Clinical implications of motor deficits related to brain tumors†

Christina Amidei and David S. Kushner

Department of Neurology and Rehabilitation, University of Illinois, 912 S. Wood Street, MC 796, Chicago, Illinois 60612 (C.A.); Department of Physical Medicine and Rehabilitation, University of Miami Miller School of Medicine, 1600 NW 10th Avenue, Miami, Florida 33136 (D.K.)

Corresponding Author: Christina Amidei, RN, PhD, FAAN, Department of Neurology and Rehabilitation, University of Illinois, 912 S. Wood Street, MC 796, Chicago, IL 60612 (camidei@uic.edu).

†NOTE: This paper is one of two articles in a series.

Motor deficits, including unilateral or bilateral weakness, plegia, ataxia, spasticity, and loss of complex movement execution, can occur during any brain tumor illness. Tumor location, treatment effects, and medications contribute to these deficits. Motor dysfunction has been associated with significant deterioration in health-related quality of life in patients with primary and metastatic brain tumors. Significant decrease in median overall survival has been reported in patients with motor deficits, although the reasons for this are unclear. Motor deficits, particularly gait impairment, contribute to significant symptom burden at end of life, and are the most common reasons for initiation of hospice care. Interventions must focus on prevention and amelioration of motor dysfunction throughout the disease course in order to preserve quality of life. The impact of exercise in prolonging survival and improving quality of life requires further study.

Keywords: functional status, motor deficits, quality of life.

More than 68 000 people in the United States are expected to be diagnosed with a primary brain tumor in 2015; these figures do not include people with brain metastases from systemic cancers, which are far more common. Overall, about 700 000 people are living with the effects of a brain tumor in the United States. Tumor histology plays a significant role in survival; the 5-year survival rate for those with malignant primary brain tumors is 34.2%, while the 5-year survival rate for those with nonmalignant tumors is 91.9%. Surviving with a brain tumor, regardless of tumor type, often means that an individual lives with the consequences of that tumor, which may include neurologic deficits. Type of neurologic deficit varies by location and disease stage, but motor deficits are common. Understanding the clinical implications of motor deficits can provide direction for interventions that may improve functional status and quality of life. This article aims to review current knowledge about motor deficits that accompany a brain tumor illness and identify implications for patient management.

Clinical Implications of Motor Deficits

What Types of Motor Deficits Occur?

A broad range of motor deficits can occur, and the incidence of specific deficits varies (Table 1). Variability in reported incidence of motor deficits is due in part to overlap and inconsistent terminology; for example, ataxia and hemiparesis may both produce gait impairment, but any of the three terms may be reported as the deficit. In addition, studies reporting incidence of motor deficits were conducted at variable time points during the brain tumor illness. No study was found that focused on specific deficits that occurred across the disease trajectory.

Focal or nonfocal motor deficits can occur. Focal deficits include hemiparesis or hemiplegia with spasticity, gait impairments, ataxia, and incoordination. These deficits are directly related to the anatomy affected by the tumor or its treatment; anatomic correlates of specific motor deficits are found in Table 2. Tumors may cross anatomic boundaries to produce a complex picture of deficits. Spastic hemiparesis/plegia occurs with involvement of upper motor neuron pathways, and usually affects groups of muscles rather than individual muscles. Location above the pons or along the homunculus determines whether weakness will be limited to the hand, arm, foot, or leg, or involve all of these areas. Balance between agonist and antagonist muscles is disrupted, resulting in paradoxical, mirror or nonvolitional movements in a paretic limb. Severity of spasticity may not correlate with extent of weakness. Gait disorders occur with involvement anywhere along upper motor neuron pathways, and usually occur with cerebellar involvement. Movements may be slower to initiate and overshoot a target; intention tremor may accompany ataxia.
deficits, apraxias may manifest as motor deficits, reflecting the weakness or sensory loss. Although considered to be cognitive ability to carry out a purposeful movement in the absence of specific functional deficits follow motor dysfunction and include loss of complex execution of movements and impairments in activities of daily living. Balance may be impaired due to a number of interrelated factors, including loss of visual cues, sensory disturbances (especially proprioceptive problems), generalized weakness, gait apraxia, and cerebellar dysfunction. Imbalance may predispose an individual to an increased risk for falls. Balance impairment is particularly prevalent in aging individuals, but has also been reported in long-term survivors of pediatric brain tumors.

