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Case study

Cognitive function surrounding resection of nonfunctioning pituitary adenomas with suprasellar extension: A prospective matched-control study

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ABSTRACT

Objective: Patients suffering from pituitary adenomas may experience cognitive dysfunctions due to hormonal imbalance or suprasellar tumor extension displacing neural structures. Progressively enlarging or symptomatic nonfunctioning pituitary adenomas with suprasellar extension are frequently resected. The literature on neurocognitive performance surrounding resection of these lesions is sparse.
Methods: A prospective matched-control study was conducted to investigate the impact of nonfunctioning pituitary adenomas with suprasellar extension on preoperative and postoperative cognitive performance. Controls were matched for age, sex, handedness, education, and profession. The neurocognitive test battery included perceptual speed, executive function, visual-spatial and verbal working memory, short- and long-term memory, verbal fluency, fluid intelligence, anxiety, and depression.
Results: Ten patients and 10 healthy controls were matched. Median suprasellar tumor extension scored 8 mm, compression of frontal lobe parenchyma was present in all cases. Median sagittal tumor diameter was 21 mm. Preoperatively, patients scored worse in perceptual speed and short-term memory tasks. All patients underwent surgical resection either through a transnasal, transsphenoidal approach or a supraorbital frontolateral keyhole approach. The short-term memory deficit disappeared one week after surgery. Perceptual speed recovered within two months after surgical therapy. None of the patients experienced worsening of cognitive function. Routine postoperative imaging at six months did not reveal displacement of neural structures or surgery-related complications in any of the patients.
Conclusion: Patients suffering from nonfunctioning pituitary adenomas with suprasellar extension may experience preoperative impairments in some neurocognitive domains that resolve within two months after surgery. The risk for cognitive deterioration with surgery appears to be low.

1. Introduction

Pituitary adenomas are benign WHO I extra-axial brain tumors. Depending on their ability to secrete hormones, they are classified either functioning or nonfunctioning. Approximately 15–30% of all pituitary adenomas are considered nonfunctioning. These patients are either diagnosed incidentally or due to mass effect on the optic pathways leading to visual alterations, headaches, or hypopituitarism [1]. Functioning pituitary adenomas may cause hyperprolactinemia [2], Cushing's disease [3], or acromegaly [4] and are associated with neurocognitive impairments in various cognitive

Abbreviations: Corsi, corsi block-tapping test; DSST, digit symbol substitution test; DST, digit span test; HADS, hospital anxiety and depression scale; KPS, Karnofsky performance status; P0, pituitary adenoma patients preoperatively; P1, pituitary adenoma patients one week after surgery; P2, pituitary adenoma patients two months after surgery; PC0, control for preoperative pituitary adenoma patients; PC1, control for postoperative pituitary adenoma patients; PC2, control for pituitary adenoma patients at follow-up; RWT, Regensburger Verbal Fluency Test; Stroop, Stroop color-word test; TMT A, trail making test A; TMT B, trail making test B; VLMT, verbal learning and memory test; WIE, Adult Intelligence Scale matrix reasoning.

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domains. In nonfunctioning pituitary adenomas, however, the suprasellar portion appears to result in neurocognitive impairments [5].

Treatment options for pituitary adenomas include observation, medical therapy, radiosurgery, surgical resection, and/or radiotherapy. Progressively enlarging or symptomatic nonfunctioning adenomas are frequently referred for surgical resection [1] via a transnasal transsphenoidal or a transcranial approach [6–8]. Adjuvant radiotherapy is administered for tumor remnants or recurrence. Radiotherapy alone may be treatment of choice in patients suffering from a poor general health or refuse surgery [9]. Each modality, especially surgery and radiotherapy, may have potential deleterious effects on cognitive performance [10]. Peace et al. found that patients undergoing transcranial tumor resection to have more deficits than patients undergoing transsphenoidal resection [11]. There is some evidence that adjuvant radiotherapy does not add risk for neurocognitive decline compared to surgical therapy alone [12,13].

The literature on neurocognitive performance surrounding resection of nonfunctioning pituitary adenomas with suprasellar extension is sparse. Specifically, the early postoperative cognitive course has not been evaluated. Here, we performed a matched-control study in these with emphasis on the early postoperative cognitive course and correlation with postoperative imaging.

