# Cognitive Rehabilitation and Problem-Solving to Improve Quality of Life of Patients With Primary Brain Tumors: A Pilot Study

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**Abstract** Caregivers of patients with brain tumors frequently identify cognitive impairment in their loved ones as their greatest burden, but only one published study has examined a cognitive-rehabilitation intervention for adults with brain tumors. Emotional distress and poor quality of life (QOL) also have been identified as important issues, yet they have been excluded from most intervention studies that target coping and mood. The primary aim of this pilot study was to determine the feasibility and tolerability of a combined cognitive-rehabilitation and problem-solving-therapy intervention for patients with brain tumors and their caregivers. In all, 19 patient/caregiver pairs were enrolled and randomized, and 13 pairs completed the 2-week trial. After receiving the intervention, 88% of patients used the study-specific strategies, and 88% indicated that they would recommend the intervention to other patients diagnosed with a brain tumor. The study intervention was described as "very helpful" or "somewhat helpful" by 88% of study participants. Caregivers were similarly enthusiastic about the intervention. The results showed that patients with brain tumors who have cognitive impairment can participate meaningfully in a structured intervention, and they supported further research into the potential effectiveness of formal rehabilitation targeting cognitive and QOL symptoms for patients with brain tumors and their caregivers.

Cognitive impairment is a major cause of disability for individuals with brain tumors and is frequently identified by patients and their caregivers as the single greatest cause of burden. For example, in a survey of such caregivers, impairments of memory, reasoning, problem-solving, and judgment were the problems cited most frequently, and physical problems (eg, balance, walking, speaking) were those cited least frequently.[1] In this same survey, cognitive problems were cited most often as the reason that patients with brain tumors were unable to return to work.

Most patients with brain tumors suffer some degree of cognitive impairment from tumor infiltration, compression, and surgical removal and/or the effects of radiation and chemotherapy[2]; several published studies have identified the specific neuropsychological domains affected and the effects of such deficits on quality of life (QOL).[1–6] A number of published studies have demonstrated the benefits of rehabilitation in patients with traumatic brain injury; these patients and their caregivers encounter cognitive challenges similar to those of patients with brain tumors.[7,8]

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Despite evidence demonstrating the benefits of a cognitive-rehabilitation program for patients with traumatic brain injuries, only one published study has examined the potential benefits of such an intervention for adults with brain tumors. Sherer and colleagues[9] found that patients with brain tumors experienced increased independence and productivity after participating in a cognitive-rehabilitation intervention. These authors asserted that patients with brain tumors "have the ability to improve their ability to function at home and in vocational and leisure pursuits and enjoy an improved level of independence and QOL given the right support."

Another source of burden and decreased QOL in patients with brain tumors is emotional distress. In a recent survey, Pelletier et al[10] found that pa-

tients with primary brain tumors suffered a high degree of depressive symptoms and that the presence of these symptoms was the most important independent predictor of poor QOL; other predictors included generalized emotional distress, fatigue, and existential concerns. Several interventional studies have been aimed at reducing distress and/or improving QOL of distressed adults with cancer.[11–13] Most recently, Nezu and others[11] published the results of a well-controlled, randomized clinical trial that provided evidence for efficacy of problem-solving therapy in distressed cancer patients; this reduction of distress was maintained at the 1-year follow-up. Similarly, another randomized trial conducted at the Mayo Clinic provided evidence for improved QOL of advanced cancer patients using a multidisciplinary, structured intervention.[13] However, these studies either specifically have not targeted patients with brain tumors or have excluded patients with cognitive dysfunction (which rules out many patients with brain tumors).

The paucity of rehabilitation investigations involving patients with brain tumors has left many questions about the feasibility of interventions in this population unanswered. Factors such as the optimal timing and the intensity of interventions are unknown. Similarly, no "gold-standard" eligibility criteria point to factors that may indicate benefit from rehabilitation interventions; these factors may include tumor grade, prognosis, patient stamina (eg, performance score, frailty, fatigue), recency of diagnosis, or severity of cognitive impairment or distress.

This pilot study was designed to address the lack of knowledge about the potential QOL benefits of rehabilitative interventions for patients with brain tumors. This project focused on cognitive dysfunction and emotional distress, two areas that may impact the QOL of these patients the most. The cognitive-rehabilitation[14] and problem-solving-therapy[11,15] interventions used here are similar in design to those individually implemented successfully with other populations. The primary aim of this study was to examine the feasibility of using these interventions in patients with recently diagnosed, primary brain tumors and their caregivers. A secondary aim was to provide preliminary evidence that a brief, structured rehabilitation intervention for patients with primary brain tumors may impact QOL positively. Another secondary aim involved gathering feedback and suggestions from patients and caregivers regarding the intervention content and procedures; this information then would be used to modify the intervention, if necessary, and to provide an intervention more effectively tailored to meet the needs of these populations.

