



# Acute phase proteins and endocrine dysfunction after traumatic brain injury in childhood

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## ABSTRACT

**Background:** Endocrine impairments, such as diabetes insipidus (DI), growth hormone deficiency (GHD) and, to a lesser degree, thyroid or cortisol deficiencies, have been reported after traumatic brain injury (TBI) in adults and much less in children both at the acute post-traumatic phase and after a lag period of time. However, no prospective data exist on the endocrine and acute phase protein response to TBI in childhood.

**Aim/Objective:** To unravel possible endocrine impairment and acute phase protein response after TBI in children hospitalized in a single pediatric Neurosurgery department.

**Methods:** Twenty-one children (11 girls), age range 1,3-12,6 years, with TBI were prospectively enrolled and studied at three phases: at the acute phase and at 6 and 12-18 months following the injury. Five out of the 21 patients dropped-out at 6 months and three more patients at 12-18 months. The endocrine and acute phase protein assessment was performed at all time-points.

**Results:** At the acute phase, GHD, as assessed by low IGF-1 levels, was found in 24% of cases, DI in 19% and subclinical hypothyroidism in 5%. Permanent endocrine dysfunctions 12-18 months after TBI were hypothyroidism and DI in 15% and low IGF-1 levels in 6%. Contrary to literature data, prolactin levels were normal during the 1st and 2nd phase, with an increase observed in 12% of the cases 12-18 months after TBI. Moreover, S100b, a biomarker of brain damage was increased in all children at all phases, indicating a persisting neuronal damage 12-18 months after TBI. All children demonstrated a good spontaneous recovery with no clinically relevant dysfunction or permanent neurological deficits.

**Conclusions:** Our results reveal a significant percentage of endocrine dysfunction in children after TBI, both at the acute phase and long after the incident. A subclinical persistent neuronal damage observed in all children calls for long-term surveillance of children post TBI.

## BACKGROUND

Endocrine impairments, such as diabetes insipidus (DI), growth hormone deficiency (GHD) and, to a lesser degree, thyroid or cortisol deficiencies, have been reported after traumatic brain injury (TBI) in adults and much less in children both at the acute post-traumatic phase and after a lag period of time. However, no prospective data exist on the endocrine and acute phase protein response to TBI in childhood. The aim of the current study was to unravel possible endocrine impairment and acute phase protein response after TBI in children hospitalized in a single pediatric Neurosurgery department.

## PATIENTS AND METHODS

Twenty-one children (11 girls) age range 1,3-12,6 years, with TBI were prospectively enrolled and studied at three phases:

- at the acute phase
- at 6 months
- at 12-18 months following the injury.

Patients' characteristics are provided in Table 1. At all time points IGF-I, T4, T3, TSH, cortisol, prolactin and the acute phase proteins hsCRP and S100b were assessed.

Patient	Age, years	Sex	Causes of injury	of	Glascow score	Coma	Sc	Tanner stage	BMiz score
1	5	F	fall		9			1	-0,98
2	11	F	Car accident		9			4	-0,08
3	9	F	fall		9			3	1,37
4	5	F	fall		12			1	1,39
5	10	F	fall		9			1	0,96
6	6	F	fall		14			1	-1,76
7	7	F	fall		15			1	-1,93
8	8	M	fall		14			1	1,25
9	6	F	fall		11			1	0,65
10	6	F	fall		10			1	0,91
11	8	M	football		15			1	0,05
12	6	M	fall		14			1	2,47
13	8	M	football		15			1	-0,13
14	6	M	fall		15			1	0,12
15	9	M	fall		9			1	-1,38
16	1	M	fall		15			1	1,76
17	6	M	fall		14			1	1,79
18	7	M	football		14			1	-2,96
19	4	F	Car accident		8			1	1,39
20	12	F	Car accident		12			4	-1,68
21	13	M	fall		11			2	-2,09
Totals	Mean age:7,28	Male: 47,6% Female:52,4%	Male: 7,2 Female:5,9	Fall 71,4% Football:14,3% Car accident:14,3%	Mean:12	GCS 13-15: 47,6% GCS 9-12 : 47,6% GCS ≤8 : 4,8%		Tanner 1: 81% Tanner 2: 4,8% Tanner 3: 4,8% Tanner 4: 9,4%	Total: 0,05 Male: 0,088 Female:0,022

TABLE 1: Demographic characteristics of the study population upon admission

## RESULTS

Endocrine abnormalities, such as GHD, as assessed by low IGF-1 levels, DI and subclinical hypothyroidism were found both at the acute phase as well as at the follow up after TBI (Table 2). Contrary to literature data, prolactin levels were normal during the 1st and 2nd phase, with an increase observed in 12% of the cases 12-18 months after TBI. S100b, a biomarker of brain damage was increased in all children at all phases, indicating a persisting neuronal damage 12-18 months after TBI (Figure 1). There were significant correlations between hormonal and acute phase proteins abnormalities (Table 3) All children demonstrated a good spontaneous recovery with no clinically relevant dysfunction or permanent neurological deficits.

