

# Multimodal MR Imaging of Corpus Callosum Abnormalities in Chronic Mild Traumatic Brain Injury within a Military Veteran Population

*Timothy Herron<sup>1</sup>, Xiaojian Kang<sup>1,2</sup>, David Woods<sup>1,2,3</sup>*

<sup>1</sup>Human Cognitive Neurophysiology Lab, Neurology, US Veterans Affairs, Martinez, CA

<sup>2</sup>Department of Neurology and Center for Neuroscience, University of California at Davis

<sup>3</sup>Center for Mind and Brain, University of California at Davis

# Background

**Traumatic Brain Injury (TBI) has often been reported to cause damage to axons within white matter, especially within the fibers of the callosal commissure even in mild (mTBI) cases [1]. However, recent reports analyzing patients having mTBI injuries with blast etiology seem to indicate that there is little or no damage within the callosum [2][3]. We collected multimodal magnetic resonance (MR) data from a small group of mTBI patients from recent military conflicts, a majority with blast injuries, in order to characterize structural features of the mid-callosal fibers relative to a matched control population and to estimate deficits in the mTBI population.**

# MR Imaging Modalities



## Philips Eclipse 1.5T Clinical MR Scanner

**Callosal Volume  
T1 Contrast**

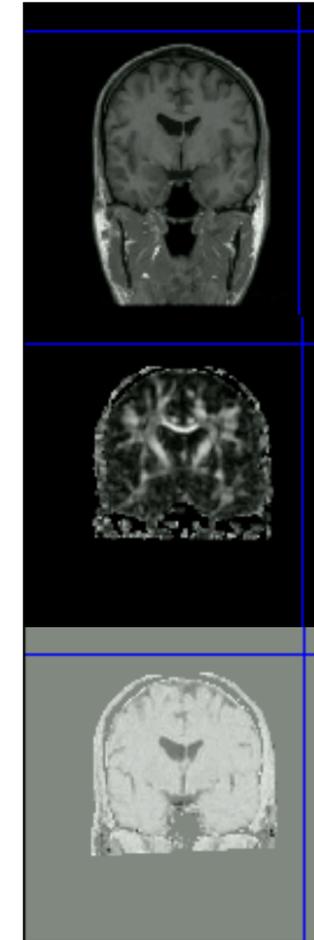
- **High Resolution T1 images** [TR/TE=15/4.47 ms, FOV = 240 mm, 256 × 256 imaging matrix, flip angle = 35°, 0.94 × 1.3 × 0.94 mm<sup>3</sup> voxels, 212 coronal slices, x2]

**Axon integrity**

- **Diffusion Tensor Images (DTI)** [cardiac-gated, single-shot spin echo EPI sequence, TR/TE = 600-1000/115.6 ms, FOV = 240 mm, 80 × 80 imaging matrix, flip angle = 90°, 3 × 3 × 3 mm<sup>3</sup> voxels, 48 axial slices, b = 1000 s/mm<sup>2</sup>], 6 direction (dual-gradient) & 2 B0 images, 4 sets]

**Myelination**

- **Magnetization Transfer Images (MTI)** [TR = 1645 ms, TE = 13.4 ms, flip angle = 20°, frequency offset = 1.5 kHz, MT pulse amplitude = 500 Hz, voxels size 1.9×1.9×2.0 mm<sup>3</sup>, x2]



**Expected direction of difference in chronic TBI patients compared to normals:**

- **High Resolution T1 images:** Callosal Area (Length and Thickness) ↓ ; Contrast ↓
- **Diffusion Tensor Images (DTI):** Fractional Anisotropy (FA) ↓ ; Radial Diffusivity (RD) ↑
- **Magnetization Transfer Images (MTI) :** Magnetization Transfer Ratio (MTR) ↓

