Neurocognitive Function Surrounding the Resection of Frontal WHO Grade I Meningiomas: A Prospective Matched-Control Study

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■ OBJECTIVE: **Patients with intracranial meningiomas can experience neurocognitive dysfunctions in specific cognitive domains depending on tumor location and size. The literature regarding cognitive function surrounding the resection of frontal meningiomas is sparse.**

■ METHODS: **We performed a prospective matched-control study to investigate the cognitive performance of frontal meningioma patients undergoing resection. The neurocognitive status 1 week and 2 months after resection was compared with the preoperative status and matched-controls. Matching was performed for age, sex, handedness, education, and profession. An extensive test battery was used to assess perceptual speed, executive function, visual-spatial and verbal working memory, short- and long-term memory, verbal fluency, fluid intelligence, anxiety, and depression.**

■ RESULTS: **Twelve patients with frontal World Health Organization grade I meningioma and 12 matched-controls underwent cognitive testing. Macroscopically, complete removal was achieved in all cases. Comparison of patients and controls revealed significant cognitive impairments in perceptual speed, executive function, short-term memory, and verbal fluency preoperatively and postoperatively. At 2 months' follow-up, perceptual speed and verbal fluency were still significantly impaired, whereas executive function and short-term memory were equal to that in the control group. None of the patients experienced cognitive deterioration after surgical therapy.**

■ CONCLUSION: **Patients with frontal meningiomas display preoperative and postoperative deficits in perceptual speed, executive function, short-term memory, and verbal fluency. The risk for cognitive deterioration owing to surgical resection is low. Within the first two months after surgery, executive function and short-term memory appear to recover.**

INTRODUCTION

Traditionally, the extent of tumor resection, progression free survival, and overall survival are the most important outcome measures in neurosurgical oncology. However, with increasingly successful treatment of brain tumors, cognitive function, cognitive rehabilitation, and health-related quality of life draw more attention.[1,2] This is of particular importance in meningioma patients in whom complete surgical resection is

Key words
- Cognition
- Frontal
- Meningioma
- Neurocognitive assessment

Abbreviations and Acronyms
CM0: Control for preoperative meningioma patients
CM1: Control for postoperative meningioma patients
CM2: Control for meningioma patients at follow-up
Corsi: Corsi block-tapping test
DST: Digit span test
DSST: Digit symbol substitution test
HADS: Hospital anxiety and depression scale
INC: Naming colors of incongruous inked color-names
M0: Meningioma patients preoperatively
M1: Meningioma patients 1 week after surgery
M2: Meningioma patients 2 months after surgery
RWT: Regensburger Verbal Fluency Test
Stroop: Stroop color-word test
TMT: Trail making test
VLMT: Verbal learning and memory test
WHO: World Health Organization
WIE: Wechsler Adult Intelligence Scale matrix reasoning

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generally curative.[3-5] Preoperative neurocognitive deficits can even affect the patient's decision to pursue therapy. Postoperative dysfunctions can impair the patient's social and professional abilities and lead to a loss of self-sufficiency. Detection of neurocognitive deficits and, at a later stage, initiation of neurocognitive rehabilitation programs are required to optimize the neurocognitive outcome.[6-8]

Numerous studies of neurocognitive function in brain tumor patients are available[2]; however, many lack adequate pretreatment assessment or control for learning effects. In addition, factors such as age, anxiety, depression, intelligence, education, and profession need to be considered for analysis, as all these factors can alter test results. Moreover, some studies do not report data for test intervals, or they did not use test intervals scheduled for specific dates. Finally, the use of inadequate test batteries, such as test batteries developed for dementia, represents another issue. Data regarding neurocognitive function in meningioma patients is sparse.[9] In particular, the early postoperative phase has not been elucidated, although this is the time when most patients return to their social and professional environment. Hence, we developed a protocol with emphasis on aforementioned factors to evaluate the neurocognitive function surrounding the resection of frontal World Health Organization (WHO) grade I meningiomas and present our results herein.