Motor deficits may occur with any type of tumor, primary or secondary, but tend to be more commonly associated with primary malignant tumors. Motor deficit was the second most commonly reported symptom by patients with malignant glioma, second only to fatigue. Motor deficits were more frequently reported in patients with glioblastoma than in those with anaplastic astrocytoma. Brain metastases contribute to paresis, ataxia, and incoordination at a frequency similar to glioblastoma. Patients with brain tumors report more motor-related symptoms than other cancer cohorts, suggesting a greater symptom burden in patients with brain tumors compared with patients who have other types of cancer.

What Causes or Contributes to Motor Deficits?
A number of factors contribute to motor deficits. Motor pathways affected by the tumor or inflammation secondary to treatment causes focal motor deficits. Surgical manipulation in motor pathways may create deficits that are slow to resolve or fail to improve. Necrosis from radiation therapy and chemotherapy may produce focal motor deficits as tumor cell death creates a local inflammatory response. Seizures may also produce focal deficits that can be challenging to distinguish from tumor progression or treatment effects.

Recently, anthracycline-based chemotherapy has been shown to produce prolonged generalized muscle weakness, probably through oxidative stress mechanisms. Other chemotherapies may produce similar muscle weakness. Corticosteroids, commonly used to control inflammation and edema in the brain, contribute to proximal muscle weakness. Individuals who develop steroid myopathy are those on dexamethasone for longer than 2 weeks at moderate to high doses. A tumor-induced systemic response may also occur, leading to significant loss of muscle mass.

### Table 1. Reported incidences of motor deficits throughout a brain tumor illness

<table>
<thead>
<tr>
<th>Type of Motor Deficit</th>
<th>Reported Incidences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemiparesis or hemiplegia</td>
<td>26%−47%</td>
</tr>
<tr>
<td>Proximal bilateral leg weakness</td>
<td>25%</td>
</tr>
<tr>
<td>Ataxia or incoordination</td>
<td>26%−91%</td>
</tr>
<tr>
<td>Spasticity</td>
<td>12%</td>
</tr>
<tr>
<td>Gait impairment</td>
<td>26%−62%</td>
</tr>
<tr>
<td>Myopathy</td>
<td>10%−44%</td>
</tr>
</tbody>
</table>

### Table 2. Anatomic correlates of focal motor deficits

<table>
<thead>
<tr>
<th>Focal Motor Deficit</th>
<th>Anatomic Correlate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemiparesis or hemiplegia</td>
<td>Frontal lobe: primary motor cortex, premotor (precentral) cortex, or supplementary motor cortex, Thalamus, Internal capsule, Brainstem</td>
</tr>
<tr>
<td>Apraxia</td>
<td>Frontal lobe: supplementary motor cortex or premotor cortex, Corpus callosum</td>
</tr>
<tr>
<td>Incoordination</td>
<td>Cerebellum, Basal ganglia, Brainstem</td>
</tr>
<tr>
<td>Ataxia</td>
<td>Cerebellum, Parietal lobe, Thalamus</td>
</tr>
<tr>
<td>Gait impairment</td>
<td>Frontal lobe: primary motor cortex, premotor (precentral) cortex, or supplementary motor cortex, Thalamus, Internal capsule, Cerebellum, Basal ganglia, Parietal lobe, Brainstem</td>
</tr>
<tr>
<td>Loss of complex execution of movements</td>
<td>Premotor cortex or supplementary motor cortex</td>
</tr>
<tr>
<td>Spasticity</td>
<td>Frontal lobe: primary motor cortex, premotor (precentral) cortex, or supplementary motor cortex, Thalamus, Internal capsule, Brainstem</td>
</tr>
</tbody>
</table>

Cognitive, visual-perceptual, and sensory impairments often coexist with focal motor deficits and compound the severity of functional impairment induced by motor deficits. Apraxia is the inability to carry out a purposeful movement in the absence of weakness or sensory loss. Although considered to be cognitive deficits, apraxias may manifest as motor deficits, reflecting the complex interplay amongst neurologic functions. Apraxias originate in the supplementary or premotor cortices. Ideomotor apraxia is the inability to execute a motor skill in spite of the intent and ability to do so. Kinetic limb ataxia is clumsiness in a limb in the absence of motor deficit; this may affect gait, producing a clumsy gait.

