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Impairment of medical decisional capacity in relation to Karnofsky Performance Status in adults with malignant brain tumor

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Background. We aimed to investigate the relationship between medical decisional capacity (MDC) and Karnofsky Performance Status (KPS) in adults with malignant brain tumors.

Methods. Participants were 71 adults with primary ($n = 26$) or metastatic ($n = 45$) brain tumors. Testing to determine KPS scores and MDC was performed as close together as possible for each patient. Participants were administered a standardized measure of medical decision-making capacity (Capacity to Consent to Treatment Instrument [CCTI]) to assess 3 treatment consent abilities (ie, *appreciation, reasoning,* and *understanding*). Capacity classifications (ie, capable, marginally capable, and incapable) were established using cut scores previously derived from healthy control CCTI performance.

Results. The majority of participants had KPS scores of 90–100 ($n = 39$), with the remainder divided between KPS scores of 70–80 ($n = 26$) and 50–60 ($n = 6$). Comparisons between persons with KPS scores of 90–100 or 70–80 revealed significant differences on the CCTI consent standards of *understanding* and *appreciation.* Participants with KPS ratings of 90–100 achieved 46% capable classifications across all CCTI standards, in contrast with 23% of participants with KPS ratings of 70–80, and 0% of participants with KPS ratings of 50–60.

Conclusions. A substantial portion of brain-tumor patients with KPS scores reflecting only minimal disability nonetheless demonstrated impairments on standardized measures of MDC. Clinicians working with this adult population should carefully screen for capacity to make clinical treatment decisions regardless of functional/performance status.

Keywords: cerebral neoplasm, cognitive function, medical decision-making, medical ethics, treatment consent.

Adults diagnosed with malignant brain tumors, either glioma or brain metastases of solid tumors, often experience cognitive, psychiatric, and physical deterioration during the course of their disease.[1,2] Malignant glioma and brain metastases are 2 of the most deadly and disabling types of BTs occurring in adults. Over the course of their illness, patients with these tumors are also presented with ongoing clinical treatment issues and are asked to make complex medical treatment and research participation choices. As a result, clinicians and researchers working with this vulnerable population have an important responsibility to ensure that these persons are capable of consenting to treatment.[3–5] This was highlighted in a recent study demonstrating that a sizable proportion of patients with brain tumors were judged incapable of consenting to neurosurgery treatment and that this incapacity was associated with degree of cognitive impairment.[6]

Our group has previously investigated medical treatment consent capacity in adults with malignant glioma.[7] We found that adults with malignant glioma demonstrated significant impairments, relative to control participants, on a standardized measure of treatment consent capacity. We did not find that demographic and clinical variables such as age, education, sex, and time from diagnosis were statistically associated with the treatment consent capacity in these patients.[7] In contrast, clinician ratings on the Karnofsky Performance Status (KPS) scale[8] were statistically correlated with patient performance on the capacity measure, suggesting a linkage between disability level and decisional capacity.

For more than 50 years, the KPS has been a standard clinical rating tool of global functional status used by clinicians and researchers in the neuro-oncology field.[2,9] The KPS scale was

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originally designed to measure the performance status of patients undergoing chemotherapy treatments for cancer.[10] Performance was defined in terms of a person's ability to carry out daily activities, including work, and his/her need for assistance. Statistically significant associations have been found between the KPS and reports of physical functioning (ie, energy level, weight loss) and also functional activities (ie, driving, grooming, work).[9] In addition, the KPS has been a commonly reported functional scale included in numerous central nervous system cancer clinical trial studies.[11–16] Although the KPS has received criticism about its psychometric characteristics (ie, reliability,[17] insensitivity to cognitive impairment[18]), it remains a standard inclusion measure for most clinical trials in neuro-oncology.

The purpose of the current study was to further examine the relationship between clinically established disability level and decisional capacity in adults with gliomas or brain metastases of solid tumors.

In our prior study, we performed only simple correlational analyses illustrating this relationship with a small sample of adults with malignant glioma. In the present study, we built upon this initial statistical association by examining, across KPS score groups, capacity performance and capacity outcome ratings (ie, capable, marginally capable, and incapable) on a standardized measure of treatment consent capacity in a larger, more diverse sample of patients with malignant BTs. We hypothesized that patients with higher KPS scores would have greater medical decision-making capacity performance compared with those with lower KPS scores.

