The hypothalamic-pituitary-adrenal axis changes in non-pituitary brain tumors survivors and the best method of diagnosis secondary adrenal insufficiency

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The number of survivors with non-pituitary brain tumors is constantly increasing and will grow up in the future. There are few data about their ACTH and DHAE-S status while prevalence of secondary adrenal insufficiency (SAI) varies depending on methods of diagnosis.

The aim of our study was to describe changes in the hypothalamic-pituitary-adrenal axis (HPAA) after craniospinal irradiation (CSI) and diagnostic utility of the basal cortisol (BC), DHAE-S and glucagon stimulation test (GST) in comparison with insulin tolerance test (ITT) in this group of patients.

Patients and methods

	Main group	Control
Diagnosis	Medulloblastoma	Healthy
Number of subjects	31 (15 females; 16 males)	11 (6 females; 5 males)
Treatment	M-2000 (total or partial resection of the tumor; chemotherapy; craniospinal irradiation (CSI): for whole brain- 35 Gy; for tumor area- 55 Gy; for spine- 32 Gy)	-
Median age at time of treatment, years	10,8 3,5 (3-15)	
Median age, years	19±3 (15-27)	25 3 (21-30)
Median follow-up, years	8,7±4,7 (2-20)	
Methods of examination	Basal ACTH, basal cortisol and DHAE-S	
	ITT with blood samples for ACTH and cortisol at 0, 15, 30, 45, 60, 90,120 min. GST with blood samples for ACTH and cortisol at 0, 90, 120, 150, 210, 240 min	
Cut-off point for SAI	Cortisol < 550nmol/l in ITT	

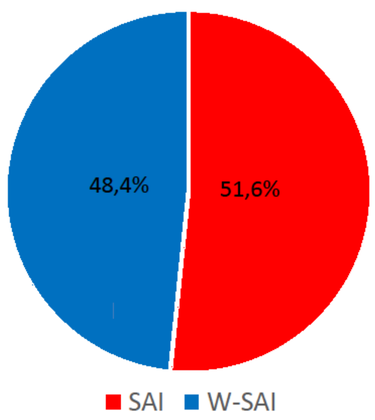
After ITT patients were divided into groups: SAI and without SAI (W-SAI).

Receiver-operating characteristic (ROC) analysis was performed to identify the thresholds for basal cortisol, DHAE-S and GST.

Cut-off points for basal cortisol and DHAE-S levels corresponding to 100% sensitivity (Se) for SAI and 100% specificity (Sp) for patients W-SAI were estimated to select a group of patients not requiring simulative tests

