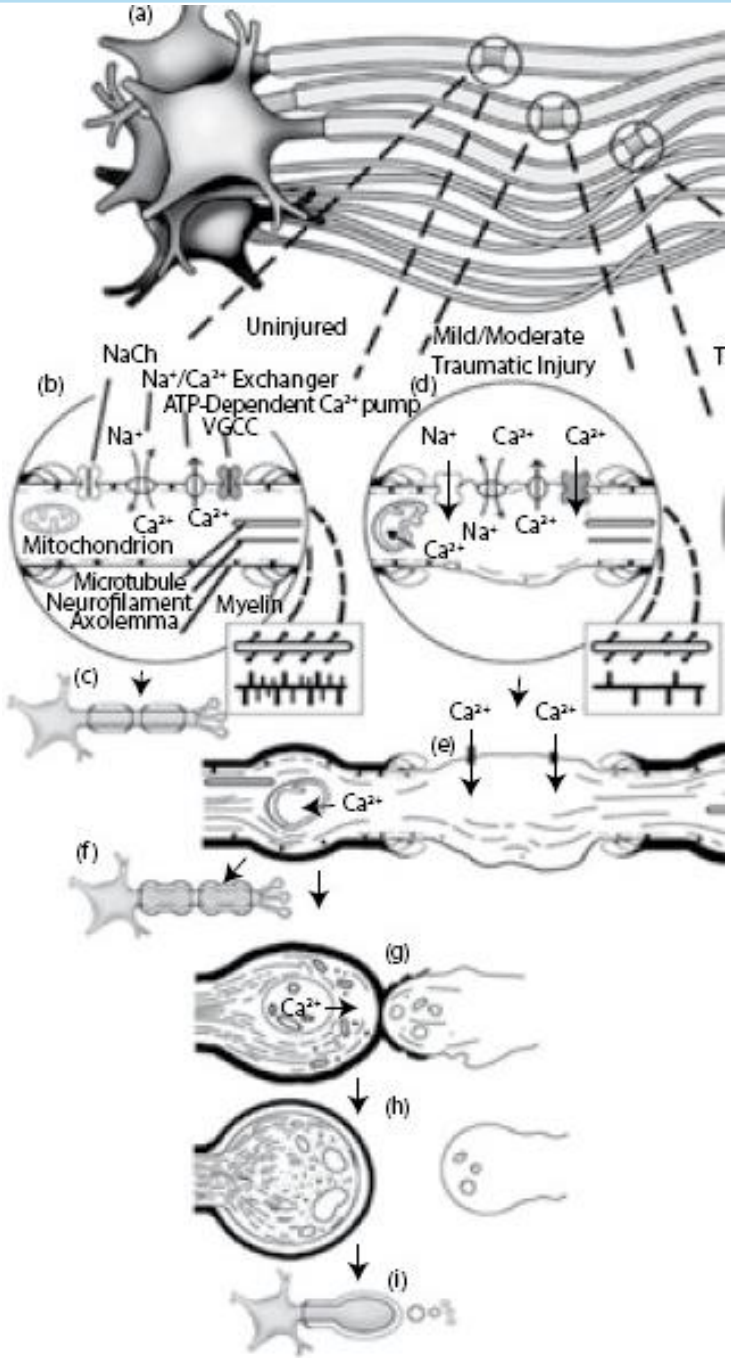
- **The severity of TBI can be quantified using a variety of measures, and the most commonly used assessment scale is the GLASGOW Coma Scale score, but also the duration of the level of consciousness, or post-traumatic amnesia.**

- **In military personnel, primary blast injury is different from a blunt impact injury; in a blast, depending on the explosive charge and distance an individual is from the detonation point, the primary overpressure can propagate over the body in less than 5 m/s; during an impact, shear waves, travel in the brain, leading to a slow evolution of the strains along the axons.**

- **Neurological damage does not all occur immediately at the moment of impact (primary injury) but evolves afterwards (secondary injury); studies have shown persistent neurocognitive deficits in approximately 15% of patients (HARTLAGE *et al.*, 2011), with symptoms of persistent post concussive syndrome (PPCS) (IVERSON *et al.*, 2006), for months to years after MTBI.**

- **Early cognitive deficits are common but usually resolve within one to three months after MTBI, but limited evidence now suggests for some, full recovery may take six months to a year (CASSIDY *et al.*, (2014).**

NEUROPATHOLOGY OF MTBI



MTBI (d) contribute to increased calcium influx via reversal of the sodium calcium exchanger and the opening of calcium channels. This impacts on the proteolysis of sodium channel inactivation that contributes to local calcium dysregulation.

Microtubular loss, neurofilament impaction, and mitochondrial damage follow, that impairs axonal transport (e). Mitochondrial bioenergetics may be linked to neuronal excitotoxicity, neuroinflammation (JOHNSON *et al.*, 2013), and ATP depletion.

These events lead intra-axonal change that elicit the collapse of the axolemma and its overlying myelin sheath resulting in lobulated and disconnected axonal segments (g).

The proximal axonal segment continues to swell, whereas the downstream fiber undergoes Wallerian change (i), that can progresses over several months post-injury (SMITH, *et al.*, 2013).

