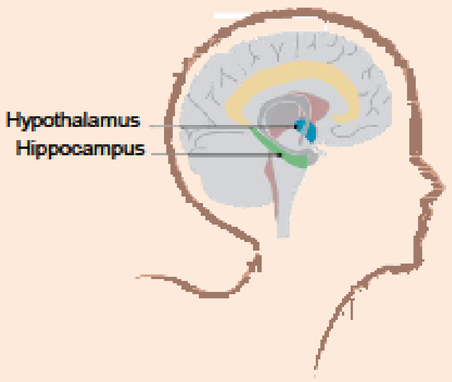

A small hypothalamic volume correlates with impaired cognitive outcome in childhood onset Craniopharyngioma

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CONCLUSIONS

- Adults with hypothalamic damage due to childhood onset craniopharyngioma have impaired memory, spatial ability and executive function.[1]
- Patients with smaller hypothalamic volume have worse cognitive outcome.
- To be able to preserve hypothalamic function we need tailored surgical and radiation strategies.
- Long term follow up should include training programs pertaining to impaired cognitive function.

INTRODUCTION

Hypothalamic damage caused by craniopharyngioma (CP) is related to memory deficits, disturbed attention, and impaired processing speed. [1]

This first study aims to establish a structure to function relationship between hypothalamic volume and cognition in adult patients with childhood-onset (CO) CP.

METHODS AND DESIGN

41 (24 women) surgically treated CO-CP patients (median age at diagnosis; 11 years) from the South Medical Region of Sweden were included.

18 pts had received cranial radiotherapy.

28 pts had panhypopituitarism, 35 were treated with ADH and 32 with GH (Table1).

Time since first operation was 23 years (range 4-49) and median age at investigation was 35 years (range 18-56).

Hypothalamic damage was found in 23 patients.

Comparisons were made with 32 healthy matched controls similar in age and sex.

All pts underwent a battery of cognitive tests. 35 pts underwent magnetic resonance imaging (MRI).

A novel delineation procedure based on T1-weighted MRI and landmarks used in histologically processed postmortem hypothalamic tissue was used to estimate hypothalamic volume.

STATISTICS

Data are presented as median and range (min-max).
Differences between patients and matched population controls were compared using Mann-Whitney U test.
Bivariate correlations were assessed using Spearman rank correlation coefficient.
A P-value < 0.05 was regarded as statistically significant.

RESULTS

CP patients with hypothalamic damage had lower cognitive performance pertaining to vocabulary (P = .02) short term memory (P = .04, P = .01), spatial ability (P = .02) and executive functions (P = .01, P = .02) (Table2).

A significantly positive correlation was found between the tests of vocabulary (r = .352, P = .04) and short term memory (r = .354, P = .04), (r = .357, P = .04) and hypothalamic volume.

Table 1. Characteristics and treatment modalities in 41 patients with childhood onset craniopharyngioma.

Pts with hypothalamic damage (n=23)			Pts without hypothalamic damage (n=18)		
Gender/ Age at invest. (y)/Age at First Operation (y)	Treatment	Hormone substitution	Gender/ Age at invest. (y)/Age at First Operation (yr)	Treatment	Hormone substitution
M/49/12	S	GH/G/T/C/ADH	M/47/5	S	GH/G/T/C/ ADH
M/43/9	S+CRT+In	G/T/C/ADH	M/46/14	S	GH/G/T/C/ ADH
M/38/16	S+CRT	GH/G/T/C/ADH	M/40/17	S	ADH*
M/37/8	S+CRT	GH/G/T/C/ADH	M/37/3	S	GH/G/T/C/ADH
M/35/16	S+CRT	GH/G/T/C/ ADH	M/36/14	S	GH/G/T/C/ ADH
M/35/6	S+CRT+In+SR	GH/G/T/C/ ADH	M/35/14	S	GH/G/T/ADH
M/33/22	S+CRT	GH/G/T/C/	M/27/4	S+CRT	GH/G/T/C/ADH
M/27/7	S+CRT	GH/G/T/C/ADH	F/49/12	S	ADH*
F/56/7	S+CRT	GH/G/T/C/	F/47/12	S	T/ADH*
F/38/20	S	G/T*	F/40/11	S	GH/G/T/C/ADH
F/33/3	S+CRT+In	GH/G/T/C/ ADH	F/38/9	S	GH/G/T/C/ ADH
F/33/5	S+CRT	GH/G/T/C/ADH	F/34/15	S	GH/G/ADH
F/32/15	S+CRT	GH/G/T/C/ ADH	F/32/10	S	GH/G/T/C/ ADH
F/29/13	S	GH/G/T/C/ ADH	F/29/17	S	GH/G/T/C/ ADH
F/28/4	S+CRT	GH/G/T/C/ ADH	F/18/6	S+In+SR	GH/G/T/C/ADH
F/40/22	S+In	GH/G/T/C/ ADH	F/41/11	S	None
M/20/9	S+CRT	None	F/30/5	S+CRT	GH/G/T/C/ ADH
F/36/12	S	GH/G/T/C/ ADH	F/25/21	S	T/ADH
F/35/29	S	GH/G/T/C/ ADH			
M/21/9	S	GH/G/T/C/ADH			
F/19/7	S	GH/G/T/C/ ADH			
F/37/9	S+CRT	GH/G/T/C/ ADH			
F/46/27	S	None			

Abbreviations: C, cortisone; CRT, cranial radiotherapy; F, female; G, gonadal steroids; In, Installation of Yttrium; M, male; SR, Stereotactic Radiosurgery; T, levothyroxine. aNot GH deficient at testing

Figure1. Hypothalamus volume in CP women (N=22) and men (N=13), with and without hypothalamic damage, compared to gender matched controls

