

## Neurocognitive Function

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Cancers of the nervous system, particularly primary malignant brain tumors, can be devastating illnesses, characterized by a very low cure rate, short survival time, and significant morbidity as the disease progresses. Malignant primary brain tumors cause profound changes in cognitive function, personality, psychological well being, and ability to perform daily activities. These changes negatively affect the productivity and independence of brain tumor patients, impacting their social functioning, financial status, and self-esteem (Sherer et al., 1997).

The effects of the tumor, tumor treatment, and other factors that have the potential to impact brain functioning and the patient's life can be differentiated by appropriate evaluation methods, which can then guide the institution of therapeutic and palliative intervention strategies. In fact, quality of life may be one of the few areas where the health care provider can have a significant impact. An appreciation of the cognitive deficits and behavioral changes that may occur in brain tumor patients can aid in the design of intervention strategies, improve the quality of patient care, and ultimately improve the overall quality of life for brain tumor patients and their families.

### **NEUROBEHAVIORAL CHANGES ASSOCIATED WITH BRAIN TUMORS**

Various factors contribute to the neurobehavioral changes associated with brain tumors. While manifestations of this disease vary substantially between patients, some general comments regarding tumor-

related and patient-related factors and their impact on cognition are warranted.

### **Location**

Brain tumors, whether primary or metastatic, almost always cause deficits of cognitive function. The type of impairment observed is in part related to the site of the lesion. For instance, left hemisphere tumors may produce language disorders that impair the patient's ability to communicate with others and comprehend spoken or written language (Haas et al., 1982). Tumors in the right hemisphere of the brain may cause deficits in visual perception and visual scanning, resulting in impaired driving skills or the inability to navigate in familiar places (Scheibel et al., 1996). Memory loss is often seen in association with tumors of either hemisphere. Impairments of frontal lobe function (executive deficits manifested by impairments of cognitive flexibility, abstraction, motivation, planning and organizational skills, ability to benefit from experience, personality changes, and so forth) are ubiquitous in brain tumor patients (Vilkki, 1992; Goldstein et al., 1993; Ackermann et al., 1996). One obvious reason is that the frontal lobes comprise one-third of the cerebrum, and a large proportion of patients has frontal tumors. However, many patients with nonfrontal tumors also exhibit executive deficits (Lilja et al., 1992). This is due in part to the fact that the frontal lobes have rich afferent and efferent connections with all other brain regions. Thus, a lesion in a nonfrontal location will disconnect the frontal lobe from information from that region and also in-

errupt modulatory frontal influences on its function. In addition, marked personality changes can occur following removal of tumors in certain regions of the brain, causing impairment in social functioning, motivation, and judgment (Meyers et al., 1992a).

### **Pathologic Type**

Individuals diagnosed with low-grade tumors that have been present for many years may have no detectable changes in brain function due to cerebral plasticity and reorganization (Meyers et al., 1992b). In contrast, patients with very rapidly growing tumors may have widespread impairment due to mass effect on adjacent brain regions (Hom and Reitan, 1984). Despite the initial differences, the cognitive functioning of patients with anaplastic astrocytoma and patients with glioblastoma multiforme do not vary appreciably following surgery (Scheibel et al., 1996). This finding illustrates the potentially beneficial effects of surgery on mass effect, intracranial pressure, and other adverse effects on distal brain regions (diaschisis).

### **Patient Characteristics**

The age of the patient also contributes to the manifestation and severity of neurobehavioral deficits. For example, older patients tend to have more malignant brain tumors, and even histologically less malignant tumors behave more aggressively in the older patient (Cohaden et al., 1985). Older patients are also at higher risk for having other concurrent neurodegenerative illnesses, such as Parkinson's disease or vascular disease. Finally, older patients may be more sensitive to the toxic side effects of treatment.

## **NEUROBEHAVIORAL CHANGES DUE TO TREATMENT**

Cognitive dysfunction in brain tumor patients is often more generalized than expected for a focal lesion. This may be due to microscopic tumor infiltration, a high rate of tumor growth causing diaschisis, or the adverse effects of treatment (Meyers, 1986). Hochberg and Slotnick (1980) found diffuse cognitive difficulties in patients who were long-term survivors of malignant astrocytomas that were unrelated to tumor type, location, other medical factors, or psy-

chiatric factors and were thought to be due to aggressive treatment. LeBaron et al. (1988) found that more than 50% of children treated for posterior fossa tumors had significant intellectual, motor, and academic problems 20 months after treatment cessation. Different adverse effects are likely attributable to radiation, chemotherapy, immunotherapy, and adjunctive medications.

### **Adverse Effects of Radiation Therapy**

Brain irradiation may be associated with delayed brain injury and related cognitive deficits. The damage from radiation treatments is generally evident several years following treatment (Leibel and Sheline, 1987) and may be progressive and irreversible. Research with monkeys has shown that brain radiation in the therapeutic range (60 Gy) causes focal areas of necrosis within 6 months (Nakagaki et al., 1976). The area of injury may present as an expanding mass of necrosis that is virtually indistinguishable from recurrent tumor or as diffuse progressive white matter disease (leukoencephalopathy). Older patients, young children, and individuals who receive concomitant high-dose chemotherapy are at greatest risk for suffering from the adverse effects of radiation. Symptoms in adults generally include memory loss, gait disturbance, weakness, and tremor. In children, dementia and severe learning disabilities may be seen following aggressive treatment (Duffner et al., 1983).