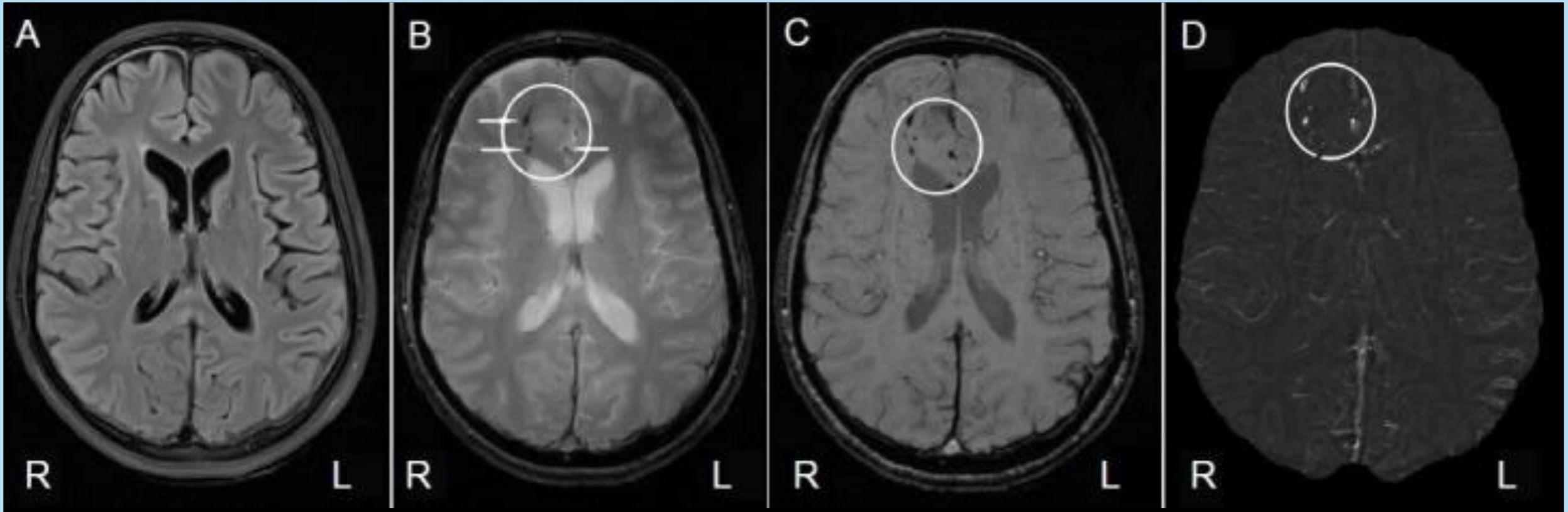
- **Traumatic axonal injury (TAI) is damage to axons caused by MTBI, it may be focal, multifocal or diffuse; the human brain is particularly prone to damage from the mechanical forces associated with rotational and linear acceleration-deceleration; severe mechanical injury produces complete transection of the axon (primary axotomy).**

- **Less severe tissue deformations produce focal pathologic abnormalities in axons that sometimes lead to delayed secondary axotomy, persistent axonal swelling and disconnection has been observed to continue for years after the initial trauma and contribute to the development of progressively greater disability, after MTBI (SMITH *et al.*, 2013).**

- **Recently, there has been renewed interest in Diffuse Axonal Injury (DAI) in MTBI; in blast injury, a primary low-intensity blast injury appears to contribute « *invisible injuries* », solely detectable at ultrastructural levels (SONG *et al.*, 2018).**

NEURO-IMAGING

BRAIN MRI IMAGING



3T (SIEMENS) MRI, 2 months after MTBI (LIU *et al.*, 2014).

(A) T2 flair imaging shows no abnormalities.

(B) Gradient Echo imaging shows three lesions in the right frontal lobe.

(C) Susceptibility-weighted imaging shows more low intensity lesions at the same location and also in the corpus callosum.

(D) Susceptibility-weighted imaging mapping shows high intensity lesions and deep veins.

- **Neuroimaging methods provide a variety of techniques to detect underlying neuropathology that results from MTBI; the most common visible abnormalities are in the form of focal encephalomalacia, hemosiderin deposition, and white matter signal abnormalities, on conventional MRI.**

- **The lack of radiological evidence has led clinicians to diagnose MTBI on the basis of non-specific clinical and cognitive self-reports symptoms (HOGE *et al.*, 2008; STEIN & McALLISTER, 2009); instead, if symptoms persist and lead to permanent disability (CARROLL *et al.*, 2004; NOLIN & HEROUX, 2006), it has been referred to as Persistent Post-Concussive Symptoms (PPCS).**

- **So MTBI is difficult to diagnose if the brain appears normal on MRI (POVLISHOCK & COBURN 1989; MITTL *et al.*, 1994; MILLER, 1996; IVERSON *et al.*, 2000; SCHEID *et al.*, 2003; HUGHES *et al.*, 2004; INGLESE *et al.*, 2005; BAZARIAN *et al.*, 2007).**

^{18}FDG BRAIN PET MOLECULAR IMAGING

- **Persistent Post-Concussive Symptoms (PPCS) include dizziness, headache, irritability, fatigue, sleep disturbances, nausea, blurred vision, hypersensitivity to light and noise, depression, anxiety, as well as deficits in attention, concentration, memory, executive function, and speed of processing (BIGLER, 2008).**