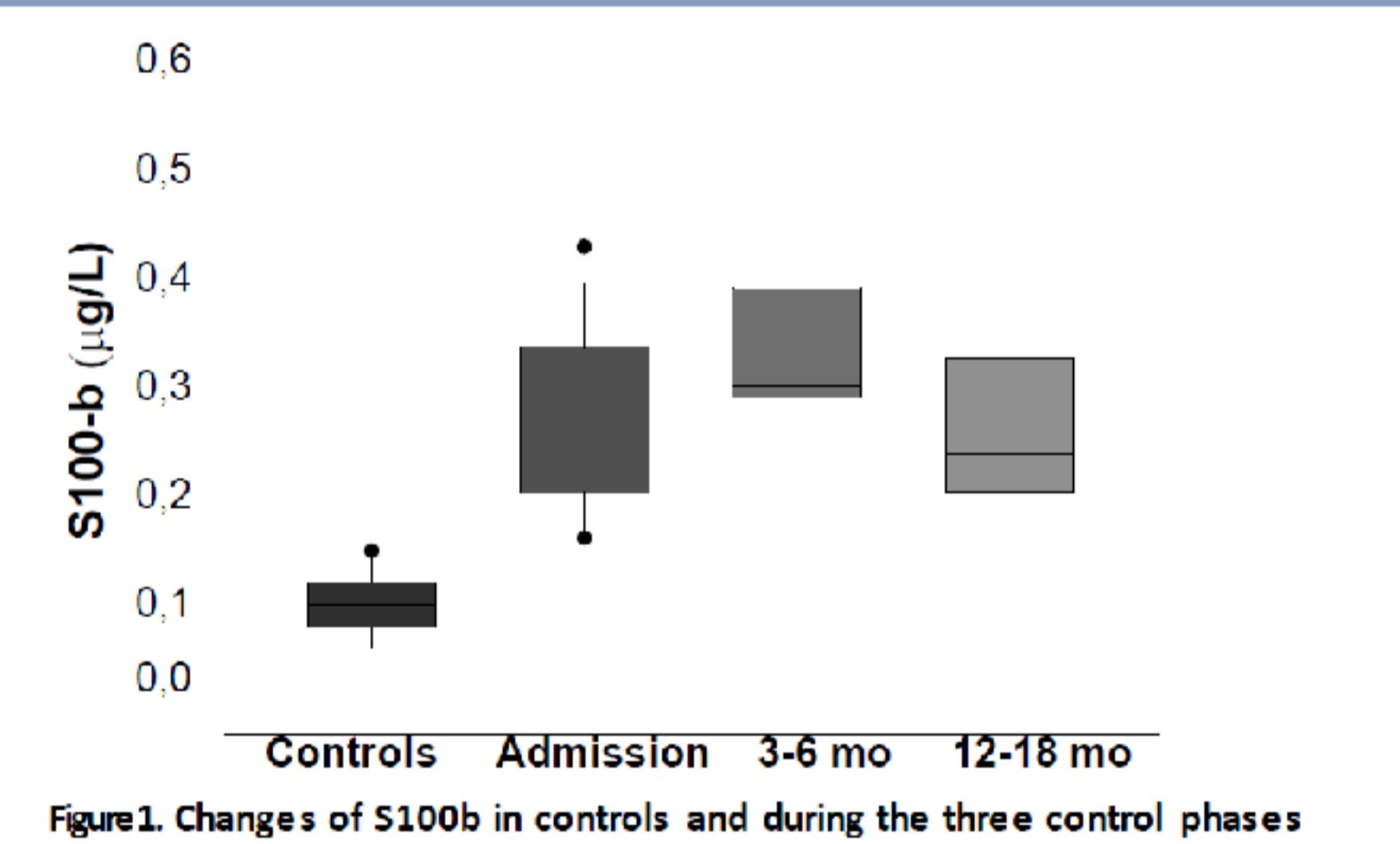


Figure 1. Changes of S100b in controls and during the three control phases

Table 2: Frequency of endocrine abnormalities on admission, 3-6 months and 12-18 months after the traumatic brain injury

	Admission	3-6 months	12-18 months
IGF-1 deficiency	24%	12,5%	6,25%
Diabetes Insipidus	19%	25%	15%
Hypercortisolemia	19%	12,5%	0%
Hypoprolactinemia	14%	6,25%	7,7%
Hyperprolactinemia	0%	0%	12,5%
Subclinical Hypothyroidism	5%	19%	15%

Table 3: Significant correlations between the parameters measured.

On Admission		3-6 months after TBI		12-18 months after TBI	
Parameters	p-value	Parameters	p-value	Parameters	p-value
Cortisol / CRP	0.03	Cortisol / TSH	0.03	PRL / TSH	0,01
Cortisol / S100b	0.03	FSH / IGF-1	0.002		
Cortisol / T4	0.04	S100b / white blood cells	0.01		
PRL / TSH	0.0000				

## CONCLUSIONS

Our results reveal a significant percentage of endocrine dysfunction in children after TBI, both at the acute phase and long after the incident. A subclinical persistent neuronal damage observed in all children calls for long-term surveillance of children post TBI.

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