2. Methods

We performed a prospective study evaluating neurocognitive dysfunction in patients with a newly-diagnosed brain tumor after approval by the local ethics committee. For the present study, we screened patients with pituitary adenomas that were admitted to the neurosurgical department of a major German academic institution from October 2014 to February 2015. Inclusion criteria were a newly-diagnosed sellar lesion with suprasellar extension compatible with a pituitary adenoma, patient consent for study participation, and a Karnofsky performance status (KPS) of 60 or more. Exclusion criteria were factors that may interfere with the patients neurocognitive performance such as history of psychiatric disorders, intake of sedative medication (tranquilizers, antipsychotic drugs), or obvious neuropsychological deficits (i.e. psychomotor impairment, lack of attention or comprehension during neurological exam). Visual deficits impairing reading or visuo-spatial skills were other exclusion criteria. Histopathology of tumor specimens obtained during surgical resection confirmed pituitary adenoma in all cases.

2.1. Neurocognitive testing

The cognitive test battery included multiple tests to assess various cognitive domains. We assessed perceptual speed, executive function, visual-spatial and verbal working memory, short- and long-term memory, and verbal fluency on a paper–pencil basis (Table 1). Moreover, fluid intelligence and the German version of the hospital anxiety and depression scale (HADS) was applied to control for potential confounders of neurocognitive function [14,15]. The sequence of neurocognitive testis was as following: DSST, DST, Corsi, verbal learning and memory test (VLMT) memorizing, Stroop, TMT A, TMT B, Regensburger Verbal Fluency Test (RWT), VLMT recognition, Wechsler Adult Intelligence Scale matrix reasoning (WIE; German adaption of WAIS-III), and HADS and required 60 to 75 min for completion.

2.2. Statistical analysis

Statistical analysis was performed using the software package SPSS (SPSS version 23; SPSS, Inc., Chicago, IL). Chi-square test, ANOVA, (repeated measures) ANCOVA, and MANCOVA were performed where appropriate. Patients and matched healthy controls were tested for homogeneity in age, gender, anxiety and depression, educational level, and intelligence. Mean ranks of education and profession were compared via the Mann–Whitney-*U* test. Preoperatively and at one week after resection, analysis of variance showed significantly reduced anxiety scores (i.e. increased anxiety level) in the patient cohort. Hence, statistical analysis was performed with the HADS anxiety score as covariate where appropriate. Statistical significance was set to $p < 0.05$. In cases of multiple comparisons, a Bonferroni correction was applied to adjust the level of statistical significance. Hence, statistical significance was set to $p < 0.025$.

3. Results

Ten patients and 10 healthy controls were enrolled (Table 2). Matching was performed for age, gender, handedness, education, and profession. Controls were assessed at the same times as the patients. Out of the 10 preoperatively tested patients, one refused

Table 1
Neurocognitive test battery.

Perceptual speed	DSST TMT A	Von Aster et al. (2006) and Tombaugh (2004)
Executive function	TMT B Stroop	Bowie and Harvey (2006) and Jensen and Rohwer (1966)
Working memory	Corsi DST	Kessels et al. (2000) and Von Aster et al. (2006)
Short-term and long-term memory	Memorizing adjusted recognition	Helmstaedter et al. (2001)
Verbal fluency	S words G/R words Forenames	Aschenbrenner et al. (2000)

Table 2
Pituitary adenoma patients' demographic and clinical data.

	Control group	Patient group	*p*-Value
No. of participants	10	10	
Age	62.0 ± 13.4	60.7 ± 11.8	0.820
Sex (F/M)	5/5	4/6	1.000
Handedness (right/left)	10/0	9/1	1.000
Anxiety preop. (HADS)	12.6 ± 2.3	9.9 ± 3.2	0.044
Depression preop. (HADS)	9.7 ± 1.3	9.5 ± 2.7	0.837
Intelligence preop. (WIE)	7.1 ± 2.6	5.6 ± 2.5	0.198
Karnofsky performance status (median (range))	N/A	90 (80–100)	
Tumor diameter (median (range))	N/A	21 mm (11–32)	
Neurological presentation Incidental/visual deterioration/other	N/A	4/5/1	