Irradiation causes injury to subcortical white matter, with larger treatment volumes causing more impairment (Gregor et al., 1996). Most studies that include neuropsychological assessment of brain tumor patients before and after radiation therapy reveal significant impairments of information-processing speed, executive functions, memory, sustained attention, and motor coordination in those with no evidence of disease recurrence (Scheibel et al., 1996; Salander et al., 1995; Archibald et al., 1994; Taphoorn et al., 1994; Imperato et al., 1990; Lieberman et al., 1982; Hochberg and Slotnick, 1980). These deficits are correlated with reduced cerebral blood flow seen on single-photon emission computed tomography imaging (Ebmeier et al., 1994).

Many studies have focused on memory deficits as the primary adverse effect of therapy in brain tumor patients. Salander et al. (1995) found that patients with malignant gliomas (grade III–IV) who were disease free and without neurologic deficits developed

impairments of verbal learning and memory but did not differ from their spouses on tests of verbal comprehension, visuospatial skills, or abstract reasoning 5 months after their initial treatment. Archibald et al. (1994) found that memory and concentration tended to be most impaired 18 months after treatment, with further declines in frontal lobe executive functions and new learning ability during the ensuing 2 years. Kleinberg et al. (1993) reported, in contrast, that 65% of their glioma patients had only mild memory deficits that did not prevent them from returning to work. However, memory impairment was rated by patient self-report and not formally tested, and it could not be determined if the patients required any assistance or compensation techniques to maintain their level of function. An excellent review of the neurobehavioral effects of radiation therapy in brain tumor patients can be found in Crossen et al. (1994).

Even radiation not directed at the brain can cause cognitive impairment. For example, a substantial percentage of patients who receive therapeutic radiation for tumors of the anterior skull base have cognitive deficits. Memory impairment was detected in 80% of patients with paranasal sinus tumors, even though the brain was not the target of irradiation (Meyers et al., 2000). The neuropsychological effects of treatment do not appear to be tightly correlated with the appearance of white matter changes on neuroimaging, although the development of white matter changes is closely correlated with radiation dose (Corn et al., 1994). This is due to both the resolution of anatomic changes on magnetic resonance imaging and the fact that many changes in brain function are caused by biochemical alterations that occur before structural abnormalities may be visualized (Ebmeier et al., 1994; van der Knaap et al., 1992).

### **Adverse Effects of Chemotherapy**

Cognitive and emotional changes reported during and after chemotherapy include memory loss, decreased information-processing speed, reduced attention, anxiety, depression, and fatigue (Meyers and Abbruzzese, 1992). Most of the older literature suggests that neurotoxic side effects of chemotherapy are acute and reversible (Weiss et al., 1974), generally resolving within 48 to 72 hours after treatment. The risk of severe delayed effects, such as leukoencephalopathy, is primarily seen following administration of higher

doses (van Dam et al., 1998), intra-arterial (Glass et al., 1986) or intraventricular administration, and concomitant radiation therapy. The neurobehavioral effects of most cancer therapy agents tend to be non-specific and diffuse, except for those that have a mechanism of action that is expected to affect focal brain regions (Meyers et al., 1997) or biologic response modifiers that are known to affect particular proinflammatory cytokines, neurotransmitters, and neuroendocrine hormones (Valentine et al., 1998). Although cognitive changes following chemotherapy have been well documented, there have been very few prospective studies investigating the long-term effects of chemotherapeutic agents on cognition.

### **Adverse Effects of Immunotherapy**

Cytokines such as interferon-alpha (IFN- $\alpha$ ) and interleukin-2 (IL-2) have been used in a number of therapeutic trials for primary brain tumors and leptomeningeal disease (LMD). These agents are known to have both acute and persistent neurotoxic side effects. Acute toxicity is characterized by fever, headache, and myalgia, which generally resolve over several days. Subacute neurotoxicity, evident within a week of starting therapy, is characterized by inattention, slowed thinking, and lack of motivation. After several months of treatment, more than two-thirds of patients develop difficulty with memory, frontal lobe executive functions (e.g., problem solving, planning, sequencing), motor coordination, and mood (Pavol et al., 1995). These neurotoxic side effects are not always reversible following treatment cessation (Meyers et al., 1991b). The route of administration is also an important consideration. Intraventricular administration of IFN- $\alpha$  has caused a reversible vegetative state in patients with LMD (Meyers et al., 1991a), and intraventricularly administered IL-2 may produce a progressive dementia in otherwise "cured" patients treated for LMD (Meyers and Yung, 1993).

### **Adverse Effects of Adjunctive Medications**

#### *Steroids*

Glucocorticoid treatment for mass effect and raised intracranial pressure is ubiquitous among brain tumor patients. However, steroids may also have adverse effects on mental and emotional functioning.

The incidence of steroid-induced psychiatric syndromes ranges from 5.7% to 50% (Lewis and Smith, 1983). These side effects include euphoria, mania, insomnia, restlessness, and increased motor activity. Some patients become anxious and depressed. Steroids are also known to have adverse effects on memory, even in normal control subjects (Wolkowitz et al., 1990), and have been implicated in the pathophysiology of major depression and Alzheimer's disease (Martignoni et al., 1992). Treatment with glucocorticoids may also potentiate the neurotoxic side effects of other agents (Sapolsky, 1985).