- **Thus MTBI affects a large number of individuals in the prime of life, where there is, to date, no consistent or reliable correlations between cognitive clinical symptoms and radiological evidence of brain injury based on conventional MRI neuroimaging.**

- **The explanation given for PPCS, when there is no discernible radiological evidence, has led some to posit a psychogenic origin (LISHMAN, 1988; MACHULDA, *et al.*, 1988; HOGE, *et al.*, 2008; BELANGER, *et al.*, 2009); HOGE *et al.*, (2008 – 2009), suggest that PPCS reported by soldiers with MTBI are entirely mediated by Post-Traumatic Stress Disorder (PTSD) and depression.**

- **So MTBI has been defined as a condition of normal structural imaging by World Health Organization guidelines (CASSIDY *et al.*, 2004), because conventional computed tomography (CCT) and MRI are not sensitive in detecting brain lesions.**

- **This lack of radiological evidence of brain injury in MTBI has led to the development of more sensitive methods like cerebral metabolic rate of glucose Positon Emission Tomography (^{18}FDG PET), more sensitive than morphological MRI, with metabolic dysfunction without structural lesions.**

- **Furthemore cognitive deficits are correlated to the volume of abnormalities (HUMAYUN *et al.*, 1989; RUFF *et al.*, 1994; ROBERTS *et al.*, 1995; GROSS *et al.*, 1996; UMILE, *et al.* 2002; PESKIND, *et al.*, 2011; PETRIE, *et al.* 2013; MENDEZ, *et al.*, 2013.**

LAVERAN'S HOSPITAL PRELIMINARY STUDY

CLINICAL AND NEUROPSYCHOLOGICAL DATA

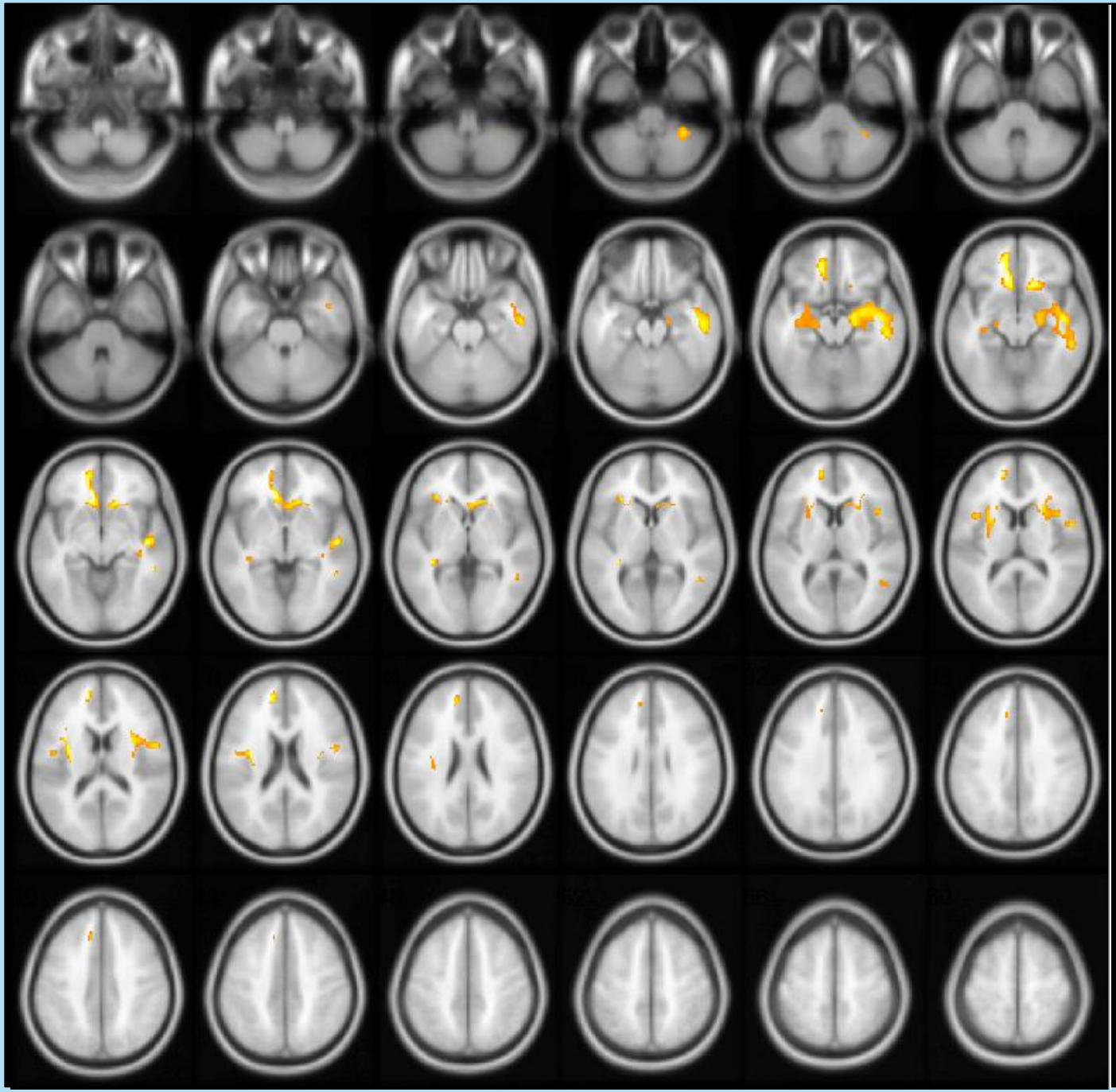
- **35 patients consulting the Physical Reeducation Medicine Department in LAVERAN Military Hospital of MARSEILLE, after MTBI in military condition: concussion (71%), whiplash (14%), Blast (2%). Sex ratio : 33/2. Age : 34 years [21-48]. Post-Traumatic-Stress-Disorders: 8 (23%).**