Methods

Seventy-one adults with brain tumors were included in the current study. All patients were diagnostically characterized by a board-certified neuro-oncologist or radiation oncologist. All tumors were intracranial lesions. Malignant gliomas were histologically verified (glioblastoma multiforme [$n = 19$], anaplastic astrocytoma [$n = 5$], and gliosarcoma [$n = 2$]). All patients with malignant glioma had received some form of brain cancer treatment (ie, surgery, radiation, and/or chemotherapy) at the time of their study participation.

Participants with brain metastases had brain tumors that spread from a non-CNS primary cancer site (non–small cell lung [$n = 15$], breast [$n = 9$], melanoma [$n = 8$], small cell lung [$n = 4$], esophageal [$n = 2$], ovarian [$n = 2$], colon [$n = 1$], gynecological [$n = 1$], mixed small and non–small cell lung [$n = 1$], head and neck [$n = 1$], and renal cell [$n = 1$]). All tumors were detected on MRI or CT scan. Further disease and treatment characteristics are presented in Table 1.

None of the study participants had a history of serious psychiatric illness, expressive aphasia, substance abuse, or coexisting medical illness adversely affecting cognition. Written informed consent was obtained from each participant and, in some cases, from their authorized legal representative. If, during the course of the study consent process, there was concern that the participant was not comprehending the study information being presented or the referring physician raised a concern about the person's consent capacity, then research consent was obtained from a family member who held legal power of attorney, and assent was obtained from the participant. The University of Alabama at Birmingham Institutional Review Board approved this study.

Table 1. Disease information

Disease Information	Number or Frequency
Months from brain tumor diagnosis	Median = 1 (mean 3.5, SD 4.2, range 1–21)
Days between CCTI assessment and KPS score assignment	Median = 4, mode = 0 (mean 6.9, SD 8.7, range 0–37)
Multiple brain tumors	28 (39%)
Tumor location by hemisphere	
Right only	19 (27%)
Left only	27 (38%)
Both	24 (34%)
Cerebellum	1 (1%)
Brain tumor treatment prior to study evaluation	59 (83%)
Type of treatment	
Surgical resection only	3 (4%)
Surgical resection and focal radiation	2 (3%)
Surgical resection and WBRT	20 (28%)
Surgical resection and focal radiation and WBRT	1 (1%)
Focal radiation only	15 (21%)
WBRT only	16 (23%)
Other	2 (3%)
Chemotherapy prior to study evaluation	52 (73%)
Antiepileptic medication	28 (39%)
Corticosteroid	30 (42%)

Abbreviations: WBRT, whole-brain radiation therapy; KPS, Karnofsky Performance Status; CCTI, capacity to consent to treatment instrument.
Note. Number of patients with percentage in parentheses for all cells except for Months from Brain Tumor Diagnosis and Days from KPS Score. Median with mean, standard deviation, and range for cells referring to Months from BT Diagnosis and Days from KPS score.

Procedures

Karnofsky Performance Status Scale

All patients received KPS ratings by their treating neuro-oncologist or radiation oncologist. KPS ratings used for the present study were collected at the clinical visit closest in time to the administration of the consent capacity measure. At the time of the KPS rating, the clinician did not know the results of the consent capacity tests.

The KPS scale consists of 11 categorical ratings in increments of 10 (ie, 100, 90, 80 . . ..) that range from 0 (dead) to 100 (normal, no complaints; no evidence of disease).[10] KPS ratings from 90 to 100 reflect the clinical status of persons able to carry on normal activity (eg, work) who are either asymptomatic (KPS = 100) or have only minor symptoms (KPS = 90). KPS ratings from 70 to 80 reflect the clinical status of persons who are symptomatic but are still independent with self-care. Individuals with KPS

scores of 80 can carry on normal activity with effort. Persons with KPS ratings of 70 are unable to engage in normal activities. KPS ratings from 50 to 60 reflect the clinical status of persons who are symptomatic, unable to carry out normal activities, and require occasional assistance (KPS = 60) or considerable assistance (KPS = 50) with self-care activities. KPS ratings from 10 to 40 reflect the clinical status of a patient with significant care needs, including hospitalization or institutionalization. The KPS clinical ratings used in this study were based upon information gathered by the clinician from the patient, family/informants, and the clinical evaluation.