### *Anticonvulsants*

For many patients, seizures are the initial symptom of a brain tumor. The overall incidence of epilepsy among brain tumor patients is estimated at 35% (Kelles and Berger, 2000). When the dosages of anticonvulsant drugs such as phenytoin (Dilantin) and carbamazepine (Tegretol) are carefully monitored, their cognitive effects are minimal (Drane and Meador, 1996). Use of phenobarbital, however, has been associated with greater adverse cognitive effects (Devinsky, 1995; Drane and Meador, 1996). Regardless of the specific medication used, too rapid an introduction of the anticonvulsant, polypharmacy, or excessive concentrations may result in changes in arousal, attention, memory, and psychomotor functioning (Kaufman, 1995). It should be noted, however, that the majority of children and adults who take these drugs experience few (if any) side effects (Bourgeois, 1998; Devinsky, 1995). In fact, at least one antiepileptic drug appears to have favorable effects on psychological well being (Meador and Baker, 1997).

### **Medical Complications**

Endocrine dysfunction due to hypothalamic/pituitary injury is also very common following radiation therapy. Thyroid dysfunction, loss of libido, and erectile dysfunction are present in a large proportion of patients. In fact, one study found that only 23% of brain tumor patients had normal thyroid, gonadal, and adrenal hormone levels following treatment (Arlt et al., 1997). Endocrine replacement therapy has the potential to improve cognition and mood in patients who have subnormal hormone levels due to hypothalamic injury related to treatment (Arlt et al., 1997).

Seizures occur in 50% to 70% of patients at some time during their illness and have a significant impact on neurobehavioral functioning and quality of life. Persistent, poorly controlled seizures reduce cognitive efficiency and exacerbate underlying cognitive deficits. Patients with seizures are often fearful of having them and may become socially isolated because of the possibility of having one in a public place or around people they know.

Anemia is a side effect of some chemotherapy regimens. For children and adults, research suggests that treatment with cisplatin (Petersdorf et al., 1993), etoposide (Chamberlain and Kormanik, 1997; Chamberlain, 1997), and high-dose carboplatin/etoposide combination therapy (Castello et al., 1990) may be complicated by anemia. Among anemic patients, the cognitive problems observed on neuropsychological testing include deficits in attention, perceptual-motor speed, memory, and verbal fluency (Brown et al., 1991; Marsh et al., 1991; Temple et al., 1995). Neurophysiological assessment of auditory evoked potentials also revealed increased latency of certain components (Brown et al., 1991; Marsh et al., 1991). These cognitive deficits and slowed evoked potentials often improve following reversal of anemia with erythropoietin (Brown et al., 1991; Marsh et al., 1991; Nissenon, 1989; Temple et al., 1995). For most patients receiving chemotherapy for a brain tumor, anemia and other treatment-related complications are medically manageable.

### **Quality of Life Issues**

Comprehensive studies of quality of life (QOL) of brain tumor patients have revealed increased emotional reactivity, lowered frustration tolerance, and reduced family functioning (Giovagnoli et al., 1996; Weitzner et al., 1996; Aiken, 1994; Taphoorn et al., 1992). Brain tumor patients at risk for poorer QOL are female, are divorced, have bilateral tumor involvement, have received chemotherapy, and have a poor performance status (Weitzner et al., 1996; Irle et al., 1994). Age, surprisingly, is not a factor in QOL or well being despite being an extremely important prognostic factor (Sneed et al., 1995). The site of the lesion also has an impact on mood. Patients with tumors in ventromedial frontal or parietal association areas are more likely to experience anxiety, irritability, and fatigue than are patients with lesions in other locations. Patients with lesions in dorsolateral frontal

and somatosensory regions tend to exhibit emotional indifference and even euphoria (Irle et al., 1994). In addition, tumor patients have been found to mimic nearly every psychiatric illness, such as obsessive-compulsive disorder (Paradis et al., 1992) and personality disorder (Meyers et al., 1992b).

Overall QOL is not as related to histopathologic diagnosis, prognosis, or age as much as it is to social support systems, personality characteristics, and access to services (Weitzner and Meyers, 1997; Lyons, 1996). The disease causes changes in life-style and roles for family members as well as for patients (Newton and Mateo, 1994). Uncertainty regarding the disease history and outcome is a source of stress for the family. Uncertainty can also be positive, however, allowing patients and their families some hope for a better-than-anticipated course (Newton and Mateo, 1994).

## DIAGNOSTIC CONSIDERATIONS

### Differential Diagnosis

Accurate diagnosis of cognitive impairment versus emotional reactions to illness and stress is important for a number of reasons. Brain tumor patients frequently have complicated treatment regimens, and compliance may be adversely affected by cognitive deficits. Problems with memory or the inability to initiate activity can negatively impact adherence to treatment regimens. Patients may be offered experimental treatments, and the decision to participate and give informed consent requires intact reasoning, the ability to weigh risks and benefits, and the appreciation of long-term consequences. Differential diagnosis of observable behavior changes may be difficult. A patient who is apathetic, withdrawn, and lacks motivation may be depressed or may have an organic brain syndrome. Levine et al. (1978) reported that 64% of general cancer patients with delirium were misdiagnosed as depressed. This number may be even greater for patients with primary brain involvement. The distinction is an important one, however, because misdiagnosis and subsequent treatment of depression in a patient with an organic brain syndrome might worsen the condition.