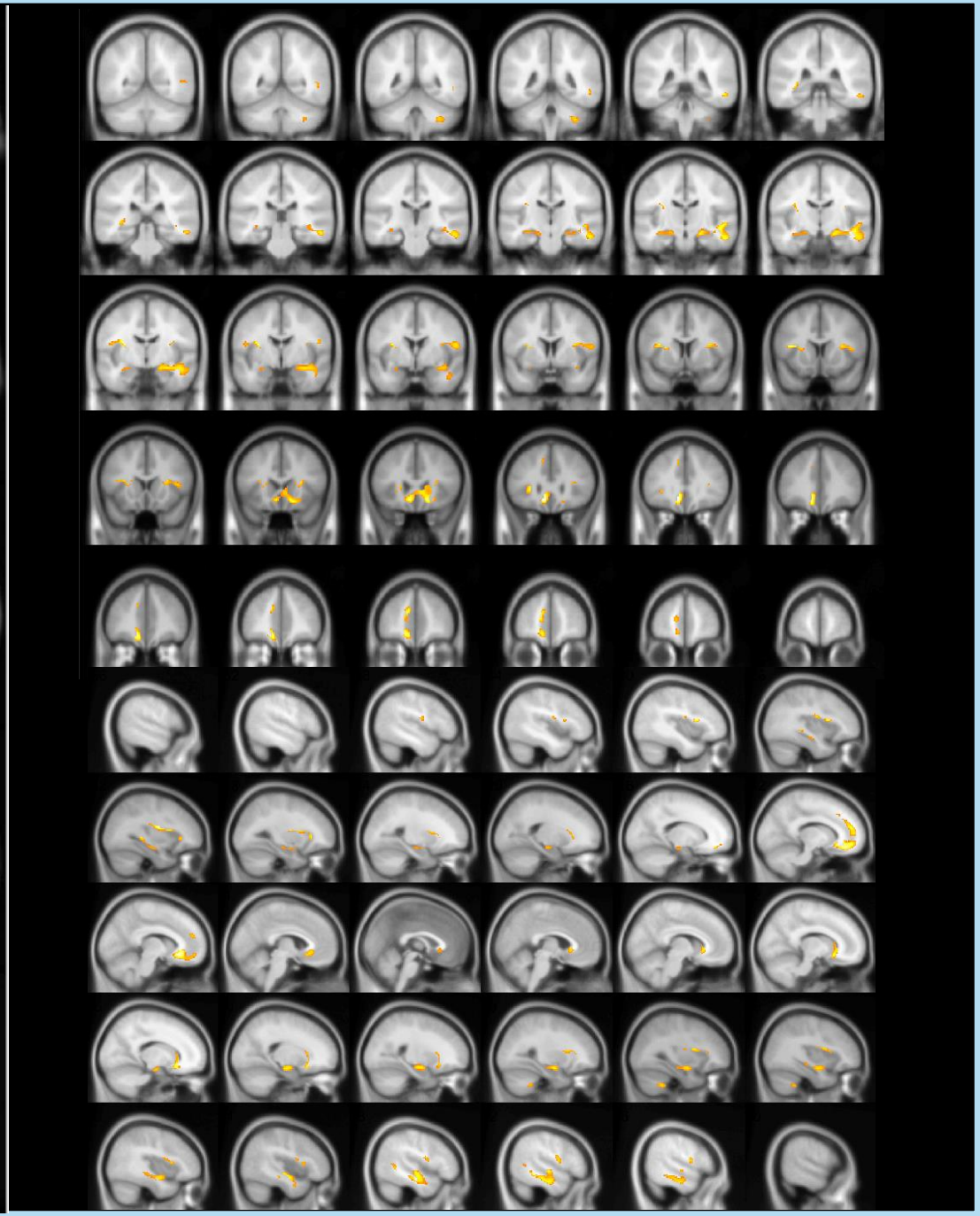
- **Multidisciplinary approach: Rehabilitation Medicine, Psychiatry (6 months to 1 year after MTBI), Neuroloy: Memory complaint [MAC NAIR (EDC)]; Mood depression [YESAVAGE (GDS)]; Global Cognition [FOLSTEIN (MMSE)], Verbal episodic memory [MICHEL (12 Words Scale)], Post-concussion Symptoms Questionnaire [RIVERMEAD].**

- **Neuropsychological evaluation. 1) Digit Span. 2) 16-item Free and Cued Recall. 3) Trail Macking Test; ZAZZO. 4) WISCONSIN; Tower of HANOÏ. 5) Semantic and Phonemic Fluency Tests. 6) BOSTON Naming Test. 7) REY–OSTERRIETH Complex Figure.**

