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Full Length Article

Neurocognitive status in patients with newly-diagnosed brain tumors in good neurological condition: The impact of tumor type, volume, and location

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ABSTRACT

Objective: Neurocognitive function is of great importance in patients with brain tumors. Even patients in good neurological condition may suffer from neurocognitive dysfunction that affects their daily living. The purpose of the present study was to identify risk factors for neurocognitive dysfunction in patients suffering from common supratentorial brain tumors with minor neurological deficits.
Methods: A prospective study evaluating neurocognitive dysfunction in patients with a newly-diagnosed brain tumor in good neurological condition was performed at a major German academic institution. Patients underwent extensive neurocognitive testing assessing perceptual speed, executive function, visual-spatial and verbal working memory, short- and long-term memory, verbal fluency, fluid intelligence, anxiety, and depression. For each patient, a healthy control was pair-matched based on age, sex, handedness, and profession.
Results: A total of 46 patients and 46 healthy controls underwent neurocognitive testing. Patients suffered from glioblastoma multiforme (10), cerebral metastasis (10), pituitary adenoma (13), or meningioma (13). There was neither any difference in age, educational level, fluid intelligence, neurological deficits, and anxiety nor in any depression scores between tumor subgroups. Overall, neurocognitive performance was significantly worse in patients compared to healthy controls. Larger tumor volume, frontal location, and left/dominant hemisphere were associated with worse executive functioning and verbal fluency. Additionally, larger tumors and left/dominant location correlated with impairments on perceptual speed tasks. Frontal tumor location was related to worse performance in visual-spatial and short- and long-term memory. Tumor type, clinical presentation, and patient self-awareness were not associated with specific neurocognitive impairments.
Conclusions: Patients suffering from newly-diagnosed brain tumors presenting in good neurological condition display neurocognitive impairments in various domains. Larger tumor volumes, frontal location, and left/dominant hemisphere are important predictors for potential neurocognitive deficits. Tumor type, clinical presentation, or self-awareness are less significant at the time of diagnosis.

1. Introduction

Neurocognitive dysfunction is a significant problem in patients that suffer from brain tumors. Whereas the success of treatment in neurosurgical oncology is traditionally measured by the extent of tumor resection, progression free survival, and overall survival, neurocognitive dysfunction has drawn attention as another important outcome measure [1–3]. Particularly in the early stages of the disease, neurocognitive impairment tends to be subtle and may therefore remain under recognized due to a lack of appropriate

Abbreviations: Corsi, Corsi block-tapping test; DSST, digit symbol substitution test; DST, digit span test; HADS, hospital anxiety and depression scale; INC, naming colors of incongruous inked color-names; KPS, Karnofsky performance status; NCS, naming colored stripes; RCN, reading color names; 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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testing and patient self-awareness. Nevertheless, it may affect the patient's social and professional abilities and ultimately may lead to a loss of self-sufficiency and quality of life. In addition, neurocognitive dysfunction may affect the patient's decision to pursue therapy. With improvements in the treatment of brain tumors such as decreased surgical morbidity and mortality, neurocognitive impairments become more relevant. While numerous studies focused on the decline of neurocognitive function in brain tumor patients following treatment, only few data are available on treatment and prevention strategies for neurocognitive deficits early in the disease course [4]. New strategies are needed to diagnose neurocognitive deficits in brain tumor patients early to initiate appropriate neurocognitive rehabilitation [5,6]. Functional magnetic resonance imaging assessing neuropsychological domains and additional intraoperative neuropsychological assessment may be useful trying to preserve cognitive function in brain tumor patients [7]. Early work by Gehring et al. showed beneficial effects of cognitive rehabilitation in patients with diffuse and anaplastic gliomas and identified predictors of improvement of neuropsychological function [5,8]. However, a fundamental understanding of the course of cognitive alteration is required to substantially address the issue of neurocognitive impairment [9]. The existing body of literature on the preoperative cognitive status is sparse. The purpose of this study was to correlate parameters such as clinical presentation, tumor type, volume, and location with neurocognitive dysfunction in patients with a newly-diagnosed supratentorial brain tumor deemed suitable for surgical resection.