Consent Capacity Measure

All study participants completed a standardized performance-based measure of treatment consent capacity. The Capacity to Consent to Treatment Instrument (CCTI) is a vignette-based measure of medical treatment decision-making capacity.[19] This measure has established reliability and validity.[19,20] Detailed administration and scoring information are presented elsewhere.[7] Participants are presented with hypothetical medical scenarios (ie, cardiovascular disease, brain cancer) and then presented with treatment alternatives. Scores are based upon participant answers to standardized questions across 4 well-established, core consent standards (*understanding, reasoning, appreciation,* and *choice*).

In the present study, only the CCTI vignette concerning cardiovascular disease was administered (Vignette B). The CCTI brain cancer vignette was omitted due to the potential for patients to confuse the hypothetical treatment scenario with their own personal brain cancer illness and treatment.

Description of CCTI Consent Standard.—As discussed, the CCTI instrument assesses 4 well-established consent capacity standards drawn from the psychiatric and dementia capacity literature.[4,21] The 4 standards are briefly described below.

Choice: simply expressing a choice for a particular treatment.
Appreciation: appreciating the personal consequences of a treatment choice.
Reasoning: providing and weighing rational reasons for and against a treatment choice.
Understanding: understanding a medical treatment condition, treatment choices, and associated treatment risk/benefits.

For the purposes of the present study, only the 3 most clinically relevant standards of *understanding, reasoning*, and *appreciation* were analyzed.

For cognitive characterization of the sample, a measure of verbal learning and memory (HVLT-R Trials 1–3),[22] phonemic verbal fluency (Controlled Oral Word Association Test[23]), and executive functioning (Trail Making Test, part B[24]) were administered. Depressive symptoms were assessed with the Beck Depression Inventory–II.[25]

Data Analyses

We divided participants into 3 groups according to their KPS rating: those scoring either 50 or 60, those scoring either 70 or 80, and those scoring either 90 or 100. Demographic and clinical variables, neuropsychological test scores, and consent capacity scores were compared between the KPS subgroups. We excluded the patients with KPS scores of 50–60 from all group-level comparisons due to the small sample size of that subgroup. Group comparisons for the demographic, clinical, and consent standards were performed using independent *t* tests or nonparametric analysis (Pearson chi-square test) where appropriate. Pearson correlations were used to examine the relationships between the KPS scores and demographic, clinical, consent capacity, and neuropsychological test scores. Significant alpha was set at $P < .05$. Tests for significance were 2-tailed. All statistical analyses were performed using SPSS 20.0 (SPSS Inc.).

The assignment of psychometrically derived cut-off scores is one approach for defining impairment[26] and has been employed in prior capacity studies by our research group.[19,27] Thus, we calculated capacity outcome classification ratings (ie, *capable, marginally capable*, or *incapable*) for each patient across each CCTI standard. In assigning outcomes, we used psychometric cutoff scores derived from control group performances on the CCTI. This group of healthy controls has previously been described.[6] A *capable* outcome was defined as a score < 1.5 SD below the control group mean or better for that particular consent standard; a *marginally capable* outcome was defined as a score ≤1.5 SD but >2.5 SD below the control group mean; and an *incapable* outcome was defined as a score ≤2.5 SD below the control group mean.

We also calculated a global capacity rating that was dichotomized as *intact* or *compromised*. Individuals with marginally capable or incapable outcomes on any of the CCTI standards were assigned a global capacity rating of *compromised*, whereas those with capable outcome ratings on all 3 of the standards were assigned a *capable* global capacity rating.

Results

Table 2 presents demographic and clinical characteristics of the participants by KPS group. Of the 71 patients, 39 had received KPS scores of 90–100 (KPS 90 $n = 33$; KPS 100 $n = 6$), 26 had KPS scores of 70–80 (KPS 70 $n = 9$; KPS 80 $n = 17$), and 6 had KPS scores of 50–60. The median and mode KPS score was 90 (range = 50–100; mean = 83.0; SD = 11.9).

Of note, when examined as a function of primary versus metastatic brain tumor, we found that the number of patients with brain metastases ($n = 17$) and malignant glioma ($n = 22$) scoring either 90 or 100 on the KPS scale was not significantly different (χ-(1) = 0.9; $P = .343$).