## Methodology and Sample

### ELIGIBILITY

Before, or upon initiation of, radiation therapy, patients with newly diagnosed primary brain tumors were referred by their radiation oncologists for clinical neuropsychological consultation to evaluate cognitive and emotional status. The diagnosis and grading of the primary brain tumor were based upon information detailed during a clinical diagnostic evaluation completed before the neuropsychological evaluation. When tumor type or grade was unclear, a final diagnosis was provided by a radiation oncologist (PDB).

The neuropsychologist provided relevant clinical care and considered patients' eligibility for enrollment into this trial. To be eligible, patients needed to be 18 years of age or older and to demonstrate mild-to-moderate cognitive impairment based on a combination of quantitative neuropsychological test data from the clinical assessment and the clinical judgment of the evaluating neuropsychologist. Patients also needed a prognosis of at least 6 months of life and the ability to attend sessions at our medical center for 2 weeks. All patients were required to have a designated caregiver available to attend all sessions.

In our setting, we were best able to offer this type of intervention while patients were receiving radiation therapy, because patients stayed in town or made daily trips to the medical center. Most of our patients traveled from across the region or even across the nation to obtain treatment. Thus, similar to those treated at many comprehensive cancer centers, patients typically do not remain in the region post treatment, so post-treatment timing of any intervention would have been difficult. Therefore, offering QOL interventions at the time of medical treatment allowed participation by the greatest number of patients.

Individuals meeting these eligibility criteria and their caregivers were invited to participate in the study; after providing signed informed consent, they were randomized to receive the intervention or standard medical care. The intervention group received six sessions of cognitive rehabilitation and six sessions of problem-solving therapy that were provided concurrently with radiation therapy over the course of 2 weeks. The standard medical care group did not receive any cognitive-rehabilitation or problem-solving intervention. Both study groups were reassessed at 2 weeks (post intervention for the intervention group) using the study questionnaires described below. Both groups were reassessed at 3 months, mainly by telephone and using study questionnaires.

A total of 19 patient-caregiver dyads were enrolled into the study. Of the 19 pairs enrolled in the study, the first 16 were randomized to their group assignment (7 controls, 9 intervention). Due to low accrual and anticipation of the ending of the enrollment period, the last three patient/caregiver dyads were not randomized and were enrolled directly into the intervention group, for a total of 7 control and 12 intervention dyads.

### MEASURES

The Compensation Techniques Questionnaire, originally developed in the Mayo Clinic Brain Injury Rehabilitation Program, was completed by patients to determine compensation techniques used before and after treatment (AR Kuppachi, unpublished data, 2003). Patients and caregivers in the intervention group each completed a study-specific Post-Study Feedback Questionnaire designed to elicit feedback on their preferences during the intervention and the skills that they found most useful.

To evaluate QOL and functional capacity, we used the

**Table 1**

Questionnaires and Timing of Data Collection for the Patient

| | BASELINE | POST INTERVENTION* | 3-MONTH FOLLOW-UP† |
|---|---|---|---|
| **Primary measure** | | | |
| Compensation techniques | X | X | X |
| End-of-study feedback | | | X |
| FACT–BR[16] | X | X | X |
| MPAI-4[17,18] | X | X | X |
| **Secondary measure** | | | |
| R-BANS[19] | X | | |
| LASA[20,21] | X | X | X |
| POMS[24] | X | X | X |
| BFI[25] | X | X | X |

Abbreviations: FACT–BR = Functional Assessment of Cancer Therapy-Brain; MPAI-4 = Mayo-Portland Adaptability Inventory-4; R-BANS = Repeatable Battery for the Assessment of Neuropsychological Status; LASA = Linear Analogue Self-Assessment scale; POMS = Profile of Mood States; BFI = Brief Fatigue Inventory

*The intervention group was tested immediately after receiving the intervention, and the standard care group was tested 2 weeks ± 5 days after study enrollment.

†For both groups, follow-up occurred 3 months ± 1 month after the post-intervention assessment or at the time of medical follow-up.

**Table 2**

Questionnaires and Timing of Data Collection for the Caregiver

| | BASELINE | POST INTERVENTION* | 3-MONTH FOLLOW-UP† |
|---|---|---|---|
| **Primary measure** | | | |
| End-of-study feedback | | | X |
| MPAI-4[17,18] | X | X | X |
| **Secondary measure** | | | |
| LASA[20,21] | X | X | X |
| CQOLC[22,23] | X | X | X |
| POMS[24] | X | X | X |

Abbreviations: MPAI-4 = Mayo-Portland Adaptability Inventory-4; LASA = Linear Analogue Self-Assessment scale; CQOLC = Caregiver Quality of Life-Cancer; POMS = Profile of Mood States

[a] The intervention group was tested immediately after receiving the intervention, and the standard care group was tested 2 weeks ± 5 days after study enrollment.