2. Methods

A prospective study evaluating neurocognitive dysfunction in patients with a newly diagnosed brain tumor was performed at the Department of Neurosurgery, Saarland University Medical Center from October 2014 to July 2015 after approval by the local ethics committee. Patients admitted to the neurosurgical department with a diagnosis of brain tumor requiring surgical resection were screened for eligibility to participate in this study. Inclusion criteria for the herein presented study were a newly diagnosed, supratentorial brain tumor based on radiographic features compatible with glioblastoma multiforme, cerebral metastasis, pituitary adenoma, and meningioma and a Karnofsky performance status (KPS) of 60 or more. Exclusion criteria were a 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) that could interfere with the neurocognitive status. To minimize the influence of neurologic deficits on the testing, patients suffering from paralysis of dominant hand, visual impairments, or aphasia were also excluded. Diagnosis was confirmed by histopathology obtained during surgical resection of the tumor. Patients were screened until 10–13 patients were enrolled per tumor type. Tumor volume was calculated from gadolinium-enhanced T1 weighted MRI-sequences using an ellipsoid/spheric equation. Healthy controls were recruited using an employee survey. Matching was performed based on age, sex, handedness, and profession. Neurocognitive assessment of healthy controls was performed between January and May 2016.

2.1. Neurocognitive testing

Neurocognitive testing was performed on a paper-and-pencil test basis to assess perceptual speed, executive function, visual-spatial and verbal working memory, fluid intelligence, short- and long-term memory, and verbal fluency.

2.1.1. Perceptual speed

The digit symbol substitution test (DSST) and trail making test A (TMT A) were applied to assess perceptual speed. The DSST consists of nine defined digit-symbol pairs. Within 90 s, the patient has to draw the corresponding symbols to a list of digits. The correct number is counted and analyzed [10]. The TMT A consists of 25 consecutive encircled targets numbered from 1 to 25 that have to be connected sequentially and time to completion is measured [11].

2.1.2. Executive function

To evaluate executive function, patients performed the trail making test B (TMT B) and Stroop color-word test (Stroop). The TMT B consists of encircled numbers from 1 to 13 and encircled letters from A to L that have to be connected in the correct numerical and alphabetical order in an alternating sequence. Time to completion is measured [12]. The Stoop is based on the time required for reading color names (RCN), naming colored stripes (NCS), and naming colors of incongruous inked color-names (INC). For analysis, the mean reaction times of congruent variables RCN and NCS are compared to the incongruent variable INC [13].

2.1.3. Working memory

The Corsi block-tapping test (Corsi) measures visual-spatial working memory. The digit span test (DST) measures verbal working memory. During the Corsi the examiner taps an increasing combination of blocks that have to be repeated in the correct order by the patient. Testing stops after two consecutive incorrect rounds. The number of correct rounds is recorded [14]. The DST consists of increasing series of digits that are read to the patient who has to recapitulate immediately to the examiner. Likewise for the Corsi, DST testing stops after two consecutive incorrect rounds. The number of correct rounds is recorded [10].

2.1.4. Fluid intelligence

The Wechsler Adult Intelligence Scale matrix reasoning (WIE; German adaption of WAIS-III) examines fluid intelligence. Patients have 5 min to answer 13 matrix reasoning quests in single choice format [10].

2.1.5. Short- and long-term memory

Short- and long-term memory was assessed by the verbal learning and memory test (VLMT). The examiner reads a list of 15 words to the patient who has to repeat these words afterwards. After 5 rounds the sum of remembered words of each round is recorded (short-term memory). After a series of other tests (30 min), the examiner reads out a list of words that contain the original 15 words from the list but also 35 distracting words. The patient has to decide for each word whether it was in the original list or not. The number of correctly recognized minus false-positive items is called adjusted recognition and quantifies both short-term and long-term memory elements [15].

2.1.6. Verbal fluency

Verbal fluency was tested using a short version of the Regensburger Verbal Fluency Test (RWT). This test consists of four subtasks. Within 60 s, the patient was asked (1) to name words beginning with the letter "S" ("S words" – phonemic (i.e. formal lexical) verbal fluency), (2) to alternately name words beginning with the letters "G" and "R" ("G/R words" – phonemic category switch), (3) to call forenames (semantic verbal fluency). The number of correct responses was recorded [16].

2.1.7. Hospital anxiety and depression scale

The German version of the hospital anxiety and depression scale (HADS) [17] was conducted to quantify potential confounders of cognitive performance [18]. The HADS is a 14-item self-rating