Many patients with brain tumors, at least early in their course, do not have overt evidence of impaired cognitive functioning on casual observation or dur-

ing routine medical examinations and yet have cognitive deficits that limit their ability to function in their normal activities. Standard assessments of performance status, such as the Karnofsky and Zubrod scales, which globally measure the patient's ability for self-care and ambulation, do not address cognitive impairments in brain tumor patients and have questionable reliability and validity (Orr and Aisner, 1986). For example, a patient who is able to walk and perform basic activities of daily living may be rated as having a good performance status even though he or she may be unreliable in following treatment regimens, lack judgement, be unable to perform his or her usual work, or have temper outbursts that compromise family function.

An informal survey of the problems and incidents reported by inpatient and outpatient neuro-oncology nurses sheds light on how these various deficits adversely affect healthcare provider-patient-family-relationships. These include

1. Inadequate insight and self-appraisal on the part of the patient. For instance, the patient may overrate his or her ability to be independent, refuse assistance in activities of daily living, and have an accident.
2. Memory problems with confabulation that may appear to represent noncompliance. For instance, the patient may inaccurately report the type, frequency, and amount of medication he or she has been taking, leading to subtherapeutic or toxic medication levels.
3. Subtle problems with language comprehension that limit the amount and type of information the patient can process and retain. Although this type of problem may not be readily identified in the hospital or clinic setting because of the high level of structure, the patient may have great difficulty following multistep, complicated instructions at home.
4. Poor initiation and maintenance of activity that may resemble a "bad attitude" or depression. This patient may have difficulty initiating and following through personal hygiene routines, performing usual work and leisure activities, and so forth.
5. Hemispatial inattention that may be manifested as "paranoia" when people approach from the unattended side or as problems in dressing and eating.



6. Subtle visuospatial problems that are manifested by the patient becoming easily lost and confused, even in familiar settings.

### Deficit Versus Handicap

The impact of a primary brain tumor on the individual is best conceptualized by the three-tiered system developed by the World Health Organization (1980). *Impairment* is the deficit of brain function caused by the disease and is assessed by neurologic and neuropsychological evaluations. *Disability* is the impact of the deficit on the patient's ability to perform activities and is assessed by performance status and functional status measures. *Handicap* is the impact of the disability on the patient's subjective well being, which includes the patient's overall comfort level and satisfaction, and is generally assessed by QOL questionnaires.

A specific cognitive deficit may or may not be handicapping to a given individual. The impact of a given impairment needs to be considered in the entire social context of the patient. Each person carries with himself or herself a unique array of environmental variables, such as education level, type of occupation, degree of social support, and access to services. These multiple factors determine the degree of handicap the brain tumor patient experiences in rejoining the mainstream of community activities and the work environment. Because of this dynamic relationship between neurologic impairment and environment, individuals with the same type and severity of deficit may experience different degrees of disability. For instance, a person who has sustained a severe verbal memory impairment may find it difficult to remain in college, but may experience few problems working in a well-established routine environment.

### Neuropsychological Assessment

Often these problems, if unrecognized, lead to inaccurate judgment on the part of the staff regarding the patient's ability for self-care, requirements for supervision or special safety measures, and reliability in following his or her therapeutic regimen. Formal neuropsychological assessment of brain function is often helpful in determining the nature and extent of cognitive impairments that are not detected in routine medical evaluations.

Neuropsychological assessment involves the administration of standardized psychometric tests that comprehensively evaluate brain functioning. These functions include attention, ability to acquire new memories, recall of stored memories, expressive speech, language comprehension, visual-perception, reasoning, emotional behavior, interpersonal behavior, and executive functions. This detailed description of intellectual status and personality characteristics allows for more rational management and planning postoperatively.

Knowledge of the patient's capabilities and limitations should be incorporated into conferences held with the patient, family members, and the healthcare team. Such information is helpful as the participants work to set realistic goals, determine the patient's capacity for independent self-care (including the ability to drive, manage finances, and handle emergencies), and determine what types of compensation and management techniques might be most useful.

### Quality of Life Assessment

The current standard of QOL assessment is multidimensional and addresses concerns that are unique to patients with brain tumors. There are several subjective QOL instruments that have been developed for patients with brain tumors, including the Functional Assessment of Cancer Therapy—Brain (FACT-Br) (Weitzner et al., 1995) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire—Brain module (EORTC QLQ-BCM) (Osoba et al., 1996). These scales differ slightly in their development methods. The core FACT and EORTC QLQ questionnaires address physical, family, social, emotional, and functional well being. The QLQ-BCM items were obtained from interviews of patients and caregivers participating in a brain cancer support group. The items for the FACT Brain module were initially developed from interviews with patients in a neuro-oncology outpatient clinic. Additional items for both of these brain tumor modules were obtained from the input of healthcare professionals, and the methods for determining reliability, validity, and internal consistency were similar.

A thorough listing of QOL tools used in general cancer settings can be found in Cella and Bonomi (1995). The PRESTON Profile (Lyons, 1996) is another tool designed for brain tumor patients and addresses several different domains, including physical,

emotional, and social functioning, relationship with family, tomorrow and the future, ongoing needs, and limited neurologic deficits. It does not address cognitive impairments and has not undergone validity or reliability assessments.