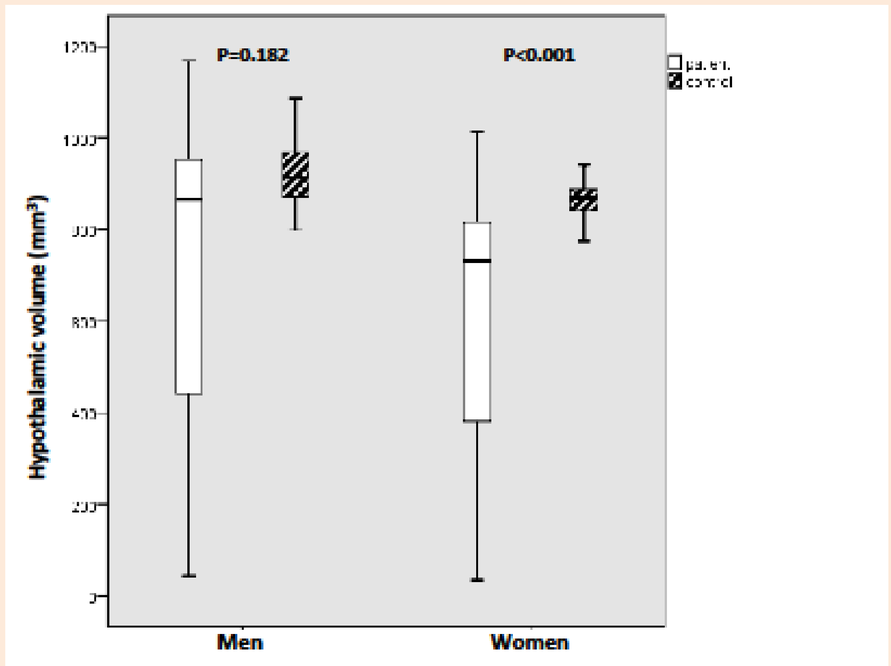

Table 2. Neuropsychological test scores of 23 childhood onset CP patients with hypothalamic damage and their controls.

	Patients (n=23)		Controls (n=23)		P-value
	Median	10th – 90th percentiles	Median	10th – 90th percentiles	
Long term memory					
Test of verbal knowledge					
WAIS Vocabulary	32	18-40	37	29-47	0.021*
Short term memory					
Verbal memory					
WAIS Digit span	28	19-33	27	20-37	0.877
RAVLT					
Trial 1	7	4-9	9	5-11	0.039*
Total score	50	31-63	58	42-70	0.079
Short delay	10	2-15	13	6-15	0.081
Long delay	10	1-15	13	7-15	0.035*
Recognition	13	10-15	15	12-15	0.013*
Visuospatial abilities					
WAIS Block Design	52	32-60	52	31-63	0.991
Rey Komplex Figure					
Immediate recall	19	5-30	25	17-29	0.021*
Delayed recall	17	6-27	25	14-29	0.016*
Recognition	21	20-23	22	19-23	0.872
Executive function					
WAIS coding	74	49-88	75	61-101	0.065
Trail Making					
Test 1	22	19-40	20	13-27	0.088
Test 2	26	20-41	21	16-31	0.122
Test 3	29	22-41	23	15-34	0.022*
Test 4	63	46-105	55	36-98	0.346
Test 5	31	17-45	22	13-32	0.005*

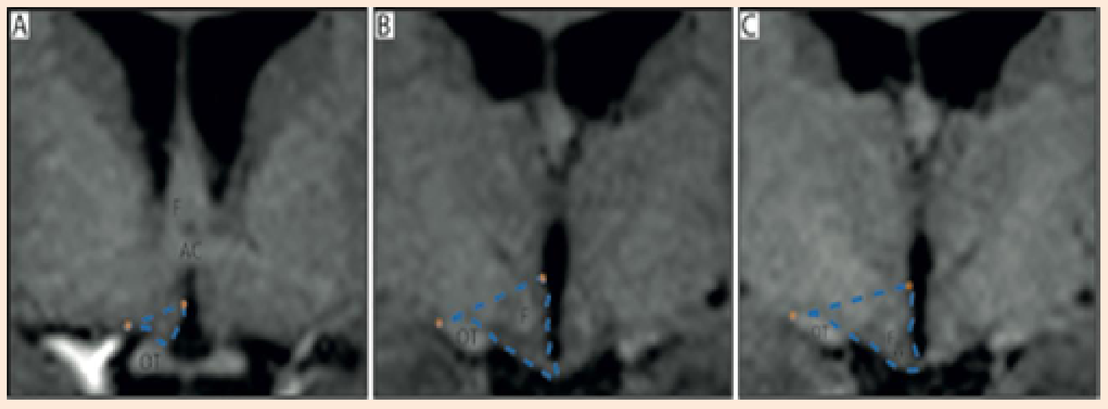

Figure 2. Overview of the boundaries used to delineate the hypothalamus. A-C represent the hypothalamic region in a coronal plane from rostral to caudal direction.
The blue dashed lines illustrate how the hypothalamic region was delineated.
Landmarks such as the hypothalamic sulcus, lateral point of the supraoptic nucleus and the medial edge of the optical tract represented by orange stars were identified for the delineation. A straight line between these two points was drawn to set the superior/lateral border of the area.
Abbreviations: anterior commissure, AC; fornix, F; optical tract, OT; mammillary body, MB.

Layout: Aletia Design, www.aletiadesign.com

1. Fjalldal et al. Hypothalamic involvement predicts cognitive performance and psychosocial health in long-term survivors of childhood craniopharyngioma. J Clin Endocrinol Metab. 2013;98:3253-62.