[b] For both groups, follow-up occurred 3 months ± 1 month after the post-intervention assessment or at the time of medical follow-up.

Functional Assessment of Cancer Therapy–Brain version (FACT–BR)[16] and the Mayo-Portland Adaptability Inventory-4 (MPAI-4).[17,18] The MPAI-4, developed to assess patients with traumatic brain injury, is a measure of functional capacity that includes ability, adjustment, and participation indices. The FACT–BR was completed by the patient, whereas the MPAI-4 was completed by the patient and by the caregiver describing the patient.

Secondary measures were used to evaluate cognitive functioning, QOL, caregiver burden, mood, and fatigue. The Repeatable Battery for the Assessment of Neuropsychological Status (R-BANS)[19] is a brief, individually administered test completed with the patient to examine multiple areas of cognitive functioning. The one-item Linear Analogue Self-Assessment (LASA) scale[20,21] that assesses overall QOL has been validated in neuro-oncology patients; both patients and caregivers completed this measure to describe their own QOL. The Caregiver QOL Index-Cancer (CQOLC)[22,23] measures the effect of a cancer patient's illness on the caregiver's QOL and is completed by the caregiver. Many of our patients had low-grade tumors that may not have led to a cancer diagnosis; therefore, we removed the word "cancer" in the title of the instrument. Also, the diagnosis of "cancer" was mentioned in the instructions; we modified the instructions to read "brain tumor" instead. None of the scale items mention cancer, so no changes to the items were required. The Profile of Mood States (POMS),[24] a measure of mood that includes a number of specific subscales, has been used extensively to assess distress in cancer populations; it was completed by both the patient and the caregiver to describe themselves. The Brief Fatigue Inventory (BFI),[25] a brief measure of the severity of fatigue and its impact on daily functioning in patients with cancer and in those being treated for the disease, was completed by the patient.

Tables 1[16–21,24,25] and 2[17,18,20–24] provide a representation of study measures administered at each time point to the patients and the caregivers.

## DESCRIPTION OF INTERVENTION

The cognitive-rehabilitation portion of the intervention was modeled after the techniques described by Sohlberg and Mateer.[14] In brief, patients and caregivers were taught to use a calendar that had a specific format as an external aid to compensate for cognitive symptoms. Patients and their caregivers completed six 50-minute sessions in an approximately 2-week period. Specific goals (Table 3)[15] provided by trained master's level psychology study personnel were developed for each session.

The portion of the intervention involving problem-solving was modeled after the techniques described by Nezu and colleagues.[11,15] In brief, the intervention involved teaching the patient and their caregiver a model of stress and a specific positive problem-solving technique for its management. This intervention also involved six 50-minute sessions over a 2-week period featuring specific goals (Table 3)[15] provided by a neuropsychologist or by a master's level behavioral therapist for each session. Cognitive-rehabilitation and problem-solving techniques were delivered concurrently.

## STATISTICAL ANALYSES

The primary aim was to assess the feasibility of the intervention. Feasibility may pertain to the ability of researchers to enroll patients in this type of intervention or to a patient's ability to participate meaningfully in one. To address the first definition and to determine "how many newly diagnosed patients with primary brain tumors will be eligible for such a trial," we tracked the number of new patients and reasons some individuals were not enrolled. To address the second definition and to answer the question "if patients are eligible, do they complete

## Table 3

Specific Goals for Cognitive-Rehabilitation and Problem-solving Therapy Sessions

| Cognitive-rehabilitation intervention |
|---|
| **Session 1** |
| Explain the purpose of a memory notebook, which is to compensate for cognitive problems by using this external device. |
| Determine whether or not the patient already uses a calendar system. |
| Introduce our calendar and orient to the format (ie, 1 day/page, specific times, action list area, date at top). |
| Have patient and caregiver verbalize difficulties they notice. |
| Strategize using the calendar for one difficulty (eg, remembering medications, entering doctors' appointments, remembering other planned outings, reducing repeated asking or questions), and agree to check off items as they are completed. |
| **Session 2** |
| Review orientation to the calendar with patient leading the way (ie, where the date is located, 1 day/page, specific times vs action list area). |
| Review patient's use of the calendar for identified area of difficulty. |
| Review checking off completed items. |
| Agree to expand the calendar for use with other areas (ie, therapist should help indicate what should go in the calendar—upcoming medical appointments, medication schedule, upcoming family events, etc). |
| **Session 3** |
| Check with patient and caregiver regarding spontaneous use of the calendar outside the session. |
| Review calendar for the previous day, today, and next day for entries and notation of completion. |
| Ask three questions for the patient to answer (ie, What is today's date? When is your next medical appointment? Did you take your medications yesterday?). |
| **Sessions 4–6** |
| Review use of the calendar and indications of completion since the last session. |
| Ask three patient-specific questions they would need the calendar to answer. |
| Ask patient and caregiver for additional difficulties, and see whether they can be incorporated into using the calendar. |
| During session 6, seek commitment from the patient and caregiver to using the calendar post treatment. |
| **Problem-solving-therapy intervention** |
| **Session 1** |
| Explain the problem-solving model of stress and the brain tumor as a major life stressor. |
| Present goals of the problem-solving intervention. |
| Present four components of a positive problem-solving orientation. |
| **Session 2** |
| Present more detailed development of the positive problem-solving orientation using the ABC method of constructive thinking and reversed advocacy role play and using feelings as cues. |
| Briefly present the steps of problem-solving: defining the problem, generating alternative solutions, deciding on a solution strategy, implementing the solution, reviewing the outcome of that implementation. |
| Present categories and specific potential tumor-related problems (eg, side effects, psychological distress, marital and family, medical interaction, sexual difficulties). |
| **Session 3** |
| Review detailed application of problem-solving steps to example problems. |
| Have the patient and caregiver choose a problem in the session to which they can apply the steps. |
| Have the patient and caregiver practice the steps on the chosen problem outside the session before session 4. |
| **Sessions 4–6** |
| Review patient and caregiver use of the strategies. |
| Review the positive problems-solving orientation or any of the steps of problem-solving, if necessary. |
| Troubleshoot any problems using the steps. |
| Continue to practice the techniques during the session. |
| Continue to refine patient and caregiver application of the steps. |