Some groups are defining QOL in clinical trials as a combination of survival and the amount of time patients have adverse effects of disease and treatment (Murray et al., 1995). This approach (quality-adjusted survival analysis) provides more information on patient function than the Karnofsky performance score (KPS). However, brain tumor patients are less likely to be free of symptoms than other cancer patients. In addition, censoring is assumed to be random and uninformative (Scott, 1997). In fact, censoring of brain tumor QOL assessments is informative when the information is missing because the patient can no longer read or understand the questions. Many cognitively impaired patients cannot complete QOL instruments, so there may be substantial amounts of missing data. If questionnaires are only given to patients who are cognitively most intact, the interpretation of the outcome of the trial may be biased.

Some investigators have caregivers assess the QOL of the patient (proxy assessment) and have reported modest correlations between patient and proxy results (Sneeuw et al., 1997). However, the similarity between the patient and proxy assessment is lower for the more cognitively impaired patients, which is exactly when the proxy assessments are most likely to be done. Patients with brain tumors, particularly in the frontal lobe, often have diminished appreciation of their disabilities and limitations and report a level of function that is not realistic. They may report a good QOL in the face of substantial mental impairment because of their lack of insight. In clinical trials, at least, subjective QOL questionnaires should be supplemented by other objective assessments of patient function.

### INTERVENTIONS AND MANAGEMENT STRATEGIES

Most individuals with brain tumors develop behavioral, emotional, and intellectual difficulties that compromise their ability to live independently and return to work. In fact, few brain tumor patients return to their usual work and activities. One study reported that only 18% of patients return to work full-time, and

10% return to work part-time (Fobair et al., 1990). The costs to the patient, family, and society include loss of self-esteem, lost income, and the necessity for disability payments. Cognitive and vocational rehabilitation have the potential to reduce the morbidity associated with this disease and its treatment, improve recovery of cognitive and emotional function, and reduce the financial costs and losses to patients, their families, and society. However, rehabilitation of brain tumor patients is in the beginning stages of development. At this time there is little established knowledge about the major rehabilitation problem areas of brain tumor patients, and no rehabilitation approaches exist to address the problems that have been specifically validated in this clinical population. Rehabilitation of brain tumor patients is given little emphasis in major reviews of rehabilitation for non-brain cancers (Hersh et al., 1988; LaBan, 1990; McGarvey, 1990; Raven, 1992). Nevertheless, there is increasing interest in the possibility of rehabilitating brain tumor patients, and initial steps toward a specialty of brain tumor rehabilitation are being taken. The goal of this section is to describe current rehabilitation methods used with brain tumor patients and to identify trends in new programs designed for this population.

### Rehabilitation Problems of Brain Tumor Patients

One obstacle to the development of specialized brain tumor rehabilitation services is identification of the major rehabilitation problems within this patient population. It has often been assumed that the rehabilitation problems of brain tumor patients are similar to those of stroke patients, survivors of traumatic brain injury (TBI), and other groups of persons receiving rehabilitation services. In fact, available data support a different and more complex picture of brain tumor patients' needs (Lehmann et al., 1978; Taphoorn et al., 1992; Marciniak et al., 1996). Brain tumor patients not only have different types of problems, but the progressive nature of their disease complicates treatment planning and decisions. Although the goals of treatment and the duration of intervention programs need to be flexible for all rehabilitation patients (Gamble et al., 1990), this is especially true for patients diagnosed with brain tumors.

It is undoubtedly true that patients with brain tumors may benefit from many of the same types of ser-

vices that are helpful for other rehabilitation populations such as stroke or TBI survivors. For example, physical therapy can improve strength and mobility; occupational therapy improves self-care skills; and speech and language therapy may help patients overcome various aphasic conditions. This group of patients, however, varies in terms of the types of problems that most frequently present for remediation. One large-scale survey found that the most frequent category of rehabilitation problem among patients with nervous system cancers was "psychological" (Lehmann et al., 1978). Problems in this category were more common than problems with ambulation, transfers, and general weakness. It is noteworthy that problems with return to work occurred at the same frequency among cancer patients as did physical disabilities. These general findings were confirmed in a study in the Netherlands of patients with slow-growing gliomas (Taphoorn et al., 1992).

In a survey of 30 caregivers of brain tumor patients, we found that the problems facing this group of patients were very different from the concerns of other medically ill populations. Using the Sickness Impact Profile (Bergner, 1977), we found that the most salient problems facing brain tumor patients were lack of energy, inability to perform usual activities around the home (i.e., paying bills, making repairs), social isolation, lack of sexual activity, generalized slowing of behavior, and problems with reasoning, memory, and concentration. In contrast to other medically ill populations, some problems were not endorsed by brain tumor caregivers as being of concern. These "nonproblems" included depression, ability to perform basic activities of daily living such as dressing and eating, ambulation, and ability to speak and be understood. Although the rehabilitation needs of brain tumor patients are becoming more widely known, there are few facilities with experience in treating this population.

Approximately 5 years ago, we surveyed acute and post-acute rehabilitation facilities across the United States to determine current clinical practice. Of the 262 questionnaires mailed out, 108 replied (41%), 77 of which were acute care facilities. Of the total group, 62% treated fewer than 10 brain tumor patients per year and 72% did not provide any specialized rehabilitation services or staff training for brain tumor patients. Problems frequently identified by these facilities included poor judgment on the part of the patient, side effects of cancer treatment, uncer-

tain medical prognosis attached to brain cancer, and emotional adjustment to cancer.