A more generalized and often proximal muscle weakness can occur due to systemic factors indirectly related to the brain tumor. This proximal muscle weakness is associated with a decrease in muscle strength and not necessarily a decrease in muscle mass. Chronic steroid use and muscle effects of tumor-induced pro-inflammatory cytokines are implicated in the myopathic changes seen in individuals with brain tumors. Generalized weakness often becomes more evident with activities that require repetitive movement, such as walking or stair climbing. Myopathic changes may also contribute to decreased exercise and activity tolerance, resulting in deconditioning. Specific functional deficits follow motor dysfunction and include loss of complex execution of movements and impairments in activities of daily living. Balance may be impaired due to a number of interrelated factors, including loss of visual cues, sensory disturbances (especially proprioceptive problems), generalized weakness, gait apraxia, and cerebellar dysfunction. Imbalance may predispose an individual to an increased risk for falls. Balance impairment is particularly prevalent in aging individuals, but has also been reported in long-term survivors of pediatric brain tumors.

Motor deficits may occur with any type of tumor, primary or secondary, but tend to be more commonly associated with primary malignant tumors. Motor deficit was the second most commonly reported symptom by patients with malignant glioma, second only to fatigue. Motor deficits were more frequently reported in patients with glioblastoma than in those with anaplastic astrocytoma. Brain metastases contribute to paresis, ataxia, and incoordination at a frequency similar to glioblastoma. Patients with brain tumors report more motor-related symptoms than other cancer cohorts, suggesting a greater symptom burden in patients with brain tumors compared with patients who have other types of cancer.
strength. This systemic response is thought to be mediated by tumor-necrosis factor-alpha and other cytokines released from tumor cells. Additional factors may contribute to generalized muscle weakness, including impaired nutrition, adverse effects of medications, and general deconditioning. 7

When Do Motor Deficits Occur?

Motor deficits can occur at any time throughout the course of a brain tumor illness. More than 70% of patients with malignant glioma report motor dysfunction as a problem at some time during the disease course. No specific trajectory of motor symptoms exists, although patterns are identifiable at different disease stages. Motor deficits present at diagnosis may improve with the addition of corticosteroids or after surgical debulking. 16,17 Extent of improvement depends on severity; dense hemiplegia present at diagnosis may improve but not resolve, while mild weakness may resolve completely. 16,17 Preoperative deficits are often related to edema from the tumor, and when tumor burden is diminished and edema controlled, motor symptoms may improve. Surgically induced motor deficits may as a result of surgical manipulation or postprocedure edema. Surgically induced motor deficits tend to improve over time, 18 but older adults may experience less improvement, possibly due to diminished physical reserve. 15 Focal motor deficits may wax and wane during treatment and are related to the local effects of treatment that cause irritation and edema. Delayed effects of treatment can also cause focal motor deficits when motor pathways are involved. Motor deficits are greater at time of recurrence than at initial diagnosis. 16,15

During palliative care, gait impairment and focal motor deficits are among the most common and distressing symptoms reported. 24 Gait impairment and motor deficits were the most common reasons for hospital admission for symptom management. Gait impairment and motor deficits occurred in 59.4% of patients with grade III or IV glioma, in 73.5% and 58.8% of patients with primary CNS lymphoma, and in 91.7% and 66.7% of patients with brain metastases, and end-of-life discussions were initiated in 79.3% of patients because of these symptoms. 7 At end of life, motor deficits account for the greatest symptom burden. 2,23 Several recent reports have identified that long-term survivors experience increased weakness, deconditioning, and overall worsening of physical function in spite of having stable disease. 1,13,19 The etiology of this is unclear and warrants further study.

Motor Deficits and Functional Status

Motor deficits contribute to a decline in functional status in people with brain tumors. Motor deficits were correlated with decline in motor subscale scores on the Functional Independence Measure (FIM) in 106 glioma patients assessed in a rehabilitation clinic. 3 Clinicians were able to identify motor deficits, but notably underestimated the long-term effects of physical impairment on functional status. 3,25,26 Further, women had lower functional scores than men with comparable motor deficits. 1,7

Decline in physical function limits ability to work. 25 Physical impairment and fatigue were second only to cognitive problems in limiting work ability in a study of work productivity in 95 individuals with malignant brain tumors. 27 Physical disability significantly decreased the likelihood of returning to work in 34 people with a brain tumor after completing a vocational rehabilitation program. 27 Motor deficits also limited driving ability, which additionally impacted ability to return to work. 25,27

