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The Role of Neuropsychology in the Assessment and Management of CNS Tumors

*Hoffnung DS**

CHI Health Alegent Creighton Clinic, Immanuel Medical Center, USA

Abstract

Neuropsychological testing plays an important role in the assessment and management of CNS tumors. Evaluation prior to the start of treatment provides insights into the functional impact of tumors and establishes a baseline against which later functioning can be compared. Testing of language and motor functions during awake surgery assists in the protection of eloquent cortex. Assessment during and after adjuvant a therapy identifies the effects of treatment, and assists in making decisions regarding palliative care. Serial testing over time may detect regrowth of tumor prior to radiographic evidence of recurrence and predict survival.

Keywords: Cognition; Surgery; Assessment; Outcome; Memory; Language

Introduction

Neuropsychology, a sub-specialty of clinical psychology, specializes in the relationship between the brain, thinking, and behavior. A neuropsychologist's expertise in assessing cognition, emotional functions, and behavior, as these functions relate to the brain and central nervous system, allows them to play an important role in the assessment and treatment of individuals diagnosed with CNS tumors. Although brain tumor localization and classification is primarily accomplished through MRI, spectroscopy, and biopsy of brain tissue, these techniques do not provide information regarding the functional impact of the tumor on thinking, emotions, and behavior. Both primary (benign or malignant) and metastatic brain tumors can produce a range of global and/or domain-specific impairments in cognitive functions, with reports in the literature varying from around 13% to over 90%, depending on the characteristics of the tumors studied, patient demographics, and treatments received [1]. Neurocognitive outcome strongly influences patient- and family-perceived quality of life of individuals treated for CNS tumors [2], and neuropsychological testing should be included in the assessment and treatment plans of all individuals with CNS tumors, when medically feasible. As Miceli et al. [3] (2011) note: "Over the past 30 years, the approach to the treatment and follow-up of patients with brain tumors has changed profoundly". With increased life expectancy comes the need for increased attention to the impact of tumor and tumor therapies on the person as a whole, and including neuropsychological evaluation prior to surgery, during awake craniotomy, during and after adjuvant therapies have been completed, and with serial testing over time should be part of the standard practice of care for the assessment and management of individuals with CNS tumors.

Evaluation prior to treatment

Neuropsychological testing involves the comprehensive assessment of neurocognitive functions across multiple domains, including attention, expressive and receptive language, visuospatial functioning, learning and memory, reasoning; fine motor speed and dexterity, and emotions and behavior. When an individual is known to have sustained a stroke or brain injury, neuropsychological testing serves to identify the impact of these insults to the brain, and also helps to distinguish between the direct effects of the lesion, the indirect effects of non-neurological factors like depression, anxiety, sleep disturbance and/or pain; and any premorbid deficits that may have been present before the 'new' insult. When a diagnosis is unknown or unclear, review of symptoms and history, and then comparison of the pattern of preserved and impaired cognitive functions seen on neuropsychological testing to the known and/or expected effects of specific medical, neurological, or psychiatric conditions leads to improved diagnostic clarity. In the case of CNS tumor, evaluation prior to surgical resection and the start of treatment provides insight into the functional impact of tumors and establishes a baseline against which later functioning can be compared.

Individuals vary greatly, and performance on neuropsychological measures can be influenced

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Correspondence:
Deborah S. Hoffnung, CHI Health Alegent Creighton Clinic, Immanuel Medical Center, 6829 North 72nd Street, Suite 4700, Omaha, NE 68122, USA, Tel: +1 402 572-2169; Fax: +1 402 572-3749; E-mail: Deborah.hoffnung@alegent.org