Despite similarities in the types of therapies employed, the nature of the problems faced by cancer patients necessitates an adjustment in the approach to rehabilitation and the goals of services. For many patients, especially those diagnosed with a malignant brain tumor, deterioration of function over time is the most likely course of the disease. Even if gains achieved in physical, occupational, or speech therapy are temporary, however, they may significantly improve the patient's QOL (Haut et al., 1991) by improving productivity and independence (Sherer et al., 1997). Although we have not completed a follow-up survey to the one described above, anecdotal evidence suggests that brain tumor patients remain woefully underserved.

### Traditional Rehabilitation Approaches

Dietz (1984) and others have described four different rehabilitation approaches applicable to cancer patients in general. In the *preventive* approach, the goal is to prevent complications that are anticipated to result from disease or treatment. An example of this approach is having mastectomy patients begin an exercise program to prevent postoperative lymphedema and deconditioning. The goal of the *restorative* approach is to return patients' functioning to the pre-disease level, which is not generally appropriate for brain tumor patients. The *supportive* approach attempts to improve a patient's functioning within the limits set by neurologic deficits, which are assumed to be permanent. In the *palliative* approach, the goal is to relieve suffering and maintain functioning during periods of disease progression. Examples of this approach are pain management and the use of exercises to preserve range of motion. Most of the rehabilitation methods used with brain tumor patients follow the supportive approach as defined above, but our experience suggests that a model that includes the preventive approach may also be useful for this population.

Implementing traditional cognitive and vocational rehabilitation for brain tumor patients is complicated by the fact that existing programs are not entirely appropriate. First, brain tumor patients have different patterns and types of cognitive deficits than do stroke or trauma patients. One study found that patients with brain tumors have milder cognitive deficits and



greater variability in the nature and extent of their deficits than people with strokes in the same neuroanatomic site (Anderson et al., 1990). Second, the natural history of the disease process differs from cerebrovascular disease or TBI. The latter two conditions are usually characterized by an acute onset and gradual recovery. In the case of brain tumors, the onset of the disease is relatively insidious, and although some recovery of function may be seen following surgery or other therapy, most patients experience a gradual deterioration of function as the tumor progresses. Hence, the goals of rehabilitation may be different from those in stroke or brain trauma rehabilitation. Finally, most existing rehabilitation programs take at least 6 months to complete and are costly (frequently more than \$20,000). Complicating the cost, funding agencies and insurance carriers may be reluctant to provide or reimburse services for brain tumor patients.

### **Inpatient Rehabilitation Programs**

Inpatient rehabilitation is indicated for those brain tumor patients who are disabled in ambulation and self-care because of neurologic deficits but who have the potential to improve. The reader is referred to comprehensive reviews of inpatient rehabilitation for stroke (Goldberg, 1991) and head injury patients (Berrol, 1992) for detailed information. The specific therapy activities used with a given patient are tailored to the patient's physical and neurobehavioral deficits and are upgraded as the patient recovers. During early stages of recovery, basic physical activities (e.g., feeding) are emphasized, whereas in later stages more advanced activities (e.g., ambulation) can be addressed. The specific therapy techniques used are based on each patient's neurologic and functional problems so that a particular problem might be treated using similar techniques regardless of whether the deficit was caused by brain tumor or stroke (Blossom and Barnhart, 1985).

In contrast to the large body of outcome research data on the inpatient rehabilitation of other neurologically impaired patient groups, there are few data reported for brain tumor patients. Feder et al. (1989) reviewed their 10 year experience with 76 patients who had undergone surgical removal of meningiomas. Despite the fact that 72% of the patients were graded on admission as having "severe" or "very severe" disabilities (criteria not stated), the majority

had marked functional improvement and virtually all surviving patients were discharged home. The average length of stay was 106 days, similar to the typical length of stay for stroke patients at the same hospital. The major single predictor of outcome was whether the tumor resection was total or subtotal. The authors note that this predictor could have represented a proxy effect of other clinical features (i.e., surgically inaccessible tumor) that are independently associated with outcome. It would be valuable to replicate this type of study with patients who have primary gliomas.

In a retrospective study of 159 cancer patients admitted to an inpatient rehabilitation program (Marciniak et al., 1996), deconditioning was the most common impairment or problem identified. Of these 159 patients, 72 had a diagnosis of primary brain tumor and the frequency of cognitive impairments was 49%. While the length of stay in the program across patient types ranged from 5 to 93 days (mean = 32, SD = 19), patients diagnosed with brain tumors remained in the program for an average of 34 days (SD = 20), with 75% eventually being discharged home. The authors concluded that inpatient rehabilitation services are beneficial for patients with a variety of cancer diagnoses, including those with primary brain tumors.

It is not currently known what proportion of brain tumor patients would benefit from acute, inpatient rehabilitation. A survey of more than 800 cancer patients in university hospitals (Lehmann et al., 1978) found that most primary physicians were not aware of rehabilitation problems in their patients or did not know what rehabilitation might offer. Because there is no established model for inpatient rehabilitation of brain tumor patients, even the predictors of length of stay and rehabilitation outcome in this population are unknown. Thus, there is a strong need for research on predictors of outcome, typical problem areas, rate of progress, utilization of different services, amount of spontaneous recovery, and complications experienced by brain tumor patients in inpatient rehabilitation.