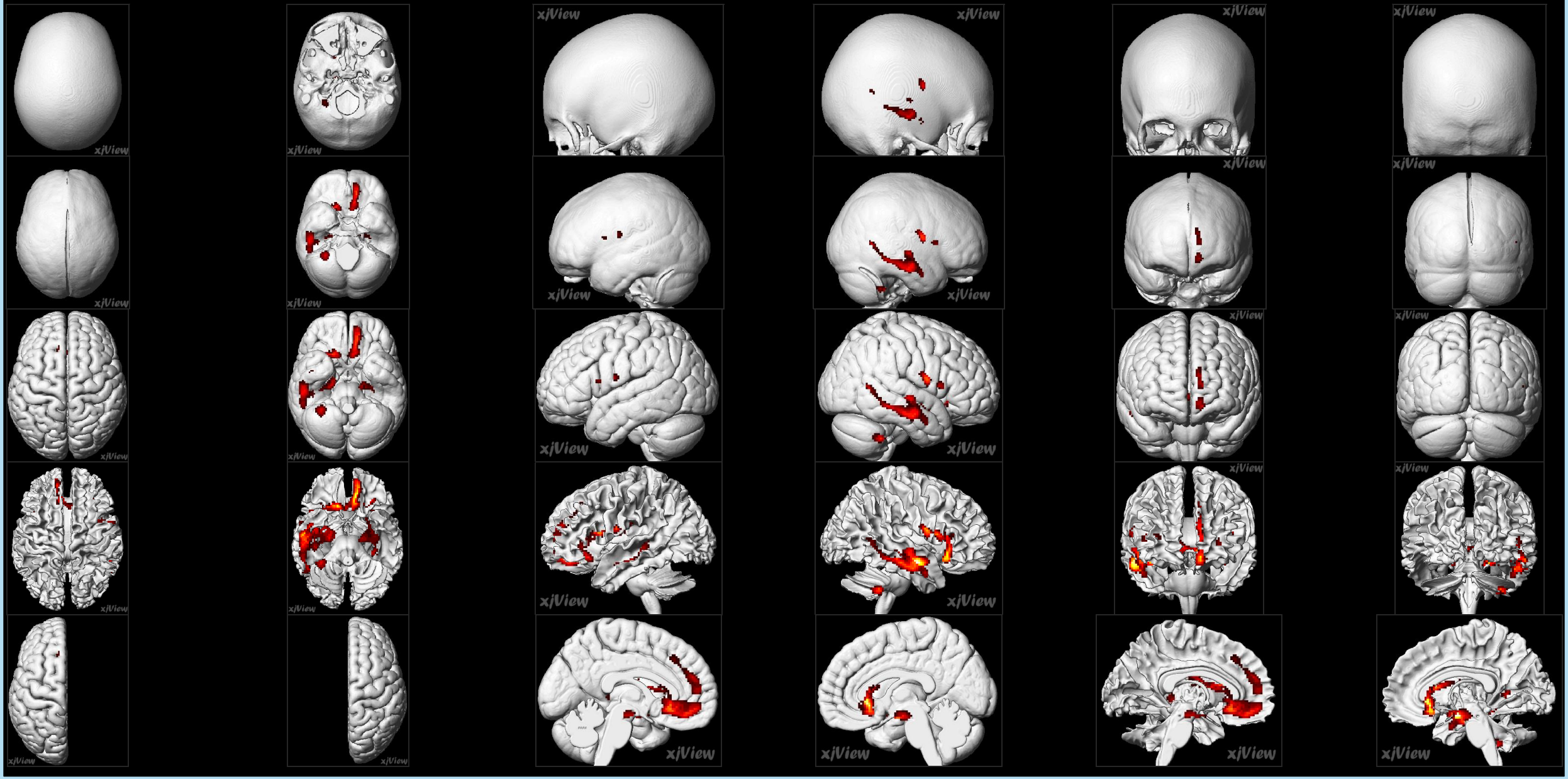
N°	IDENTITY	SEX	AGE	MTBI	LOSS OF CONSIOUSNESS	PTSD	GDS	MMSE	RL/RI 16	MRI	TEP SCAN
1	BAL Corinne	F	52	Concussion	+	+	18	26	16/16	Abnormal	Abnormal
2	BEN Mohamed	M	28	Concussion	-	-	24	25	15/16	Normal	Abnormal
3	CLE Thomas	M	48	Whiplash	-	-	9	28	16/16	Normal	Abnormal
4	FEL David	M	48	Concussion	+	+	29	22	15/16	Normal	Abnormal
5	FOR Nino	M	33	Concussion	+	-	11	24	15/16	Normal	Abnormal
6	GAI Franck	M	51	Concussion	+	-	11	27	15/16	Abnormal	Abnormal
7	IDR Audris	M	25	Whiplash	-	+	15	28	11:16	Normal	Abnormal
8	IER Remi	M	46	Concussion	+	-	27	25	16/16	Normal	Normal
9	JEG Marc-Ant	M	31	Concussion	+	-	9	28	16/16	Normal	Normal
10	MOU Magomed	M	46	Concussion + Blast	+	+	20	26	16/16	Abnormal	Abnormal
11	NEG Guillaume	M	30	Concussion	+		14	28	13/16	Abnormal	Normal
12	ODA Newton	M	51			-	20				Normal
13	OGO Roman	M	25	Concussion	+	-	20		14/16	Abnormal	Abnormal
14	PIG Nicolas	M	32	Concussion	-	+				Normal	Normal
15	PLU Stéphane	M	35	Concussion	+	-		29	16/16	Abnormal	Normal
16	QUI Christophe	M	51	Concussion	-	-			14/16	Normal	Abnormal
17	SHR Nirad	M	32	Concussion	+	+	26	24	16/16	Normal	Abnormal
18	SIL Roli	M	32	Concussion	+	-	2	27	16/16	Abnormal	Abnormal
19	SOU Ibrahim	M	35	Concussion	+	-	21	27	16/16	Normal	Normal
20	TOF Piotr	M	34	Concussion	+	-	18	21	16/16	Abnormal	Abnormal
21	TUA Venceslav	M	51	Concussion	+	-	5	27	15/16	Abnormal	Abnormal