Patients with KPS scores of 90 or 100 were younger but not significantly more educated than patients with KPS scores of 70 or 80. Worse cognitive function was exhibited by patients with lower KPS scores. As KPS scores decreased, depressive symptoms increased. Although not included in the group comparisons, patients with KPS scores of either 50 or 60 reported higher levels of depressive symptoms.

Overall, KPS scores were significantly correlated with the following: age ($r = -0.294$; $P = .013$), verbal learning/memory ($r = 0.453$; $P < .001$), phonemic/letter fluency ($r = 0.367$; $P < .002$), executive functioning ($r = 0.474$; $P < .001$), depressive symptoms ($r = -0.280$; $P = .034$), CCTI *understanding* ($r = 0.452$; $P < .001$), and CCTI *reasoning* ($r = 0.472$; $P < .001$).

Table 2. Comparisons on demographic and clinical variables by Karnofsky Performance Status group[†]

Variable	KPS Scale Rating			t/χ^2	*P*
	90–100 (*n* = 39)	70–80 (*n* = 26)	50–60 (*n* = 6)		
Demographic Variables					
Age, y	53.5 (13.2)	60.4 (10.2)	59.3 (6.2)	2.3	.028
Education, y	14.6 (2.7)	13.3 (2.9)	13.3 (2.5)	1.8	.072
Sex (m/f)	18/21	14/12	2/4	0.4	.617
Race*				2.0	.207
Caucasian	37 (94.9)	22 (84.6)	5 (83.3)		
African-American	2 (5.1)	3 (11.5)	1 (16.7)		
Other	0	1 (3.8)	0		
Cognitive variables (range)					
HVLT Trials 1–3 Total (0–36)	21.1 (6.1)	15.0 (6.1)	12.7 (4.3)	3.9	<.001
Phonemic fluency	29.3 (13.3)	20.0 (11.3)	16.5 (11.5)	2.9	.018
TMT B	125.4 (77.8)	193.7 (103.0)	253.7 (80.3)	3.0	.004
Mood variable					
BDI (0–63)	9.1 (5.9)	11.5 (9.0)	22.5 (16.3)	1.2	.237

Note. Values are mean (SD).
[†]Comparisons only between KPS 90–100 and KPS 70–80 groups. Chi-square tests were conducted for sex and race. For all other group comparisons, independent *t* tests were conducted. Phonemic fluency was measured with the Controlled Oral Word Association Test.
*Race was analyzed as a dichotomous variable (Caucasian compared with Other).
Abbreviations: BDI, Beck Depression Inventory; HVLT, Hopkins Verbal Learning Test; TMT, Trail Making Test.

Significant correlations were not observed between KPS scores and either education ($r = 0.196$; $P = .104$) or CCTI *appreciation* ($r = 0.197$; $P = .099$).

Table 3 presents CCTI standard performance by KPS group. With respect to treatment consent capacity, the patients with KPS ratings of 90 or 100 had consistently higher scores across each of the 3 CCTI standards than the group with scores of 70 or 80. However, statistically significant differences were only observed for the CCTI *understanding* and *appreciation* standards.

Table 4 presents the capacity outcomes across each of the 3 core CCTI standards by KPS group. On the *understanding* standard, capacity compromise (ie, marginal or incapable classifications) was seen in 39% of patients with KPS ratings 90–100; 69% of patients with KPS ratings 70–80, and 83% of patients with KPS ratings 50–60. The number of patients with capable capacity classification ratings on the *understanding* standard was significantly higher ($P = .013$) in the KPS 90–100 group than the KPS 70 or 80 group.

Similarly, on the *reasoning* standard, 28% of participants with KPS ratings of 90–100 showed capacity compromise, while 54% of participants with KPS ratings of 70–80 showed capacity compromise. The number of patients demonstrating capacity compromise was significantly higher for the group with KPS scores of 70–80 ($P = .004$). Of the participants with KPS ratings of 50–60, all showed capacity compromise.

Finally, on the *appreciation* standard, 13% of participants with KPS ratings of 90–100 displayed capacity compromise; 31% of participants with KPS ratings of 70–80 showed compromise; and 33% of participants with KPS ratings of 50–60 showed compromise. Significantly greater capacity compromise on the *appreciation* standard was observed for KPS scores of 70–80 compared with scores of 90–100 ($P = .033$).