Source: Nezu et al[15]

## Table 4

Reasons Patients Were Not Enrolled (n = 141)

| REASON | n (%) |
|---|---|
| No cognitive deficit | 54 (38%) |
| Patient declined neuropsychological referral | 23 (16%) |
| Unknown | 19 (13%) |
| Alternative research protocol | 14 (10%) |
| No support person | 8 (6%) |
| Prognosis < 6 months | 8 (6%) |
| Severe cognitive impairment | 5 (3.5%) |
| No-showed or cancelled appointment | 5 (3.5%) |
| Not remaining at center long enough for intervention | 3 (2%) |
| Non-English speaking | 1 (1%) |
| Not continuing treatment at our center | 1 (1%) |

the trial and learn and utilize the intervention?" we captured the percentage of patients using study-specific strategies on the Compensation Technique Questionnaire.

To address tolerability or patient satisfaction, the percentage of patients and caregivers who found the intervention helpful, the portion of the intervention that patients considered to be most helpful, and the percentage of participants who would recommend the intervention to others, we used the Post-Study Feedback Questionnaire.

Demographic, tumor, and treatment data were described using means, medians, and percentages, as appropriate. The primary quantitative measures of interest were the FACT–BR and the MPAI-4. For each measure, scores from the same group (treatment or control) at different time points were compared using the Wilcoxon signed rank test, and scores from different groups at the same time point (baseline, post intervention, and follow-up) were compared using the Wilcoxon rank sum test, all having a 0.05 level of significance. Because feasibility and tolerability were the primary focus, the analyses for secondary endpoints were descriptive and qualitative.

## Results

Over the course of 2 years, 160 new patients with primary brain tumors were seen by our radiation oncology department. Of those 160 patients, 19 were enrolled. Table 4 reports the various reasons the remaining 141 were not enrolled. For example, 38% of patients referred did not have mild-to-moderate cognitive impairment and, therefore, were ineligible for the study; this was the most common reason patients were not enrolled. Targeting newly diagnosed patients early in the courses of both their disease and treatment likely is the reason so few patients demonstrated cognitive impairment.

In this sample, 74% (14/19) of the patients were seen for the intervention up to 2 months from the time of diagnosis; one patient was seen within 3 months of diagnosis. The remaining four patients were substantially farther from diagnosis at 22 months, 27 months, 41 months, and 87 months; this last patient originally was diagnosed 87 months prior and was seen