^{18}FDG-PET METABOLIC BRAIN-IMAGING DATA





PET Hypométabolism (p<0.005 k >83) 21 MBTBI, compared to 14 normal subjects, age and sex matched



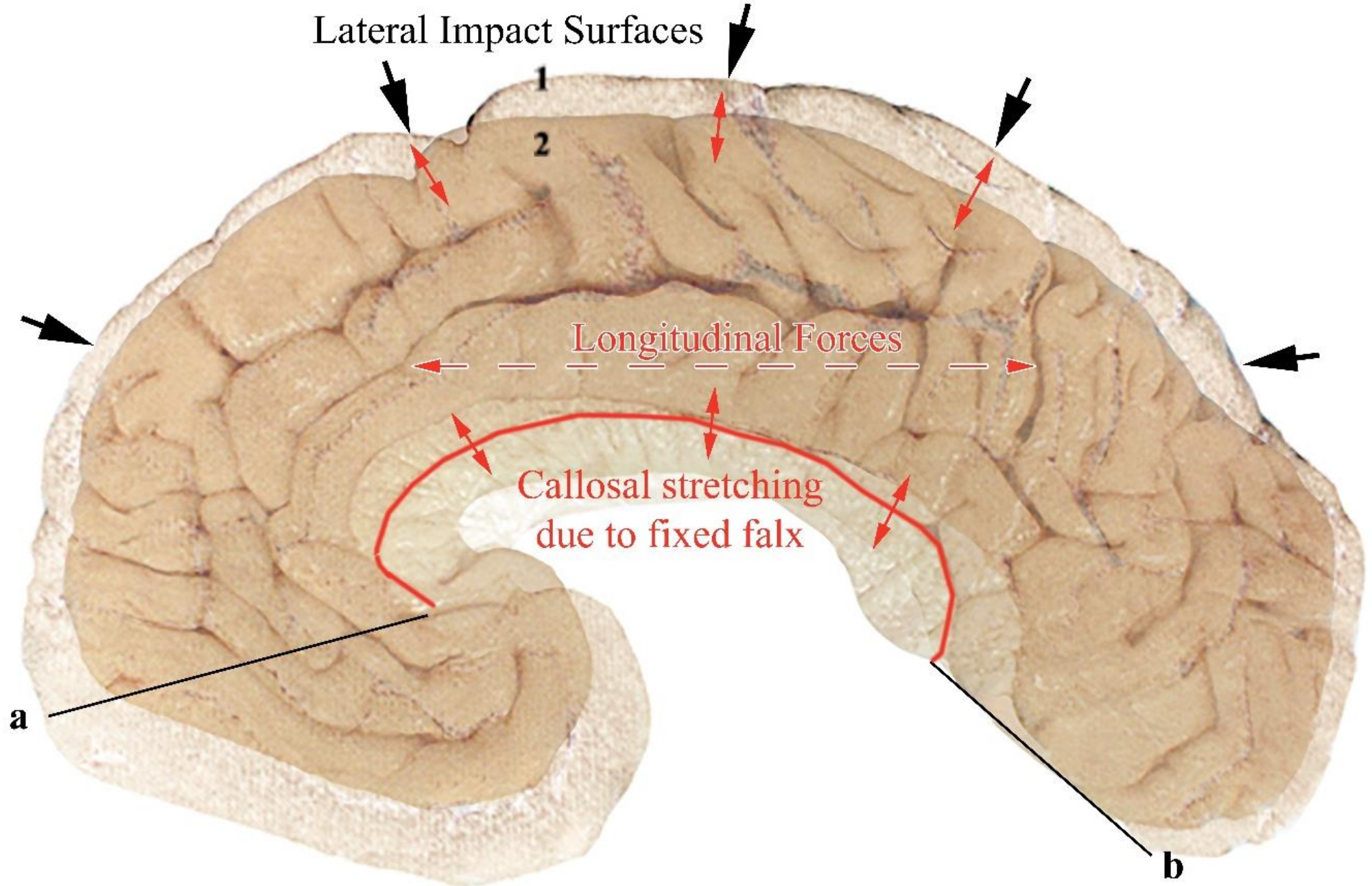
CINGULUM IN MILD TRAUMATIC BRAIN INJURY

CINGULATE GYRUS

- **Atrophy of the Posterior Cingulate Cortex (PCC) was primarily responsible for the overall reduction of Cingulate Gyrus (CG) surface area in MTBI subjects (YOUNT *et al.*, 2002).**