# MRI Processing

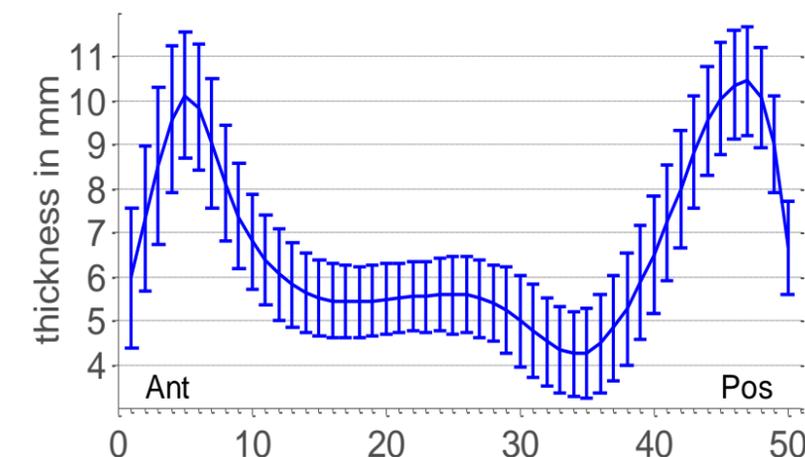
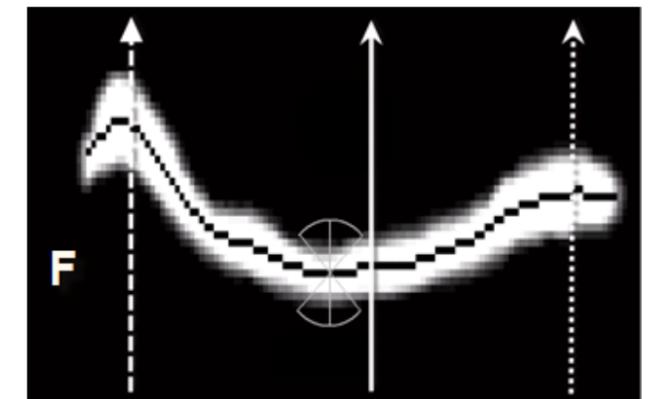
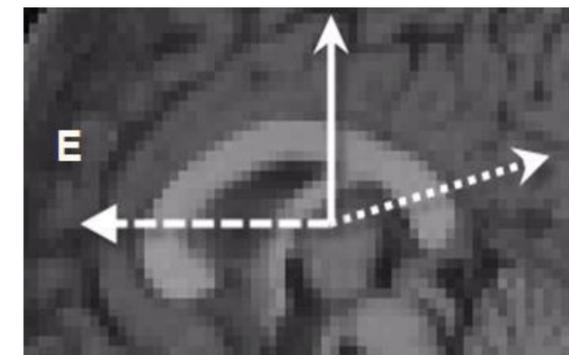
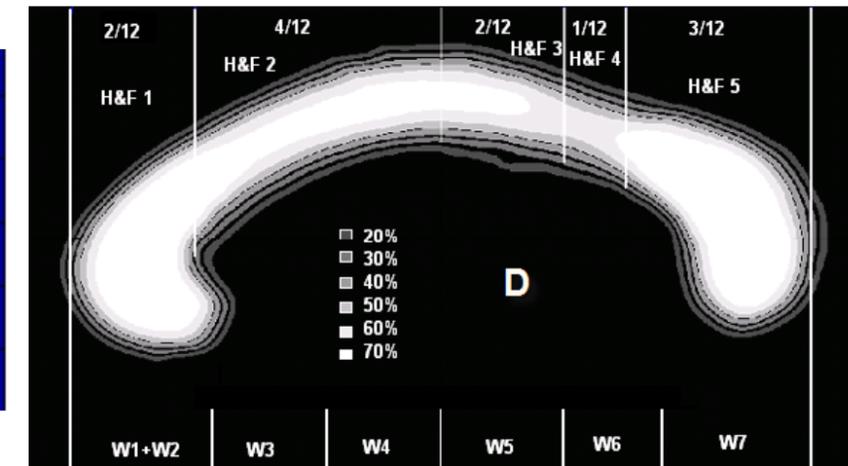
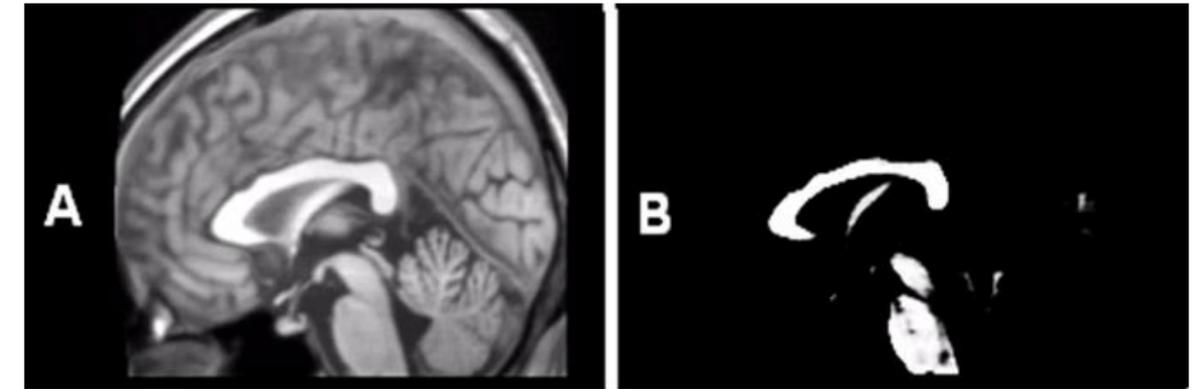
C8 measures midsagittal cross-sectional thickness and area of the human corpus callosum from high-resolution T1 in vivo MR images that have been preprocessed using affine normalization (A) and tissue segmentation (B).