**Table 5**

Patient Demographic, Tumor, and Treatment Characteristics

| VARIABLE | PATIENTS ENROLLED | | STUDY COMPLETERS | |
|---|---|---|---|---|
| | CONTROL (n = 7) | INTERVENTION (n = 12) | CONTROL (n = 5) | INTERVENTION (n = 8) |
| Age (year) | | | | |
| Median | 60 | 46.5 | 56 | 46.5 |
| Range | 31–71 | 30–78 | 31–70 | 31–78 |
| Mean (SD) | 56.6 (13.9) | 49.8 (16.4) | 52.8 (14.7) | 48.8 (16.4) |
| Male gender, n (%) | 4 (57.1%) | 7 (58.3%) | 3 (60%) | 5 (62.5%) |
| Tumor type | | | | |
| Meningioma, n (%) | 0 | 2 (16.7%) | 0 | 2 (25%) |
| Glioma, n (%) | 7 (100%) | 10 (83.3%) | 5 (100%) | 6 (75%) |
| Tumor grade | | | | |
| Low, n (%) | 1 (14.3%) | 5 (41.7%) | 1 (20%) | 3 (37.5%) |
| High, n (%) | 6 (85.7%) | 7 (58.3%) | 4 (80%) | 5 (62.5%) |
| Hemisphere | | | | |
| Right, n (%) | 1 (14.3%) | 2 (16.7%) | 0 | 0 |
| Left, n (%) | 5 (71.4%) | 9 (75%) | 5 (100%) | 8 (100%) |
| Both, n (%) | 1 (14.3%) | 1 (8.3%) | 0 | 0 |
| Neurosurgery (yes), n (%) | 3 (42.9%) | 7 (58.3%) | 2 (40%) | 5 (40%) |
| Radiation therapy (yes), n (%) | 7 (100%) | 11 (91.7%) | 5 (100%) | 7 (87.5%) |
| Chemotherapy (yes), n (%) | 5 (71.4%) | 7 (58.3%) | 4 (80%) | 5 (62.5%) |
| ECOG performance status* | | | | |
| 0, n (%) | 4 (57.1%) | 6 (58.3%) | 3 (60%) | 4 (50%) |
| 1, n (%) | 2 (28.6%) | 5 (41.7%) | 1 (20%) | 4 (50%) |
| 2, n (%) | 1 (14.3%) | 0 | 1 (20%) | 0 |

Abbreviations: SD = standard deviation; ECOG = Eastern Cooperative Oncology Group

*Performance status is missing for the one patient in the intervention group who dropped out after enrollment and randomization but before the intervention sessions began.

for recurrence within the past 3 months. All patients were seen during the radiation therapy period (range, 1–36 days after radiation therapy began; mean, 15 days after radiation therapy began) for the intervention.

A challenge of staff working at a comprehensive cancer center is competing protocols. During the enrollment period, a competing QOL intervention began enrolling patients. That protocol was designed to target QOL in emotionally distressed patients with advanced-cancer; therefore, patients with high-grade brain tumors were considered eligible for that trial if they were relatively intact cognitively as measured by a brief mental-status exam. Presumably, the 10% of patients referred to that alternative protocol did not have cognitive impairment and would not have been eligible for our trial; however, we cannot state this with certainty, because we did not evaluate their cognitive function. Thus, nearly half (48%) of the patients not enrolled may have been ineligible because they lacked cognitive impairment.

In all, 16% of patients declined to be referred to the clinical neuropsychologist for clinical evaluation and never were evaluated either clinically or for potential eligibility for the trial. Poor prognosis and lack of a caregiver were relatively rare reasons patients were not enrolled (6% each). Remaining reasons included severe cognitive impairment (3.5%), not presenting for a clinical neuropsychology appointment (3.5%), not remaining at the medical center long enough to complete the intervention (2%), not speaking English (1%), and not continuing treatment at our center (1%).

## PATIENT PARTICIPATION

There were 12 intervention patients and 7 control patients enrolled in the trial. Of them, 18 completed the pre-intervention assessment. One patient concerned about the time commitment dropped out after being randomized to the intervention group. Fourteen of 18 patients (8 intervention and 6 control patients) completed the post-intervention assessment. One control patient dropped out due to tumor progression and new-onset seizures. Further, two intervention patients dropped out, one because of caregiver unwillingness to accompany the patient to the intervention and the other because of fatigue during treatment.

Thirteen patients completed the entire study through the 3-month follow-up date (eight intervention and five control patients). One control patient did not complete the 3-month follow-up assessment due to tumor progression.

Table 5 presents demographic, tumor, and treatment characteristics for patients who enrolled in the study (n = 19) and those who completed the study (n = 13).

**Table 6**

Mean Total Raw Scores for Study Completers on Primary Study Measures

| MEASURE | GROUP | PRE INTERVENTION (SD; MEDIAN) | POST INTERVENTION (SD; MEDIAN) | 3-MONTH FOLLOW-UP (SD; MEDIAN) |
|---|---|---|---|---|
| FACT–BR[16] | Control (n = 5) | 132 (18.4; 125) | 139 (15.3; 136.5) | 140 (9.0; 143) |
| | Intervention (n = 8) | 117 (32.1; 127) | 130 (13.3; 129.5) | 130 (18.0; 128.5) |
| MPAI-4[17,18] | Control (n = 5) | | | |
| | Self-rating | 20.0 (9.5; 19) | 18.8 (7.5; 17.0) | 16.2 (5.45; 18.0) |
| | Proxy rating* | 27.4 (16.0; 24) | 31.6 (13.5; 35.0) | 25.4 (18.6; 14.0) |
| | Intervention (n = 8) | | | |
| | Self-rating | 35.8 (20.2; 28.5) | 26.0 (11.3; 25) | 24.3 (15.7; 21.5) |
| | Proxy rating* | 30.7 (15.3; 27.5) | 25.8 (14.6; 23.5) | 20.0 (11.9; 18.5) |

Abbreviations: SD = standard deviations; FACT–BR = Functional Assessment of Cancer Therapy–Brain; MPAI-4 = Mayo-Portland Adaptability Inventory-4

*Proxy rating by caregiver

## IMPLEMENTATION OF STRATEGIES

As measured by the Compensation Techniques Questionnaire, after receiving the intervention, 88% (7/8) of patients were using the study-specific strategies a minimum of several times per week and a maximum of several times per day. One patient was unable to implement the study-specific strategies.