- **Furthermore, it is plausible that direct mechanical deformation of the medial surface of the CG could strike the falx cerebri and stretching of the opposite hemisphere, causing injury; concussion could force any level of cingulate cortex to strike the falx, causing injury.**

- **Diffuse changes in cerebral Gray Matter (GM), observed following MTBI, are found one year after the injury; changes related to MTBI occur in limbic system and poorer performance in attention tests also correlated with decreased GM concentration in CG (GALE *et al.*, 2005).**

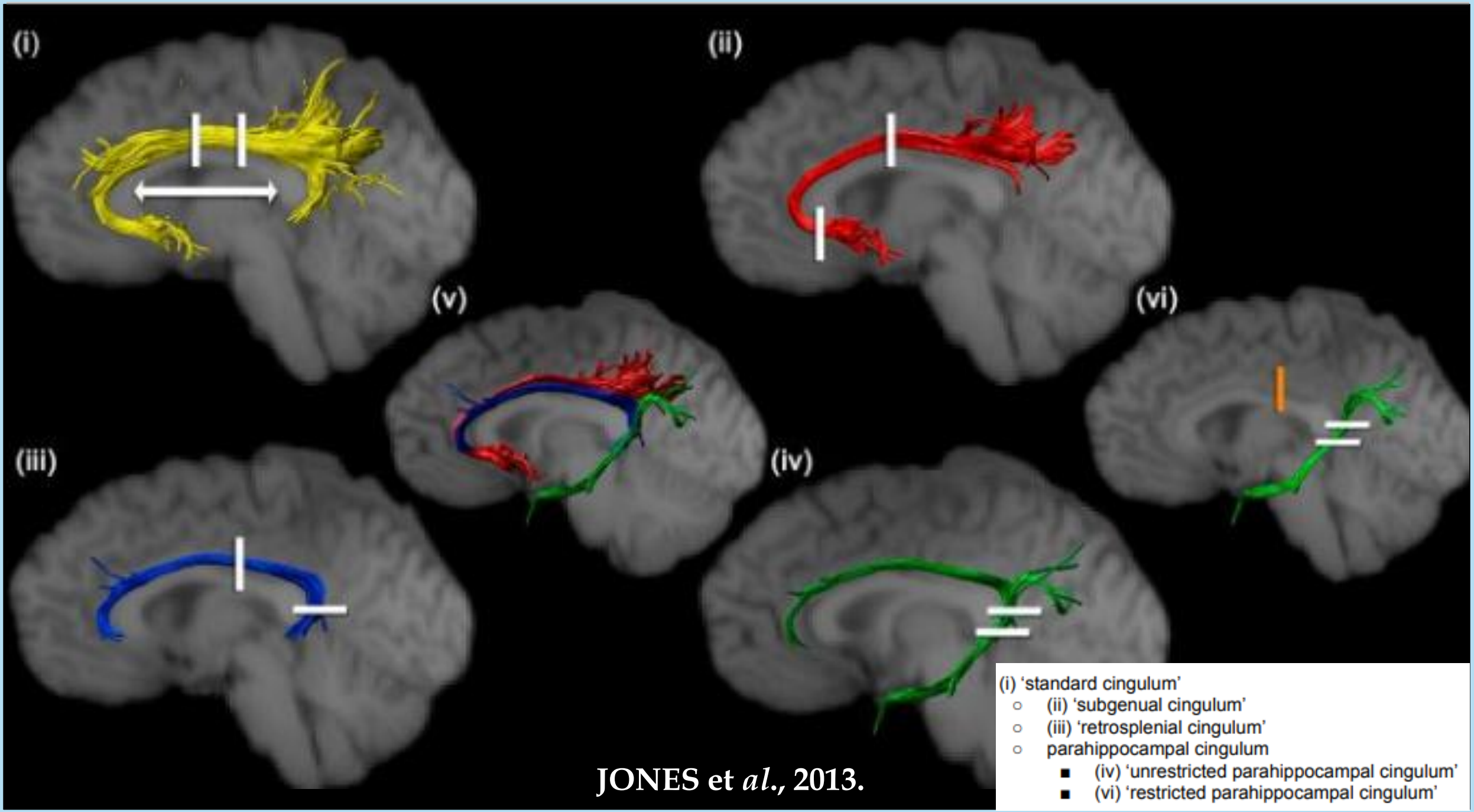

Lateral Impact Surfaces
1
2
Longitudinal Forces
Callosal stretching
due to fixed falx
a
b

CINGULATE BUNDLE

- **The Cingulate Bundle (CB) constitutes an association of long and short fibers that connect the cingulate cortex to the para-hippocampal gyrus, the prefrontal cortex, and cortical association areas in parietal and occipital lobes (MUFSON & PANDYA, 1984).**

- **After curving around the splenium, CB projects along the inferior surface of the hippocampus and diffuse towards his anterior pole (MORI & AGGARWAL, 2014) ; The Cingulate Gyrus (CG) receives sensory inputs from the neocortex (frontal, parietal, occipital, and temporal lobes).**

- **MTBI affects the global organization of brain networks of PAPEZ circuit, which control cognition and emotion, through Cingulum and supports the notion of a disconnection syndrome.**