Areas are computed for geometrically defined callosal compartments (D) for isolated callosal WM (C). Thickness is sampled along a median line within the corpus callosum (F) according to a radial method of spacing (E).

C8 produces consistent, reliable callosal measurement estimates comparable to those from manually-segmented callosa [4].

Multimodal data coregistered to T1 image & values extracted from (D) partitions and on median line.

Callosal thicknesses defined as the shortest line segment passing through a medial line point (F). Areas defined as total sums of WM segmentation values within geometric partitions.



**OASIS-152**  
[6] thickness means (s.d. error bars).

# mTBI Patients

16 mTBI patients, veterans from OIF/OEF/OND conflicts, where 8 report blast as the primary cause of mTBI and 5 others having experienced concussive blast in combat. An age (mean 36 y.o.), sex (all male), handedness (all RH), and education-matched (14 yrs) control group of 27 subjects (14 veterans) were also imaged.

Subject Code	Age (yrs)	Education (yrs)	Active Combat	Enlisted Combat	# of Combat Personnel	OEF/OIF*	LOC (any)	TBI Hospitalization	PTA (any)	Fight/Hit Blunt Object	Explosion/Blast	Fall	MVA	PostTBI Headaches	Sports	Tinnitus*	Chronic Pain*	Sleep Disorder*	CFQ Score*	PCL Score*			
	24	12	X	X	X		3+	X		X	X								X	X	60	54	
	28	12	X	X	X						x						X		X	X	85	66	
	43	14	X	X	X		3+	X	X	X	X						X	X	X	X	101	80	
	41	14						X		X	X			X	x		X	X	X	X	46	45	
	25	15	X	X	X			X	X	X	X						X		X	X	87	64	
	25	12	X	X	X		2		X				x				X	X		X	60	57	
	29	12	X	X	X			X									X					85	54
	43	.	X	X			1										X		X	X	.	62	
	28	14		X	X					X												64	43
	29	13	X	X	X		1						x				X	X				59	27
	61	18	X	X	X			X	X	X	X		X	X	X		X	X		X	64	52	
	27	15	X	X	X			X									X	X		X	88	72	
	48	13	X	X	X		1	X									X	X	X	X	77	59	
	50	20	X	X			3+	X						X	X		X	X	X	X	96	62	
	49	12	X		X					X	x			X	x	x	X	X	X		68	47	
	28	14	X	X	X		1	X	X	X	x	X	X	X	X		X	X			89	68	
	36	14	88%	88%	88%			63%	31%	19%	38%	81%	25%	25%	19%	56%	75%	63%	69%	75	57		