At the 3-month follow-up, 50% of patients (4/8) continued using the strategies a minimum of several times per week and a maximum of several times per day. Another three patients were using the strategies once per week or less. Thus, 88% were using the strategies at least once per week at follow-up. Again, one patient could not implement the strategies during the intervention and, therefore, was not using any at follow-up.

## PATIENT SATISFACTION

On the feedback questionnaire, 88% (7/8) of intervention participants described the study intervention as "very helpful" or "somewhat helpful." Half of the patients considered the cognitive-rehabilitation component to be helpful, whereas 25% found the problem-solving-therapy component to be most helpful, and 25% believed that both were equally helpful. Of those who received the intervention, 88% (7/8) would recommend the treatment to another person diagnosed with a brain tumor.

Similarly, 88% (7/8) of the caregivers described the study intervention as "very helpful" or "somewhat helpful." Half of the caregivers found the cognitive-rehabilitation component to be most helpful, and the remaining 50% found the problem-solving-therapy component to be most helpful. Of those who received the intervention, 100% of the caregivers would recommend the treatment to another person diagnosed with a brain tumor.

## QOL

The FACT–BR was the primary QOL measure, and higher scores indicated better QOL. Table 6[16–18] shows the mean and median scores for each group at each time point. There was no statistically significant difference between the control and intervention groups on the FACT–BR total score at any assessment time point. Overall, this group of patients reported rather good QOL, with *t* scores falling within the average-to-above-average range ($t$ = 40–63) when compared with the normative sample.[16] Only three observations fell below the average range across all patients and all three time points.

No significant change in FACT–BR total scores was found over time within each group. Review of the mean scores across time suggested a possible trend toward improvement in QOL for both groups. On the subscales related to social/family well-being, emotional well-being, functional well-being, or additional concerns specific to brain tumors, there were no significant changes across time within groups. However, on the subscale for physical well-being, the score for the intervention group was significantly better at the 3-month follow-up than it was at the pre-intervention evaluation ($P$ = 0.04). The mean difference was 3.25 raw score points (95% confidence interval [CI], 0.07–6.43).

Secondary QOL measures included the LASA and the CQOLC (Table 7).[20–25] On the LASA, scores ranged from 6–8 out of 10, with higher scores indicating better QOL for each group at each time point. This finding suggested a positive QOL for patients and caregivers throughout the study. When compared with a normative comparison group of caregivers of individuals who had different types of cancer and who currently were being treated actively,[26] *t* scores on the CQOLC ranged from 48–55 across groups and measurement points, suggesting that caregiver QOL was average or better when compared with that of other caregivers of patients receiving treatment.

## FUNCTIONAL STATUS

The MPAI-4 was the primary measure of functional status; lower scores indicated better functional status. Table 6[16–18] shows the overall scores on both the self-rated version and the caregiver-rated version of the MPAI-4 at each assessment time point. Across both groups, there was a tendency for functional status reported by the patient to improve over time ($P$ = 0.06), but there was no difference in functional status across groups. There was also no difference in the caregivers'

**Table 7**

Mean Total Raw Scores for Study Completers on Secondary Study Measures

| MEASURE/GROUP | PRE INTERVENTION (SD; MEDIAN) | POST INTERVENTION (SD; MEDIAN) | 3-MONTH FOLLOW-UP (SD; MEDIAN) |
|---|---|---|---|
| **Patient LASA[20,21]** | | | |
| Control (n = 5) | 8.4 (2.5; 9.0) | 8.0 (1.9; 7.0) | 8.4 (1.8; 9.0) |
| Intervention (n = 8) | 7.4 (1.7; 7.5) | 7.4 (2.4; 8.0) | 8.0 (1.7; 8.0) |
| **Caregiver LASA[20,21]** | | | |
| Control (n = 5) | 7.0 (2.5; 7.0) | 7.8 (1.5; 8.0) | 7.8 (2.5; 8.0) |
| Intervention (n = 8) | 6.5 (2.4; 7.0) | 6.8 (1.8; 7.0) | 7.1 (2.3; 8.0) |
| **CQOLC[22,23]** | | | |
| Control (n = 5) | 93 (17.4; 101) | 102 (11.7; 104) | 107 (18.5; 110) |
| Intervention (n = 8) | 95 (20.1; 102) | 98 (19.5; 102) | 98 (20.6; 103) |
| **POMS Patient[24]** | | | |
| Control (n = 5) | 81 (2.3; 81.7) | 76 (9.4; 80) | 79 (8.7; 80.0) |
| Intervention (n = 8) | 65 (24.6; 74.2) | 72 (7.0; 71.7) | 76 (11.3; 80.0) |
| **POMS Caregiver[24]** | | | |
| Control (n = 5) | 67 (15.1; 74.2) | 73 (8.3; 75.8) | 74 (23.9; 80.0) |
| Intervention (n = 8) | 70 (12.8; 72.5) | 73 (16.5; 78.1) | 73 (16.1; 80.0) |
| **BFI[25]** | | | |
| Control (n = 5) | 2.6 (3.0; 1.2) | 1.8 (1.7; 1.1) | 3.0 (3.5; 1.1) |
| Intervention (n = 8) | 4.4 (2.5; 3.8) | 4.2 (2.7; 4.4) | 3.2 (2.8; 2.5) |