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by a wide range of factors, including age, gender, socioeconomic and cultural circumstances, education, sensory or motor deficits, and longstanding (non-pathological) weaknesses in language, attention, and/or memory [4]. Evaluation prior to surgical resection and adjuvant therapies identifies individual cognitive differences unrelated to the tumor and/or treatment effects, so that later testing is a more accurate assessment of the effects of treatment. Neuropsychological testing can also identify functional disability that is not captured in imaging and/or neurologic exams, and not predicted by tumor type or volume [5]. While rapidly progressing tumors may cause significant physical and cognitive impairment due to increased intracranial pressure and lesion momentum that outpaces brain plasticity, slowly growing tumors may still allow the brain to adapt to the physical presence of the tumor, but affect cognitive functions less predictably [6]. For example, Noll et al. [7] (2015) noted greater difficulties in verbal learning, processing speed, executive functions, and language in a sample of individuals with histopathologically-confirmed grade IV gliomas in the LEFT temporal lobe relative to those with grade II and grade III lesions; and Meyers & Cantor (2003) provided the example of an individual who showed no evidence of language, memory, or other cognitive impairment after extensive resection of a large LEFT hemisphere tumor that had likely been present for 20 plus years, versus an individual who developed global aphasia, alexia, and agraphia over a period of two weeks secondary to the presence of a smaller but rapidly progressing tumor in the same region [8]. On the other hand, Cochereau and colleagues' (2016) analysis of individuals with incidentally-discovered WHO grade II gliomas noted disturbed functions on a set of neurocognitive tests administered the day before surgery in 60% of the patients studied (53% with executive dysfunction, 20% working memory impairment, and 6% with attentional disturbances), none of whom had shown any other obvious clinical consequences of their tumor (e.g., seizures, sensory or motor complaints) [9]. When a wait-and-see attitude is being considered, identification of the cognitive consequences of tumor could spur the decision to perform resection earlier, or reassure the patient and treatment team that continued observation is acceptable in the absence of signs of functional impairment.

Awake craniotomy

Another role for neuropsychology in the assessment and management of CNS tumors is the evaluation of cognitive and sensorimotor functions during awake craniotomy. There is a growing body of evidence that suggests better outcomes, including longer progression-free survival and superior seizure control, with greater extent of resection (EOR) and decreased contrast-enhancing residual tumor volume [10,11]. However, in patients with tumors infiltrating regions of 'functional' brain, the extent of resection may be limited by the desire to preserve cognitive and motor functions, and in the absence of clear parameters regarding the location of these eloquent regions, the surgeon may be less prone to perform an extensive resection [12]. Analyses dating back to Ojemann's seminal cortical stimulation studies in the 1970s have shown that the cortical whereabouts of language and other cognitive functions varies from person to person, and this makes it risky to rely solely on anatomical landmarks and imaging to identify these regions in the individual patient [13]. Functional imaging techniques like MRI or PET can identify the areas that *participate* in language, motor, and sensory functions, whereas electrocortical stimulation mapping of neurocognitive functions during awake craniotomy allows for the specification of sites that are *essential* for preservation of these functions. During the awake craniotomy, the neuropsychologist administers naming, repetition, and automatic speech tasks; monitors for (involuntary) movements in the mouth, face, and hands; and directs the patient to notice any sensory symptoms as the surgeon stimulates selected sites on the surface of the brain. Speech hesitancy or arrest, involuntary movements, and the patient's reporting of unusual sensations are reported back to surgeon in 'real time', and this allows for the demarcation of cortex with an essential role in language, motor, and/or sensory functions that should be preserved, from areas that can be safely included in the approach to, and resection of, the tumor. As De Witt Hamer et al.[14] found in their 2012 meta-analysis of intraoperative stimulation in individuals undergoing surgical resection of gliomas, the use of direct electrical stimulation allowed for a better EOR (75% of tumor resected completely versus 58% without stimulation), and was associated with a lower risk of late postoperative neurological deficits (3.4% versus 8.2%). Current efforts are now turning to the development of techniques to identify and spare other non-linguistic cognitive functions, like executive skills, attention, working memory, and praxis, which are not presently mapped, and which may not fare as well after tumor removal [15].