### **Cognitive Rehabilitation**

With the establishment of postacute day-treatment rehabilitation programs in the late 1970s and early 1980s, the needs of patients with moderate to severe TBI began to be more formally addressed (Ben-Yishay

et al., 1982; Prigatano et al., 1986). Many of these programs adopted a holistic approach to rehabilitation, incorporating various activities designed to facilitate patient progress and adaptation (Prigatano and Ben-Yishay, 1999). As reviewed in depth by Prigatano (1999), the major components of a holistic neuropsychological rehabilitation program include the establishment of a therapeutic milieu, cognitive rehabilitation or retraining sessions, psychotherapy, involvement and education of family members, and a protected work trial. Whereas the early aim of such activities was to restore cerebral functioning to the highest degree possible, more contemporary cognitive remediation programs strive to manage the individual's disability rather than treat the underlying impairment (Wilson, 1997). Although there is little evidence that cognitive retraining (the restorative approach) directly improves higher cerebral functioning in adults after acquired brain injury (Prigatano, 1999), there are benefits to participation in cognitive rehabilitation programs. Initially, cognitive retraining sessions may help patients better understand the nature and degree of their impairment or disability and, as they progress through the program, cognitive rehabilitation helps them use residual skills to improve their abilities to problem solve and adapt.

Modification of special programs dedicated to rehabilitating the neurobehavioral problems of TBI patients are being developed for brain tumor patients (e.g., Sherer et al., 1997). The most common type of neurobehavioral-oriented program is the day-treatment program with emphasis on cognitive and vocational rehabilitation. Although these programs are frequently affiliated with an inpatient rehabilitation program, many are located in the community to provide better access to resources.

The first step in cognitive and vocational rehabilitation is to identify realistic goals for the patient, often through formal neuropsychological and vocational testing to identify preserved skills. The major therapeutic strategy is to train patients to compensate for their neurobehavioral deficits at home and on the job. Brain tumor patients would appear to be excellent candidates for cognitive rehabilitation because patients with focal lesions and relatively restricted cognitive deficits may be in a better position than persons with more diffuse impairments to recognize the need to use compensatory strategies (Prigatano, 1999). Typical areas targeted for retraining include memory, problem solving, and social behavior. In ex-

amining the efficacy of cognitive remediation, the greatest success has been in compensating for memory disorders (Baddeley et al., 1995). For instance, patients with memory deficits may compensate by using written reminders, alarm watches, pagers, and other devices. Unfortunately, the efficacy of compensation strategies in addressing deficits in other areas of functioning (i.e., judgment and problem solving) has not been conclusively demonstrated (von Cramon and Matthes-von Cramen, 1992). For some patients, a major treatment goal may be to improve the appropriateness of behavior. This may include teaching the patient to inhibit socially inappropriate remarks or to improve frustration tolerance. Patients and family members often need counseling about the need to accept less demanding jobs, which are not as financially rewarding and prestigious.

The majority of the brain tumor patients seen in our clinic are experiencing cognitive difficulties. Feelings of confusion and frustration often accompany cognitive changes and can affect not only the patient but also those persons close to him or her. For many patients, whether they are newly diagnosed or already in treatment, a neuropsychological assessment can be helpful in delineating the individual patient's cognitive strengths and weaknesses as well as validating the concerns of patients and their families. In some instances, the neuropsychological evaluation provides concrete evidence of impairment for the patient who is unable or unwilling to acknowledge that impact of the disease and/or their treatment on cognition.

Many of our patients reside out of state or at a distance from the facility, which prohibits frequent visits for cognitive remediation. Although referrals to accredited rehabilitation facilities are provided when appropriate, some patients benefit from an intensive "problem-solving" approach that can be completed in conjunction with scheduled clinic visits. Maintaining a strong therapeutic alliance with the patient and close professional relationships with speech and language pathologists, physical therapists, occupational therapists, psychiatrists, and primary care physicians are crucial to the success of this approach.

### Vocational Rehabilitation

In our needs assessment survey of brain tumor patients, we found that more than 40% were unable to work. Not all of these individuals are candidates for vocational rehabilitation, but there are those who

could benefit greatly. Modification of programs dedicated to vocational rehabilitation of TBI patients may prove beneficial for brain tumor patients.

A newer vocational rehabilitation approach that has been successful and cost-effective with TBI patients is *supported employment*. In this approach, patients who are capable of holding employment are placed directly in jobs and are initially assisted by a job coach who trains the patient to perform the work and acts as the patient's direct supervisor. As the patient becomes more independent on the job, the job coach decreases the amount of supervision until job coaching is unnecessary. The supported employment approach can be modified for patients returning to a position in which a job coach may not be appropriate by assigning a co-worker to act as a mentor to the patient as he or she resumes the job responsibilities. These vocational rehabilitation approaches are reviewed by Wehman and Kreutzer (1990).

### Pharmacologic Strategies

Neurobehavioral slowing is the hallmark of frontal lobe dysfunction and treatment-related adverse effects in brain tumor patients. The syndrome of neurobehavioral slowing is generally due to involvement of the monamine pathways of the frontal-brain stem reticular system. In addition, catecholamines have an important role in the modulation of attention and working memory.