Motor deficits can improve with rehabilitation, regardless of tumor type, and functional gains can be attained with rehabilitation even when motor deficits do not improve. 3 Functional gains in mobility, locomotion, and self-care attained with rehabilitation of brain tumor patients was comparable to those gained after in-patient rehabilitation for other types of neurologic disability. 3,6 Further functional improvements were noted for at least 3 months after program completion, and functional gains were able to be attained even while undergoing tumor treatment. Khan et al 17 randomized patients to a treatment group that received an outpatient multidisciplinary rehabilitation program or to a control group that received usual care in their community. Gains in scores on FIM subscales were significantly greater in the multidisciplinary rehabilitation group, and were sustained for at least 6 months. 12 Similarly, patients with malignant brain tumors achieved gains in functional status with a home rehabilitation program. 10

Motor Deficits and Quality of Life

Decreased functional status may negatively affect quality of life. Decline in physical function has been found to be predictive of decline in global quality of life and health-related quality of life in both patients with primary and metastatic brain tumors. 10,15,24,28 Physical function has been found to be a significant contributor to quality of life, and predictive of global quality of life in both patients with primary and metastatic brain tumors. 16,15,26,28 Motor deficits correlate with a significant impact on individual physical, role, emotional, and social functional domains on the QLQ-C30. 14,15 Yet other studies identify no relationship between physical function and quality of life. Physical function was found to have no correlation with quality of life in a study by Gazzotti et al, 10 but the participants’ mean functional status on the Barthel Index was 98.7, indicating that factors other than functional status may influence quality of life for those without motor or functional deficits. Osoba et al 15 also found no correlation between functional status and quality of life, but the participant functional levels were again fairly high. When comparing people with advanced brain cancer to those with other types of advanced cancer, motor deficits contributed to overall quality of life to a greater degree in the brain cancer group. 15 However, quality of life is affected by many factors other than functional status, and Porter et al 26 suggest that non-clinical factors might have greater relevance for quality of life than functional measures alone.

Motor deficits and physical functional status are correlated with quality of life subscale measures of fatigue, cognitive function, and depression in a number of studies. 4,12,26,28 This raises the question of whether physical function, fatigue, cognitive function, and depression comprise a symptom cluster deserving of independent analysis.

Motor Deficits and Survival

The presence of motor deficits has been found to negatively impact survival. Chaichana et al 18 evaluated preoperative factors that contributed to survival in 393 glioblastoma patients that...
had undergone surgical resection. After controlling for factors known to contribute to outcome (extent of resection and use of adjuvant therapies), they found preoperative motor deficit to be an independent predictor of significantly shorter survival in adults. Similarly, McGirt et al. found patients with surgically acquired deficits had a significantly shorter survival time than those who did not develop new perioperative deficits. In their retrospective review of 306 patients, those who developed a new or worsened perioperative motor deficit had a 3.9 month reduction in median survival. Both authors were unable to identify the cause for decrease in survival, but suggested that the impact of motor deficit on functional outcome and quality of life were the probable mechanisms for decreased survival. In a study of 48 patients with primary brain tumors, quality of life measures including leg weakness, unsteady gait, and incoordination were found not only to be predictive of recurrence, but survival as well. Leg weakness and gait speed have been found to be independent predictors of survival in other cancer types as well.

Rehabilitative approaches focusing on improving functional status and quality of life have the potential to enhance survival, especially in those with motor deficits. Tang et al. evaluated the impact of functional improvements in 63 patients with brain tumors who underwent an inpatient rehabilitation program. Significant improvements in overall FIM scores were noted at discharge, with improvements in motor subscales having the most significant contribution to the increase in overall FIM score. The authors suggested that improved physical function may have benefits beyond improved quality of life. Extent of functional improvement was also predictive of survival; those with the highest functional independence scores at discharge had the longest survival.

Exercise

Exercise may be of benefit in preventing weakness and loss of physical function in people with brain tumors. People with malignant brain tumors have been found to have less daily physical activity than their age-matched cancer counterparts; reasons for this are not known. Physical activity and exercise have long been known to positively affect overall functional status, and more than 80 studies now support the benefits of exercise in cancer survivors. Structured exercise programs have been deemed safe and well tolerated in people with cancer, and a number of prominent organizations now provide physical activity and exercise guidelines for people with cancer. The American Cancer Society has acknowledged that exercise is safe and feasible during cancer treatment and can improve not only physical function, but quality of life as well. Exercise may improve mood and fatigue and, therefore, perceived quality of life. Exercise has also been shown to improve gait control, which is of significance for patients with brain tumors. In this context, physical activity and exercise may be viewed as complementary to medical therapies for patients with malignant brain tumors.