Relevant features of the 16 mTBI patients. Table includes demographics (age, education), type of military service (Enlisted Service, Combat, Theater: OEF/OIF=Operation Iraqi Freedom or Operation Enduring Freedom), mTBI characteristics (LOC= loss of consciousness, PTA = post-traumatic amnesia), mTBI etiology, ongoing health issues (headaches, tinnitus, chronic pain, sleep disorders), and the cognitive failures questionnaire score (CFQ) as well as the Post-Traumatic Checklist (PCL-military) score. \* indicates a significant difference from controls (t-test or sign test).

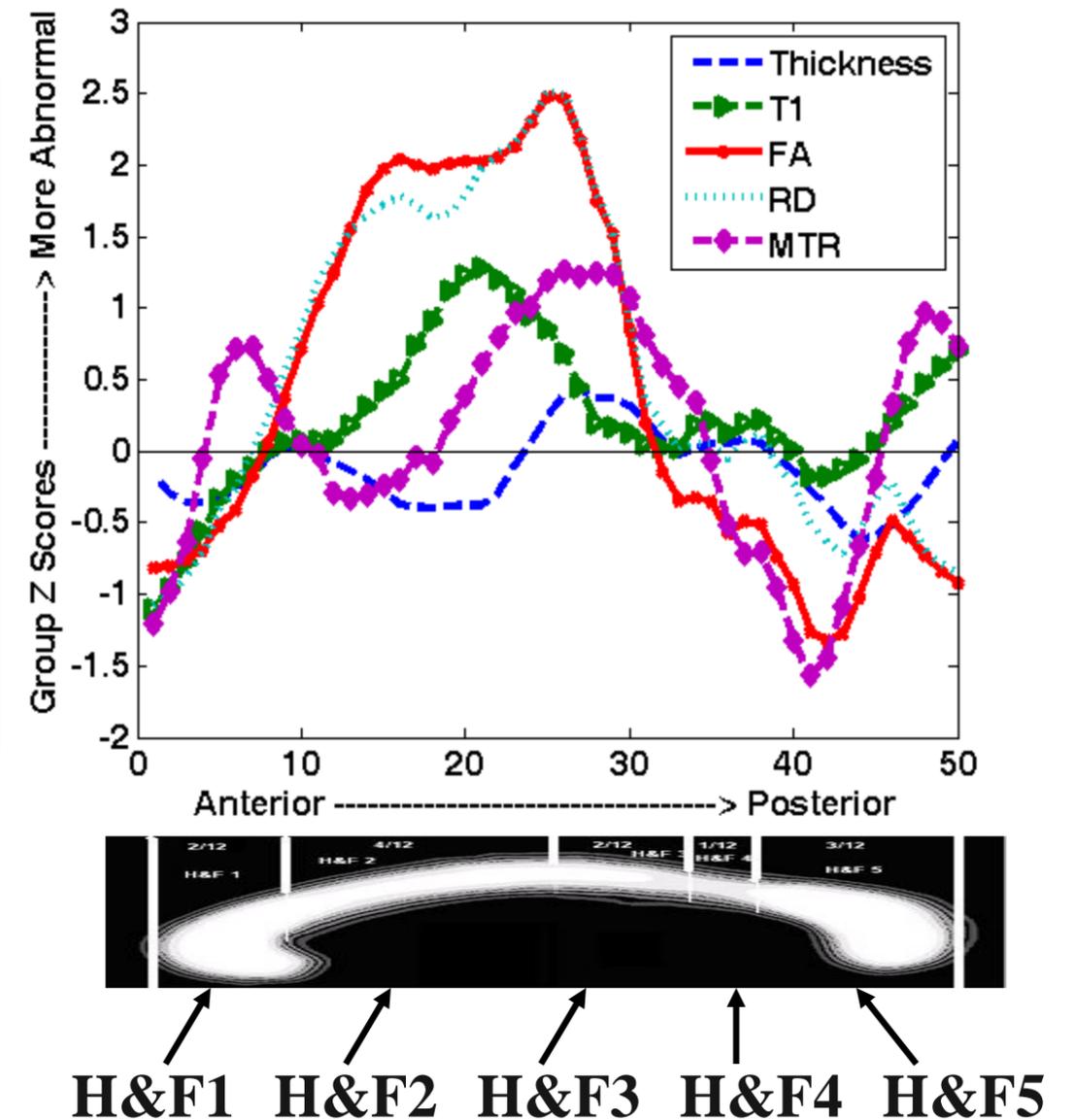
# Results

There was a significant group deficit in mTBI patient diffusion scores (FA) in the anterior mid-body of the callosum.

However, only a few of the 16 patients had significant abnormalities (e.g.  $Z > 2$ ) in the anterior mid-body in any of the imaging modalities, including FA, with most subjects only showing at most weak deficit trends.

Further, *within* the mTBI group there was a  $r = -0.64$  Pearson correlation between PCL scores and FA values in the anterior midbody H&F2 ( $r = 0.79$  between RD and PCL). [Also a  $r = +0.66$  between RD and CFQ (cognitive failures).]

Only FA was abnormally low (and RD generally high) in the anterior midbody region. But without significantly reduced fat content (T1 & MTR) and no callosal thickness difference.



	H&F1	H&F2	H&F3	H&F4	H&F5
<b>FA</b>	0.60	<b>2.47</b>	-0.10	-0.09	-0.20
w/ cov	0.24	0.55	0.29	0.00	0.21

FA group differences in z-score equivalents with row 2 covarying out intracranial volume and overall post traumatic checklist (PCL) scores.

# Conclusion

We find no evidence of robust TBI-specific deficits in the mid-sagittal corpus callosum, even though 12/16 patients of our small sample experienced LOC, PTA, and/or hospitalization from their primary mTBI [5]. However the patient group differed from the (age, sex, education, handedness) matched controls in several respects: the patients suffered from higher levels of pain, sleep disorders, post-traumatic stress and tinnitus in addition to having experienced more combat.

## Acknowledgements

We would like to thank the OASIS project [6] for use of their data. This work is supported by the VA Research Service through grant (VA RR&D B6120R).