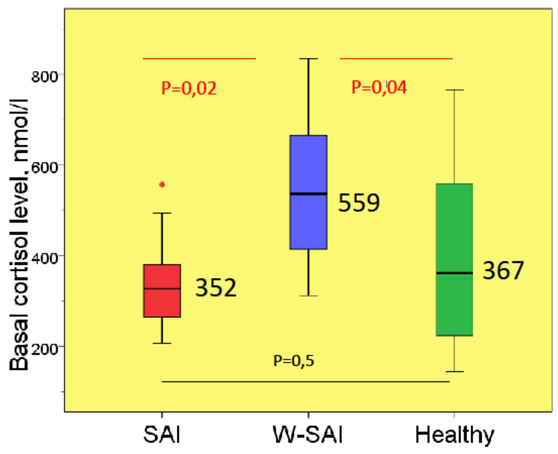
Results

The frequency of SAI following CSI

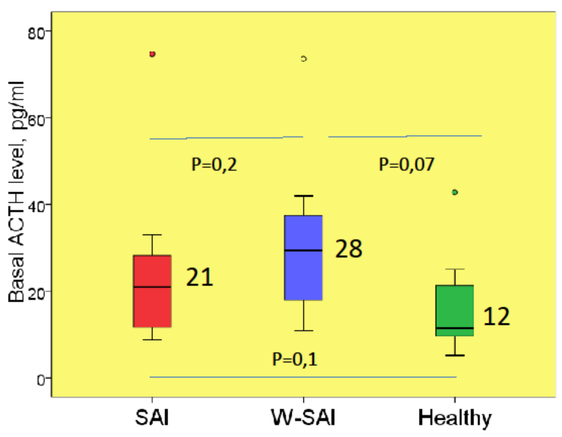


16/31 (51,6%) had SAI by ITT

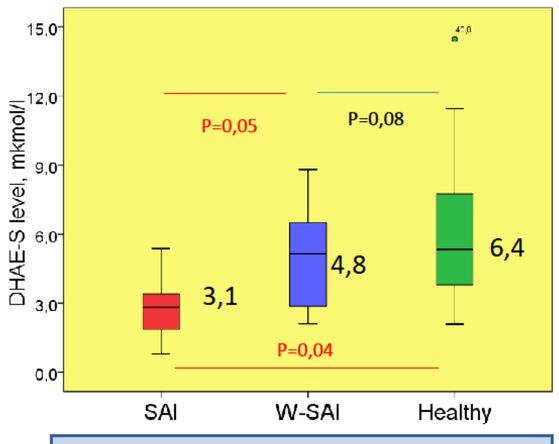
Mean levels of basal hormone (median; 25, 75 percentiles) for subgroups



BC was significantly higher in W-SAI patients compared to healthy controls and SAI



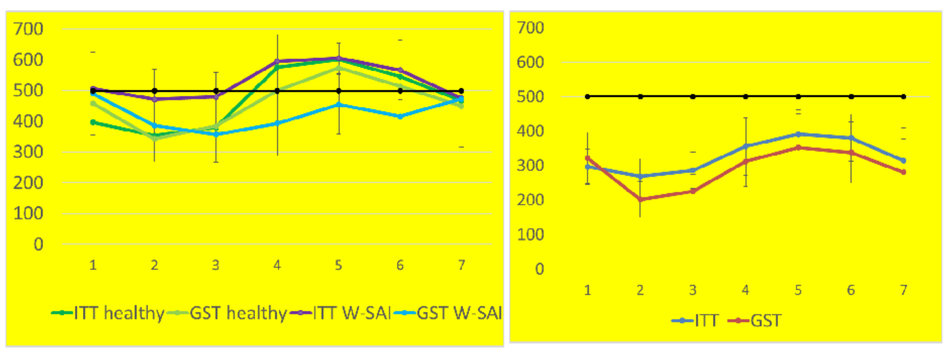
ACTH was the same



SAI-patients had DHAE-S lower than W-SAI and healthy controls

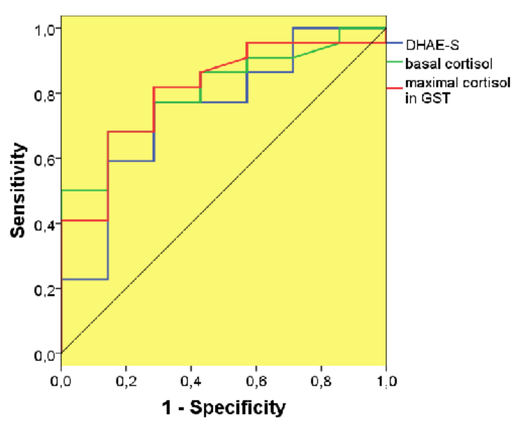
Cortisol level during ITT and GST, nmol/l

healthy and W-SAI	SAI



GST and ITT had the same peak ACTH and cortisol level (p=0,15 and p=0,6, Wilcoxon test). SAI had cortisol level significantly lower than healthy and W-SAI (p<0,01)

ROC- analysis



Area under curve	
Basal cortisol	0,808
DHAE-S	0,747
Maximal cortisol level in GST	0,808

Cut-off points of hormones when simulative tests not require

Hormone	100% Se (patient has SAI)	100% Sp (patient w-SAI)
Basal cortisol, nmol/l	150	500
DHAE-S, pg/ml	2,2	5,7
Cortisol level during GST	250	560

Conclusion:

1. Prevalence of SAI after CRT is high.
2. Patients W-SAI had tendency to increased BC while SAI had lower DHEA-S level.
3. GST may be used as screening simulative test when ITT is contraindicated while BC and DHAE-S levels are in a grey zone.

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