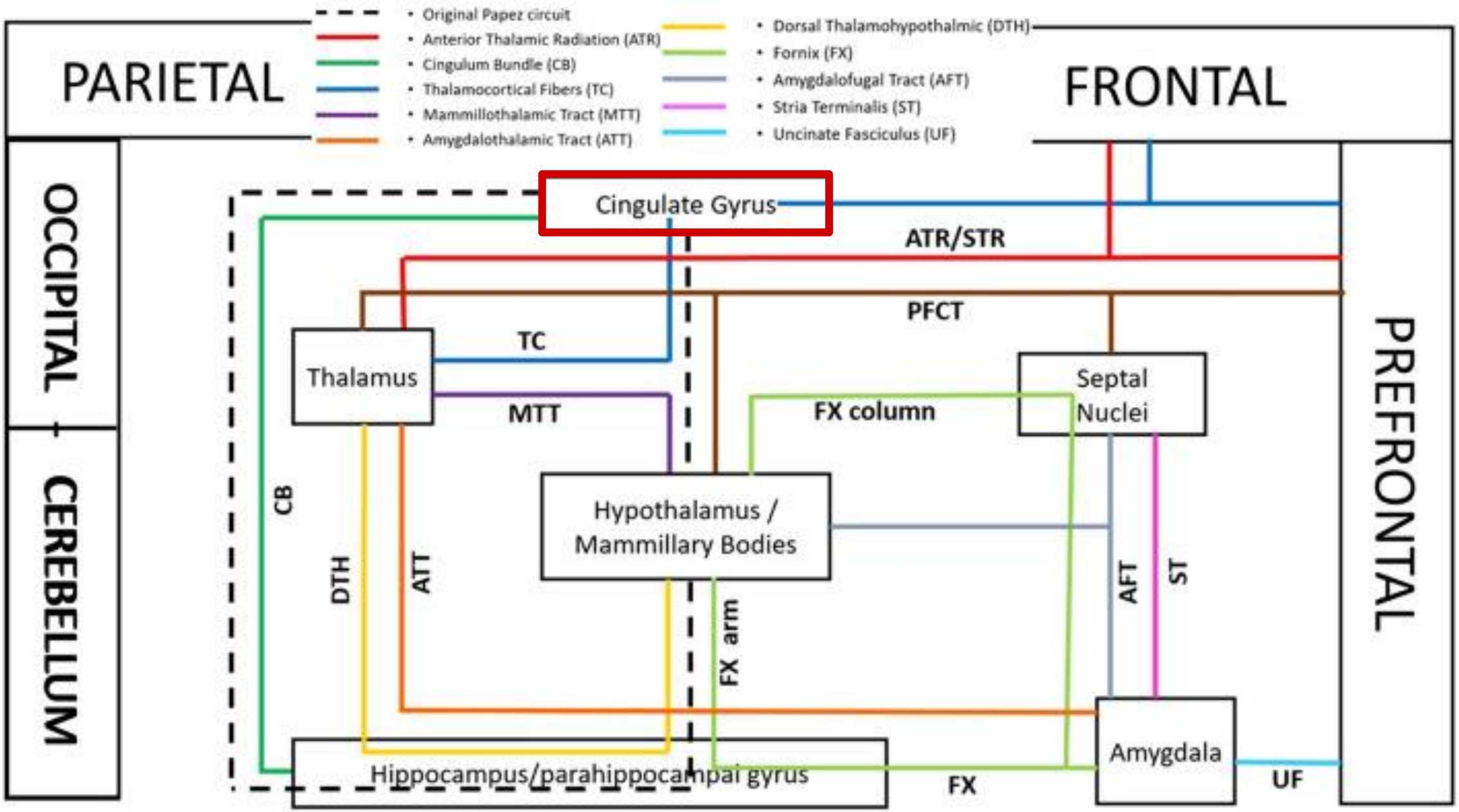
JONES et *al.*, 2013.

CONCLUSION

- **Systematic multidisciplinary management and regular monitoring within a cohort, significantly improve the diagnosis and treatment of MTBI; in addition, in military situation, the problem of rehabilitation and aptitude, arises at the highest level.**

- **The specialization and professionalization of multidisciplinary teams is a guarantee of a good medico-military expertise.**

- **Alongside the neuropsychological assessment and anatomical neuroimaging (MRI), functional neuroimaging (^{18}FDG brain PET) provides a strong argument in the neuropsychology-neuroimaging correlations, especially when the morphological MRI is normal.**



KAMALI *et al.*, 2023

MTBI AND GUILLAUME APOLINAIRE'S SYNDROME

Portrait of Guillaume APOLLINAIRE from Pablo PICASSO

TRISTESSE D’UNE ETOILE

« Une belle Minerve est l'enfant de ma tête
Une étoile de sang me couronne à jamais
La raison est au fond et le ciel est au faîte
Du chef où dès longtemps Déesse tu t'armais. »

« C'est pourquoi de mes maux ce n'était pas le pire
Ce trou presque mortel et qui s'est étoilé
Mais le secret malheur qui nourrit mon délire
Est bien plus grand qu'aucune âme ait jamais celé. »

« Et je porte avec moi cette ardente souffrance
Comme le vers luisant tient son corps enflammé
Comme au cœur du soldat il palpite la FRANCE
Et comme au cœur du lys le pollen parfumé. »

THANK YOU FOR ATTENTION