Assessment during and after adjuvant therapies

Neuropsychological testing after surgery, but before adjuvant therapies are started, may predict survival. In Johnson et al.[16] (retrospective) analysis of 91 patients with newly diagnosed glioblastoma who completed neuropsychological assessment after tumor resection, cognitive impairment, as measured by specific neuropsychological tests (and particularly, measures of executive function and attention), was independently associated with poor prognosis, even within patient subgroups defined by RTOG Recursive Partitioning Analysis (RPA) class. The treatments used to combat CNS tumor also put healthy brain tissue at risk, and screening of neurocognitive functions with neuropsychological measures during and after treatment with chemotherapy and radiation can provide information that may be missed with a brief mental status exam. As Meyers and Wefel emphasized in their 2003 review of endpoints used in brain tumor clinical trials, the MMSE is a weak tool for detecting declines in memory and executive functioning in individuals being treated for brain tumor [17], and measurements that assess an individual's ability to perform activities of daily living, such as the widely used Karnofsky Performance Score (KPS) do not address cognitive functions at all. Instead, a battery of neurocognitive measures selected for brevity, repeatability, reliability and validity, and sensitivity to change can more effectively delineate the specific effects of treatment, guide the selection of supportive therapies (e.g., medications and rehabilitation) that might ameliorate difficulties with arousal, attention, and memory; and also identify grounds for pausing or discontinuing neurotoxic therapies, such as the presence of chemotherapy and/or radiation-induced encephalopathy [18,19].

Repeating neuropsychological testing over time

Monitoring of cognitive functions over time has the potential to do more than just characterize the functional status of individuals who have undergone treatment for CNS tumors. Serial neuropsychological testing can also reveal regrowth of tumor weeks to months before there is radiographic evidence of progression [20,21], and the presence and degree of cognitive decline that remains after adjuvant treatments may also predict survival. In their analysis of 56 individuals with recurrent brain tumors tested prior to receiving investigational treatments and then at intervals coincided with planned MRI scans,

Meyers & Hess (2003) noted meaningful deterioration on measures of cognitive functioning (but not measures of QOL of ADL functioning) almost a month before radiographic evidence of progression was noted on MRI [21]. In another study described by Meyers and Brown (2006), 60% of patients with malignant gliomas tested after 8 months of treatment (with accelerated fractionated radiation therapy and concomitant chemotherapy) demonstrated declines in memory functions, and 40% demonstrated declines in executive functions and bilateral fine motor coordination relative to their own pre-treatment scores, despite radiographically stable disease. When patients were divided into groups according to whether they lived 3 or more years after treatment, those with better performance on measures of memory, visuomotor scanning speed and executive functions were more likely to have longer survival rates than those that showed more significant deficits on testing 8 months after therapy [22].

Conclusion

In conclusion, neuropsychological testing contributes positively to the assessment and management of individuals with CNS tumors. Although tumors of the central nervous system may have different medical outcomes based on size, grade, and site of tumor growth, all have the potential to affect neurocognitive and neurobehavioral functions, and cognitive dysfunction associated with disease-related factors, as well as the adverse effects of cancer therapies, is a significant problem among individuals with brain tumors. The annualized net cost of care for patients with CNS tumors, who undergo surgical resection, chemotherapy and/or radiation, treatment with medications for management of symptoms, repeat neuroimaging studies, and follow-up visits with Neurosurgery and Oncology has been estimated at $108,000 - $138,000 in 2010 U.S. dollars during the initial phase of treatment (depending on age and sex), and another $9,000 per year for continued care up until the last year of life [23]. Although neuropsychological testing might add $1500-$3000 per year in additional treatment costs (depending on length of battery and regional cost of assessment), its obvious value to clinical decision making and improvement of outcomes should make it a standard of practice for the assessment and management of individuals with CNS tumors.

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