Abbreviations: SD = standard deviations; LASA = Linear Analogue Self-Assessment scale; CQOLC = Caregiver Quality of Life-Cancer; POMS = Profile of Mood States; BFI = Brief Fatigue Inventory

ratings of functional status across groups or across time. Finally, there was no significant difference between self-ratings and caregiver ratings of functional status.

## COGNITIVE DATA

Table 8[19] shows the data from the R-BANS index scores for each group at enrollment. Index scores have a mean of 100 and a standard deviation of 15, with higher scores indicating better cognitive functioning. Baseline data suggested that the control group completing the study was more impaired on the measure of immediate memory than was the intervention group completing the study despite, random assignment of all but three subjects ($P = 0.03$). Not surprisingly, both groups appeared to be weak on memory and attention tasks when compared with the normative sample; these cognitive domains are specific targets for the types of interventions provided in this study.

An aim of the study was to re-evaluate all patients with the R-BANS at the 3-month follow-up point in anticipation that patients would return at that time for other medically necessary follow-ups. However, contrary to expectations, most patients did not return at that time for in-person follow-up; instead, they often chose to be followed by physicians closer to home. Questionnaires were completed via telephone if the person was not returning for in-person evaluation. However, the R-BANS cannot be administered via telephone, so most patients did not complete the R-BANS at follow-up.

## MOOD AND FATIGUE

The final secondary measures included the POMS for both the caregiver and the patient and the BFI for the patient. Table 7[20–25] documents means, standard deviations, and median scores on these measures at each assessment time point. The

**Table 8**

R-BANS[19] Index Score Mean at Enrollment by Treatment Group for All Enrolled and All Completing the Study

| | PATIENTS ENROLLED | | STUDY COMPLETERS | |
|---|---|---|---|---|
| INDEX | CONTROL (n = 7) (SD; MEDIAN) | INTERVENTION (n = 12) (SD; MEDIAN) | CONTROL (n = 5) (SD; MEDIAN) | INTERVENTION (n =8 ) (SD; MEDIAN) |
| Immediate memory | 70 (17.8; 65.0) | 85 (12.8; 82.0) | 65 (12.3; 65.0) | 84 (14.4; 80.5) |
| Visuo-construction | 92 (16.7; 89.0) | 88 (18.3; 91.5) | 97 (14.8; 92.0) | 89 (16.5; 91.5) |
| Language | 85 (6.9; 85.0) | 86 (16.0; 83.5) | 85 (8.4; 83.0) | 88 (16.4; 85.0) |
| Attention | 77 (13.5; 75.0) | 77 (28.0; 69.5) | 77 (9.5; 75.0) | 77 (23.7; 69.5) |
| Delayed memory | 72 (19.0; 75.0) | 83 (21.0; 94.0) | 71 (13.5; 75.0) | 82 (18.8; 88.5) |
| Total | 73 (13.4; 75.0) | 79 (20.0; 75.5) | 73 (9.3; 75.0) | 80 (18.6; 75.5) |

Abbreviations: R-BANS = Repeatable Battery for the Assessment of Neuropsychological Status; SDs = standard deviation

POMS scores are converted to a scale of 0–100, with higher scores indicating better emotional status. In general, scores of 70 and higher suggest good emotional adjustment; using this criterion, the POMS scores of this sample suggested rather good emotional status of patients and caregivers throughout the study. Specifically, over 77% of the individual patient's scores and 74% of the individual caregiver's scores were above 70 across group and assessment time points.

Possible BFI scores ranged from 0–10, with higher scores indicating more fatigue. Similar to that seen with mood and QOL data, the majority of patients experienced only mild fatigue during the course of the study even though they were receiving radiation therapy. Specifically, 62% of patient scores across groups and assessment time points were in the no-to-mild-fatigue range (< 4), 20% of patient scores were in the moderate-fatigue range (4–6), and 18% of patient scores were in the severe-fatigue range (7–10).