The use of neurostimulants in the brain-injured population has been shown to increase participation in therapy by improving arousal and attention (Kaelin et al., 1996). Methylphenidate (Table 26-1) has proven efficacious in improving the cognitive and emotional symptoms of human immunodeficiency virus (Brown, 1995), alleviating apathy in a patient with multiple subcortical infarcts (Watanabe et al., 1995), improving attention and functional outcome in brain-injured adults (Kaelin et al., 1996), and en-

hancing recovery rates in moderately severe brain-injured patients (Plenger et al., 1996). Stimulant treatment also has been useful for concentration difficulties, psychomotor retardation, and fatigue frequently seen in brain tumor patients and helped to elevate mood (Meyers et al., 1998). A conservative dose of 10 mg bid significantly improved cognitive function as assessed by objective tests, and doses in excess of 30 mg bid were well tolerated. Subjective improvements included improved gait, increased stamina and motivation to perform activities, and improved bladder control. There were no significant side effects, and many patients taking steroids were able to decrease their dose (Meyers et al., 1998). Long-term experience with this agent is lacking to determine if tolerance to therapeutic effects can develop.

### Education, Support, and Strategies for Caregivers

Family involvement is an important component of the patient's rehabilitation. Prigatano (1999) offers some guidelines for the establishment of a good working alliance with family members. These guidelines include listening carefully to the perspective of the family member, viewing family members as consultants, providing clear expectations of their role and level of involvement, incorporating educational materials and discussions, and recognizing that part of the therapist's job is to engage family members.

In addition to providing rehabilitation to appropriate brain tumor patients, patients' family members should be offered education and emotional support. Problems of brain tumor patients' spouses and caregivers are receiving increasing attention (Haut et al., 1991). In our experience, families of brain tumor patients are burdened by the patients' cognitive and behavioral changes in addition to the typical psychological problems of coping with cancer in a family member. They may have particular difficulty dealing with neurologically caused personality changes such as loss of initiative, quick mood changes, loss of control over emotions, and lack of insight into limitations. Support groups for brain tumor patients and their family members may be of great benefit. In our support group, one meeting each month is devoted to a topic discussion or lecture on an area of interest such as seizure medications. The other meeting each month is for open discussion and is more sup-

**Table 26-1.** Neurocognitive Functions Improved by the Use of Methylphenidate

Speed of information processing
Memory
Word retrieval
Executive function
Fine motor speed

portive in nature. Similar programs are available at other cancer centers, partly through the advocacy efforts of the National Brain Tumor Foundation ([www.brainumor.org](http://www.brainumor.org)) and support from the American Brain Tumor Association ([www.abta.org](http://www.abta.org)).

National Brain Tumor Foundation  
414 Thirteenth Street, Suite 700  
Oakland, CA 94612-2603  
[www.brainumor.org](http://www.brainumor.org)  
800-934-2873

American Brain Tumor Association  
2720 River Road  
Des Plaines, IL 60018  
[www.abta.org](http://www.abta.org)  
800-886-2282

### CONCLUSION

At the present time, rehabilitation efforts for brain tumor patients and, indeed, for cancer patients in general have focused on symptom management (i.e., pain control), psychological support, nutritional support, and management of the medical complications of treatment (McLaughlin, 1984). There are increasing numbers of services available for the totally disabled and terminally ill, but not for those individuals who may have milder, yet incapacitating deficits. A "good outcome" for brain tumor patients is often considered by medical personnel to be preservation of life and possibly rehabilitation of motor deficits by physical therapy. However, there has been little or no effort to offer cognitive and vocational rehabilitation to brain tumor patients who may have the ability and desire to return to work following the acute phase of their illness (Conti, 1990). According to the former commissioner of the Rehabilitation Services Administration of the U.S. Department of Education, "It is RSA's position that persons disabled by cancer may be eligible for vocational rehabilitation services and that such services should be provided if the individual wants to work and can work even if for a limited period of time" (U.S. D.H.E.W., 1980).

The current lack of sophisticated rehabilitation effort is due to several factors. One reason is a lack of awareness on the part of rehabilitation professionals, patients, and medical caregivers about ser-

vices that are available. Second, many brain tumor patients may not be encouraged to seek rehabilitation because they may not have marked sensory, linguistic, or motor deficits such as those seen in stroke patients even though most experience problems in executing work-related activities. Finally, there may be concern about expending resources on individuals who may eventually die from their disease. However, the resources expended on brain tumor patients may compare favorably with those expended on patients with heart disease, diabetic complications, mental disorders, and other chronic disabling conditions. In addition, these disorders share the possibility that the condition will progress or recur.

Along with formal rehabilitation, helping brain tumor patients attain an acceptable QOL may include helping them to accept the permanent changes, both cognitive and social, that having brain cancer might cause. Among the most disturbing losses sustained by the brain tumor patient are the loss of self-esteem, the loss of work and working relationships, and the loss of self-confidence. Brain tumor patients and their families may need to invest their efforts in new activities and interests and learn to enjoy leisure. Families may need to have occasional respite from their caretaking responsibilities. Quality of life needs to be defined on a highly individualized basis, requiring a great deal of flexibility on the part of the healthcare team, consultative services, and the patients and families. The need for continued psychosocial and neuropsychological assessment, rehabilitation, and counseling services will continue to grow as brain tumor patients survive for increasingly longer periods of time.

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