Table 3. Karnofsky Performance Status group on the Capacity to Consent to Treatment Instrument

Variable	Range	KPS Scale Rating			*t**	*P*
		90–100 (*n* = 39)	70–80 (*n* = 26)	50–60 (*n* = 6)		
CCTI Standards						
Understanding	(0–44)	28.5 (7.8)	20.9 (9.8)	14.7 (12.4)	3.5	.001
Reasoning	(0–7)	3.7 (1.8)	2.8 (2.2)	1.0 (1.1)	1.9	.058
Appreciation	(0–4)	3.4 (0.9)	2.8 (1.4)	2.8 (1.6)	2.2	.033

Note. Values are mean (SD).
*Independent *t* tests were conducted comparing the KPS of 90–100 versus 70–80 groups.

In terms of global capacity rating, only 46% (18/39) of participants with KPS ratings of 90–100 received capable classifications across all 3 CCTI standards. All patients with KPS of 100 were classified as capable per their performance across all 3 of the CCTI standards. For participants with KPS scores of 70–80, only 23% (6/26) received capable classifications across all 3 CCTI standards. For participants with KPS scores of 50–60, none of the 6 persons received capable classifications across all 3 standards. Of note, in the 90–100 KPS group the proportion of intact versus impaired global capacity rating was not different between patients with

Table 4. Capacity to Consent to Treatment Instrument ratings by Karnofsky performance status group

	KPS Rating			χ^{2*}	*P*
	90–100* (*n* = 39)	70–80 (*n* = 26)	50–60 (*n* = 6)		
CCTI Standards					
Understanding				8.8	.013
Capable	24 (61.5)	8 (30.8)	1 (16.7)		
Marginal	11 (28.2)	8 (30.8)	0 (0)		
Incapable	4 (10.3)	10 (38.5)	5 (83.3)		
Reasoning				11.1	.004
Capable	28 (71.8)	12 (46.2)	0 (0)		
Marginal	8 (20.5)	3 (11.5)	3 (50.0)		
Incapable	3 (7.7)	11 (42.3)	3 (50.0)		
Appreciation				6.8	.033
Capable	34 (87.2)	18 (69.2)	4 (66.7)		
Marginal	4 (10.3)	2 (7.7)	1 (16.7)		
Incapable	1 (2.6)	6 (23.1)	1 (16.7)		

Note. Chi-square tests compared intact performance (ie, capable) and impaired performance (ie, marginal or incapable).
*All patients with KPS 100 were classified as capable per their CCTI performances across each of the 3 CCTI standards.
Analyses were only conducted for the KPS groups of 90–100 versus 70–80 due to insufficient sample sizes of the KPS 100 group (*n* = 6) and KPS 50–60 group (*n* = 6).

brain metastases (*n* = 17) or malignant glioma (*n* = 22); $\chi^2(1) = 0.1$; *P* = .753.

Discussion

The current study expanded upon our prior finding of a significant correlation between KPS ratings and treatment consent capacity performance as measured by the CCTI in patients with malignant glioma.[7] Similar to our prior study, we found that KPS scores were correlated with performance on 2 of 3 CCTI standards (*understanding* and *reasoning*), and in which higher KPS scores were associated with higher CCTI performances. In addition, when each consent standard was examined at the group level (see Table 3), it was found that the group with the highest KPS scores (ie, 90–100) performed better than the group with KPS score of 70–80 on the most complex capacity standard (*understanding*) as well as the *appreciation* standard. For the *reasoning* standard, the same performance trend was noted (ie, higher scores by the 90–100 KPS group) but not to a level of statistical significance. Not unexpectedly, the smaller KPS group with scores of 50–60 displayed lower scores across all 3 CCTI standards compared with the other 2 groups. These findings highlighted that clinical disease progression, as measured by a clinician-based functional disability rating, can be associated with complex decision-making ability. However, when examined at the individual level, we found that a sizable proportion of patients with high KPS ratings (ie, clinician-determined minimal symptoms and no disability, KPS = 90–100) nonetheless showed impairments on a standardized measure of medical treatment consent capacity when compared with a noncancer control group. These impairments emerged in the form of both diminished CCTI raw score performance and compromised CCTI capacity classification ratings. Of particular note was that only 46% of patients with KPS ratings of 90–100 were assigned capable classification ratings for all 3 CCTI standards examined (S3–S5).