## References

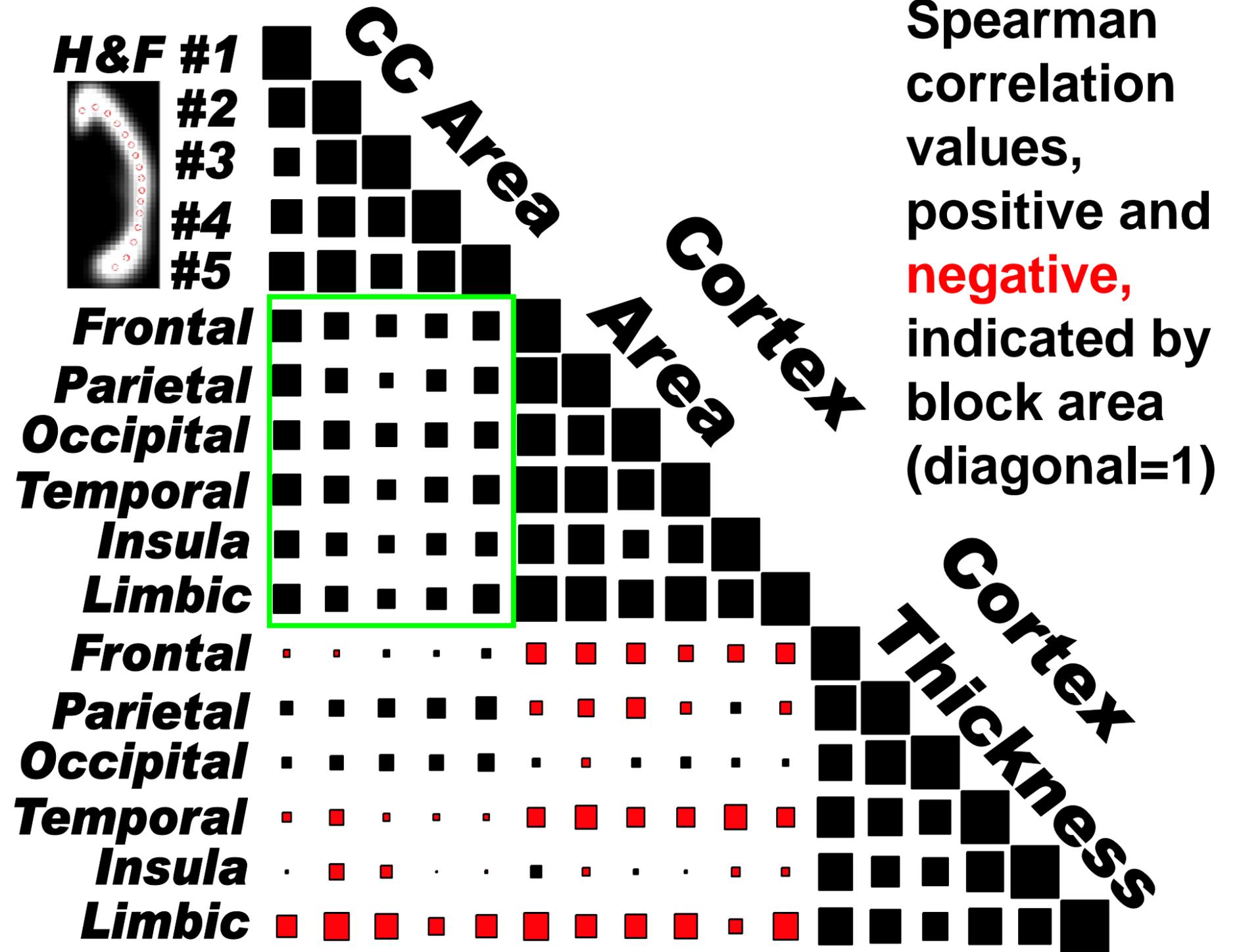
- [1] Aoki et al, *J Neurol Neurosurg Psychiatry*, 2012, 83:870-876.
- [2] Levin et al., *J Neurotrauma*, 2010, 27:683–694.
- [3] Davenport et al., *Neuroimage*, 2012 Feb 1;59(3):2017-24.
- [4] Herron et al, *Front Neuroinform*, 2012, 6: 25. [www.nitrc.org/projects/c8c8](http://www.nitrc.org/projects/c8c8).
- [5] Matthews et al., *Psychiatry Research: Neuroimaging*, 204 (2012) 149–154.
- [6] Marcus et al, *J. Cog. Neuro.*, 19(9), 2007. [www.oasis-brains.org](http://www.oasis-brains.org)



# Callosal/Cortical Correlations

Callosal measurements may relate to many parts of the cortex affected by mTBI in addition to being damaged [1].

138 young normal high-res. T1s (1.5T, age mean 26, 69 F) added to 152 OASIS young normals (3T, age mean 23, 82 F) [6], processed using FreeSurfer for lobar cortical areas and cortical thicknesses.



Spearman correlation values, positive and **negative**, indicated by block area (diagonal=1)

Correlations have age, gender, and scanner partialled out.

# Basic callosal relationships

1231 T1 images from the 1000 Functional Connectome Project image database [4] were used to study demographic, brain size, and callosal, relationships.

