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

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Introduction

- Traumatic axonal injury (TAI) has been shown to be an important part in all severities of the traumatic brain injury (TBI), using different sensitive magnetic resonance imaging (MRI) techniques.
- MRI findings early after the injury have been associated with clinical outcome.
- Messori et al (2003) have demonstrated haemorrhagic TAI lesions to appear less conspicious with time, but no earlier studies have assesed how non-haemorrhagic TAI lesions evolve in number and volume from the acute to the chronic stage.

AIM: to prospectively assess the evolution of TAI detected by structural MRI in patients with moderate to severe TBI during the first year post-injury and relate the findings with outcome.

Methods

- 58 patients with TBI (Glasgow Coma Scale score 3-13) were examined with MRI at median 7 days, 3 and 12 months post-injury.
- TAI lesions were evaluated blinded for patient information and categorized into 3 stages based on location; hemispheres, corpus callosum and brainstem.
- The number of T2*-weighted gradient echo (GRE) and fluid-attenuated inversion recovery (FLAIR) lesions were counted and FLAIR lesion volumes were segmented and an inter-rater reliability calculated.
- Outcome was assessed 12 months post-injury by Glasgow Outcome Scale Extended.

Results

- In the early MRI, 31% had brainstem lesions compared with 17% at 3 months (p=0.008).
- In the FLAIR sequences number and volumes of lesions were reduced at 3 months (Table 1), while in T2*GRE sequences the number of lesions were first reduced at 12 months (Table 2).

Table 1: Total traumatic axonal injury volume in the FLAIR sequence (non-hemorrhagic lesions)

		Early MRI		3 months MRI			12 months MRI		
	Location of lesion	Vol (mm^3)	SD	Vol (mm^3)	SD	p-value*	Vol (mm^3)	SD	p-value**
Moderate TBI (n=28)	Hemispheres	426.9	(936.8)	145.4	(321.7)	**0.003**	119.0	(342.7)	0.78
	Corpus Callosum	481.6	(1014.2)	86.5	(426.4)	**0.001**	21.1	(111.7)	0.59
	Brainstem	52.0	(179.0)	0		**0.012**	0		n.a.
	Thalamus/BG/Cerebellum	194.4	(796.0)	10.5	(55.3)	**0.049**	8.2	(43.5)	0.98
	Total	*1181.0*	*(1873.8)*	*245.9*	*(544.8)*	***<0.001***	*129.4*	*(343.4)*	*0.66*
Severe TBI (n=25)	Hemispheres	927.1	(1295.3)	227.6	(475.3)	**0.005**	414.70	(870.1)	0.45
	Corpus Callosum	1833.8	(2890.1)	230.4	(576.4)	**<0.001**	277.1	(628.1)	0.90
	Brainstem	533.6	(1712.7)	135.2	(309.8)	0.14	153.9	(363.8)	0.95
	Thalamus/BG/Cerebellum	426.0	(1545.9)	68.6	(235.2)	0.16	18.4	(90.2)	0.84
	Total	*4116.1*	*(6281.5)*	*983.6*	*(1760.1)*	***<0.001***	*649.8*	*1441.9*	*0.68*

The data are reported in means with their standard deviation (SD). Patients with chronic gliotic changes (n=6) are excluded.
* The p-value represents the difference between early and 3 months MRI (longitudinal mixed effects model)
** The p-value represents the difference between 3 months and 12 months MRI (longitudinal mixed effects model)

- FLAIR lesion volume in early MRI predicted worse outcome in multivariable analyses with adjustment for age, GCS score and pupil dilation (p=0.04). Subgroup analysis of moderate TBI patients showed only age (p=0.003) and Rotterdam CT score (p=0.007) to be assosicated with outcome.
- The inter-rater reliability was excellent for FLAIR volume and number of T2*GRE lesions.

Table 2: Number of TAI lesions in T2*GRE sequences (hemorrhagic lesions)

Location of lesion	Early MRI mean (SD)	3 months MRI mean (SD)	p-value*	12 months MRI mean (SD)	p-value**
	n=58	*n=58*		*n=55*	
Hemispheres	12.1 (9.8)	12.6 (10.3)	0.44	11.7 (10.6)	0.091
Corpus callosum	3.2 (6.3)	3.2 (6.4)	0.97	2.3 (4.0)	**0.017**
Brainstem	1.4 (4.5)	1.1 (4.5)	0.11	1.0 (3.6)	0.39
Total	18.4 *(21.4)*	*18.7 (22.7)*	*0.76*	*16.4 (19.0)*	***0.007***

* The p-value represents the difference between early and 3 months MRI (longitudinal model)
** The p-value represents the difference between 3 months and 12 months MRI (longitudinal model)
The few lesions counted in thalamus, basal ganglia and cerebellum are not presented in this table

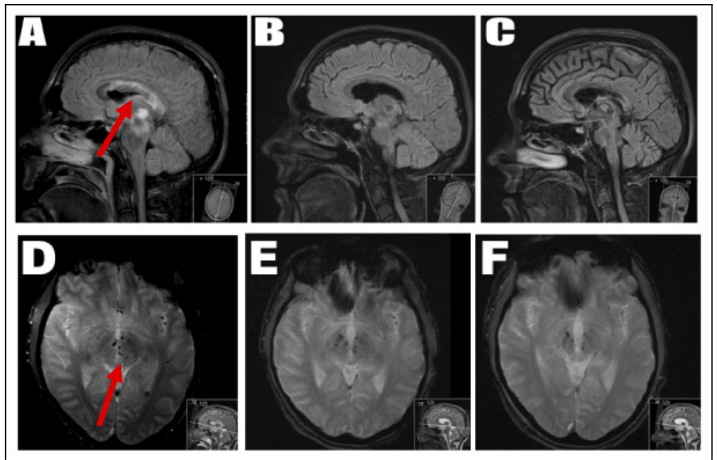

Figure A-C show sagittal midline FLAIR images of the same patient performed at three different time points (4 days, 3 months and 12 months). The first examination (A) shows lesions both in the corpus callosum, thalamus and the brain stem. At 3 and 12 months (B and C) these lesions have disappeared, but we find sequleae with atrophy. Figure D-E shows transverse T2*GRE images of the same patient at the same time intervals. Multiple, bilateral haemorrhagic lesions are found in the brain stem that persist during the follow up period.

Conclusions

- **This is the first study to demonstrate and quantify the attenuation of non-hemorrhagic TAI lesions during the first year post-injury, most importantly the disappearance of brainstem lesions during the initial 3 months. Hemorrhagic TAI lesions attenuate first after 3 months.**
- **Only FLAIR lesion volumes in early MRI predict clinical outcome after adjustment for other known prognostic factors, but this association was not found for moderate TBI.**