## Discussion

This study demonstrated the feasibility of patient participation in and patient satisfaction with a cognitive rehabilitation and problem-solving intervention for patients with primary brain tumors. In spite of their serious medical diagnoses and their cognitive impairment, most enrolled patients completed the study. Extremely positive feedback indicated that patients and their caregivers found the intervention helpful; they also indicated that they would recommend the intervention to other patients.

Specifically, 88% of patients were able to learn the study-specific strategies and to continue using the strategies to some degree after 3 months. Also, 88% of those who received the intervention described it as helpful and indicated that they would recommend the intervention to other patients with brain tumors. Caregivers were similarly enthusiastic about the intervention strategies. This indicated that use of this type of intervention is feasible during radiation treatment for a subset of patients with newly diagnosed brain tumors who are experiencing cognitive impairment. Given these findings, future research should involve a large, randomized clinical trial that evaluates the impact of a cognitive-rehabilitation and problem-solving therapy intervention on functional status, mood, and QOL. Future research should seek more information on how such specific patient factors as tumor location or concurrent chemotherapy may impact the efficacy of the intervention.

In spite of the presence of cognitive impairment, scores of both intervention- and control-group questionnaires indicated that patients were well adjusted and had average-to-above-average QOL. Qualitative review of the scores showed that QOL in this sample appeared to remain stable, or even improve, in some participants across the study period. In this small sample, there were no statistically significant changes on measures of QOL or emotional status. However, this small trial was not powered to detect statistical changes.

Patients were selected based upon cognitive impairment, not upon poor QOL or for emotional distress. This may be important for those designing future research. Specifically, it may be reasonable to target patients reporting poor QOL, poor functional performance in day-to-day activities, and/or emotional distress for interventions. Alternatively, a larger study could compare subgroups with higher and lower baseline distress to determine which may benefit most from rehabilitation.

One hypothesis is that the relatively high QOL scores for patients in this trial reflected their cognitive impairment and, therefore, decreased awareness of deficits. The MPAI-4 findings, however, suggested that this was not the case. Specifically, the MPAI-4 measures functional impairment secondary to cognitive impairment; it was completed by both the patient and the caregiver describing the patient. There was no difference between the patient and caregiver ratings, suggesting that patients rated their functional impairment accurately and had adequate insight into their cognitive and functional impairments. Therefore, it is unlikely that higher QOL scores in this trial were due to some lack of awareness of deficits.

Only a small percentage of all patients with newly diagnosed brain tumors who were receiving radiation therapy and who were screened for eligibility had measurable cognitive impairment. A brain tumor likely causes less cognitive impairment than would a more sudden-onset process (eg, stroke), even when lesions are equated for volume and area of impact.[27] These patients simply may have been too early in their disease course to expect much measurable impairment.

The specific targeting of this newly diagnosed, relatively small subset with objective cognitive impairment restricted the pool of eligible participants. But the results showed that most eligible patients did enroll, and most completed the study and gave positive feedback about their experience. Recruitment could be improved in future studies by including patients in a later disease course or experiencing recurrence; a greater percentage of these patients likely would have cognitive impairment. Another possibility, currently in development in our center, is to include patients *before* cognitive impairment develops and to provide education and allow them to learn and implement compensatory strategies before they experience deficits. Larger studies that include both impaired and unimpaired patients could determine which group benefits most from treatment. There also may be a role for briefer education-oriented contacts for all patients and their caregivers, with more intensive interventions given to the minority of patients having significant cognitive impairment.

In all, 33% (4/12) of those enrolled did not complete the intervention. This occurred for a variety of reasons, including patient concern about the time commitment (n = 1), fatigue during radiation (n = 1), and caregiver unwillingness to continue participation (n = 2). It is difficult to modify the intervention based upon these concerns, since each was cited by just one or two participants. However, design of a larger trial could include greater schedule flexibility to accommodate fatigue and allow multiple caregivers per patient to ease the scheduling burden on caregivers.

Finally, an important consideration for a future, larger trial would be relevant stratification factors. Potential factors could include tumor location. For example, in this study, left hemisphere tumors were present in the majority of patients and in all who completed the study. Thus, tumor location would be an important variable for patient stratification. Similarly, concurrent chemotherapy or neurosurgical history may impact cognitive functioning and/or the ability to complete rehabilitation; they represent additional factors to consider for a larger trial.

## Conclusion

These results provided an encouraging foundation for larger-scale studies on cognitive and QOL interventions for patients with brain tumors. The patients in this study could tolerate the intensive intervention and the rather extensive pre- and post-treatment evaluations. Future research could use similar measures over a longer time span to evaluate whether such cognitive and psychological interventions may help prevent or slow declines in QOL that are related to disease progression.

Past studies established the value of formal cognitive assessment of patients with brain tumors.[28–30] Hopefully, this study will help to lay the foundation for taking the next step: empirical validation of neurocognitive-rehabilitation techniques that will enhance QOL for patients with brain tumors and their caregivers.

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