A more exciting question is whether physical activity and exercise can prevent disease progression, prevent metastasis, and extend survival. Exercise has been associated with a cancer mortality risk reduction of 15% to 67% in persons with glioblastoma, non-small cell lung cancer and ovarian cancer. However, doses and types of exercise varied widely, and prescriptive guidelines for exercise duration, frequency, and intensity are not yet delineated. Recent evidence suggests that exercise modulates metabolic pathways that influence cancer biology. Exercise has been shown to decrease insulin-like growth factor, increase natural killer cell function, decrease in C-reactive protein, and decrease methylation. These factors may provide a biological rationale for the benefits of exercise in people with cancer.

Practice and Research Implications

Implications for practice and research can be gleaned from information presented in this brief review. Ongoing neurologic assessment through the course of a brain tumor illness is essential, as a broad range of motor deficits can occur. Assessment of the motor system typically includes muscle mass, strength, and tone, as well as assessment of coordination, gait, and posture. Physical examination of the person with a brain tumor should extend beyond a detailed neurologic examination to include a functional assessment that also encompasses balance and fall risk, ability to perform activities of daily living, and activity tolerance. Functional assessment may be a more critical measure over time, because of the impact of functional status on quality of life. Functional assessment tools, such as the FIM or Barthel Index, may be useful in monitoring objective changes over time. Patient self-report measures of the impact of motor deficits on functional status and quality of life should be incorporated into the overall assessment. Such measures not only enhance patient participation in treatment decisions, but may also provide valuable insight into functional impairments that have been missed in the examination. As deficits are identified, the multifactorial cause for the deficits should be considered and interventions instituted as appropriate. Patients may interpret new motor deficits as indicative of disease progression. Significance of the deficits should be clarified with the patient as interventions are planned.

Motor deficits are potentially modifiable factors that affect functional status, quality of life, and possibly even survival. Evidence supports the benefits of rehabilitation in improving functional status and quality of life for patients with brain tumors and interventions instituted at any sign of functional decline. Patient referral to physiatry and rehabilitative services should be considered an integral component of care, with a focus on maintaining motor function to the greatest degree possible for as long as possible. Physical and occupational therapies are beneficial throughout the disease course and may have some benefit even at end of life in promoting comfort and easing care. Although evidence supports that motor deficits and functional declines adversely affect quality of life and survival, it is not known whether addressing these deficits will prolong survival. The complex interactions between functional status, quality of life, and survival continue to be studied; data to date suggest that the primary benefit of improving physical function lies in improving quality of life. While survival measures are important, outcome measures beyond survival are equally significant, particularly to patients. Management strategies may be optimized for people with brain tumors when care is focused on factors that predict quality of life.

Motor function may be part of a symptom cluster with fatigue, mood, and cognitive function on quality of life measures. This
suggests that decline in motor function may add to fatigue, and adversely affect mood and cognitive function. It also suggests that improving motor function may also ameliorate fatigue, and improve mood and cognition. These potential interactions require additional attention both in clinical and research settings.

Health benefits of exercise for individuals with cancer have been delineated, as well as the positive impact of exercise on quality of life. Additional research is needed to determine whether individuals with brain tumors have specific physical or functional limitations that limit this benefit. However, it remains reasonable to consider structured exercise as a complementary therapy in the overall management plan. Further research is essential in delineating the appropriate prescriptive exercise guidelines for brain tumor survivors.

A number of studies recently have focused on identifying and treating cognitive consequences of a brain tumor illness; lesser attention has been paid to motor deficits accompanying the disease. Additional studies should focus on several questions raised in this review, including the reasons for a greater symptom burden with brain tumors as compared with other cancers. As individuals survive with brain tumors, the long-term reports of worsening motor deficits and physical functioning in spite of stable or absent disease warrant additional study in order to preserve quality of life.

**Conclusion**

Recognition of the clinical implications of motor deficits following a brain tumor diagnosis is growing, as is acceptance of rehabilitation throughout the disease course. Preventing and treating motor deficits may improve functional status and enhance quality of life. Exercise is a complementary treatment modality that deserves further study as to its role in improving quality of life and prolonging survival.

**Funding**

Christina Amidei has no funding to report related to this work. David Kushner has no funding to report related to this work.

**Conflict of interest statement.** C. A. has no conflict of interest to declare related to this work. D. K. has no conflict of interest to declare related to this work.

**References**