METHODS

Following approval by the local ethics committee, a prospective study evaluating neurocognitive function in patients with a newly diagnosed brain tumor was performed at a major German academic institution. From October 2014 to February 2015, all patients who were admitted to the neurosurgical department with a new diagnosis of a brain tumor requiring surgical resection were screened for meningioma diagnosis. For the presented study, inclusion criteria were a newly diagnosed, supratentorial brain tumor based on radiographic features compatible with a meningioma, patient consent for study participation, and a Karnofsky performance status score of 60 or more. Exclusion criteria were the following factors that potentially interfere with the patients neurocognitive performance: history of psychiatric disorders, intake of sedative medication (tranquilizers, antipsychotic drugs), or obvious neuropsychological deficits (e.g., psychomotor impairment, lack of attention or comprehension during neurological examination). Patients with paralysis of the dominant hand, disabling visual deficits, or aphasia were also excluded because of potential interference with test performance that could obscure adequate analysis. Diagnosis was confirmed with histopathologic analysis of specimens obtained during surgical resection of the tumor. Controls were recruited using an employee survey and eventually tested between January and May 2016. Imaging material was independently studied by a consultant neuroradiologist (A.S.) and a neurosurgical resident (P.H.). Discrepancies were resolved by discussion.

Neurocognitive Testing

We assessed perceptual speed, executive function, visual-spatial and verbal working memory, fluid intelligence, short- and long-term memory, and verbal fluency on a paper-pencil basis preoperatively, at 1 week postoperatively, and 2 months after resection at follow-up (Table 1). Moreover, the German version of the hospital anxiety and depression scale (HADS) was applied to control for potential confounders of neurocognitive function.

Perceptual Speed. Perceptual speed was assessed using the digit symbol substitution test (DSST) and trail making test (TMT) A.[10,11]

Executive Function. The TMT B and Stroop color-word test (Stroop) were applied to evaluate executive function.[12,13]

Working Memory. The Corsi block-tapping test (Corsi) and the digit span test (DST) were performed to measure visuospatial and verbal working memory.[10,14]

Fluid Intelligence. The Wechsler Adult Intelligence Scale matrix reasoning (WIE; German adaption of WAIS-III) was conducted to examines fluid intelligence[10]

Short- and Long-Term Memory. Short- and long-term memory was assessed with the memorizing and adjusted recognition elements of the verbal learning and memory test (VLMT).[15]

Verbal Fluency. Verbal fluency was tested using three elements of the Regensburger Verbal Fluency Test (RWT)[16]:

- S words—phonemic (i.e. formal lexical) verbal fluency
- G/R words—phonemic category switch
- Forenames—semantic verbal fluency.

Hospital Anxiety and Depression Scale. The German version of the HADS was applied to control for potential confounders of cognitive performance.[17,18]

Sequence of neurocognitive testing was DSST, DST, Corsi, VLMT Memorizing, Stroop, TMT A, TMT B, RWT, VLMT Recognition, WIE, and HADS, requiring 60 to 75 minutes for completion.

Statistical Analysis

Statistical analysis was performed using the software package SPSS (SPSS version 23; SPSS, Inc., Chicago, Illinois, USA). We performed a χ^2 test, analysis of variance, (repeated measures) analysis of covariance, and multivariate analysis of covariance. Patient groups and their matched-control groups were tested for homogeneity in age, sex, anxiety and depression, educational level, and intelligence. The Mann-Whitney U test was applied to compare mean ranks of education and job between the patient and control groups. Statistical analysis was performed with the HADS score as a covariate when appropriate. Bonferroni correction for multiple comparisons was applied and level of statistical significance set to $P < 0.025$.

RESULTS

Twelve consecutive frontal meningioma patients and 12 healthy matched controls were enrolled (Table 2). Matching was performed for the following variables: age, sex, handedness, education, and profession. Of the 12 patients who underwent preoperative testing, 10 and 11 patients were tested