Consistent with our prior work,[7] a high proportion of brain-tumor patients displayed substantial capacity compromise on the cognitively challenging and clinically stringent standard of *understanding*. In this study, a high rate of impairment was found even in the 90–100 KPS group. On the *understanding* standard, 39% of individuals in the 90–100 KPS group had scores in the psychometrically defined impaired range compared with controls. A sizable proportion of participants in this group also scored at impaired levels for the *reasoning* (28% of participants) and *appreciation* (13%) standards. Both the *reasoning* and *appreciation* capacity standards are viewed as less stringent and complex than the *understanding* standard, but they continue to prove difficult for a sizeable minority of brain-tumor patients.[7] Based on our preliminary correlation analyses and our prior work with a smaller sample of brain-tumor patients,[7] there likely exists a complex pattern of cognitive abilities, socio-demographic (ie, educational background), and clinical variables (eg, disease duration, medications) that may affect individual decision-making abilities even for relatively functionally intact patients. Such clarification awaits future investigation.

The current study provided two central points. First, our findings suggest that patients with lower KPS scores (ie, 70–80) have significantly impaired capacity performance as compared with those having higher KPS scores (ie, 90–100). Although the sample size was quite small for the KPS of 50–60 and KPS of 100 groups, our preliminary findings suggest that decisional capacity may be most impaired in patients with KPS scores less than 70 and least impaired in patients with KPS scores of 100. Second, impaired decision-making capacity performance was present in a sizeable portion of patients with high KPS scores who were judged to have minimal levels of clinician-rated functional disability (ie, KPS score of 90). Thus, KPS should not be used as a proxy for consent capacity, and capacity assessments should be conducted more frequently in this patient population.

The present study has several limitations. First, the sample for the KPS rating groups of 100 and of 50–60 were very small and could not be analyzed as individual groups, so we could not make any conclusions regarding participants with these KPS scores. However, we did present descriptive results for these subgroups to more fully represent this patient population. We realize that we have taken a conservative approach by excluding the participants in the 50–60 group, but we wanted our sample to be comparable to the samples typically included in clinical trials. Future investigations of medical decision-making capacity in patients with lower KPS scores (<70) may improve our understanding of the relationship between functional status and consent capacity in patients with greater levels of functional disability. Second, our study was limited to cross-sectional analyses; future studies that assess all patients early in the diagnostic process and then follow them longitudinally with clinical rating tools, cognitive testing, and consent capacity instruments

will help us more fully understand the progression of consent capacity changes over the disease course. A third study limitation was the inherent psychometric limitations of the KPS. Prior studies have noted that KPS ratings continue to be widely incorporated into clinical trial research as part of standard study inclusion criteria and outcome measurement.[2] However, the KPS has also been shown to have only limited utility as a measure of quality of life, cognitive function, and even functional status.[2] One group has proposed standardized, behavior-anchored questions regarding physical and role activities as the basis for KPS ratings, which in turn could lead to enhanced reliability and validity.[9] Fourth, the CCTI capacity outcomes were generated psychometrically for scientific purposes and do not represent actual clinical capacity judgments or legal capacity judgments (which are reserved for legal professionals and the courts). We also note that our cutoff threshold of 2.5 SD may seem rather conservative, but our intent was not to overestimate capacity compromise based upon psychometric cut-off points. Finally, the use of standardized medical vignettes does not directly assess patients' capacity to make decisions regarding their own personal treatment situation. However, in clinical practice, a patient obtaining a low score on the CCTI standards could be followed up with a more detailed assessment of capacity tailored to his or her individual circumstances using a different tool or approach.[28]

Despite these limitations, the current study highlights the importance of carefully assessing consent capacity in patients with brain tumors before making clinical decisions concerning their medical treatment, regardless of performance status. The study's findings have potentially important implications for clinical practice. First, patients with KPS ratings indicating only minimal disability could nonetheless have diminished decisional capacity across clinical situations that include the clinician presenting them with information regarding various clinical trials and experimental therapy options. In addition, decisions to continue cancer-directed therapy or transition to a quality-of-life focus with palliative and/or hospice care are also potential clinical scenarios. Accordingly, clinicians and researchers working with brain-tumor patients should carefully screen for capacity to make clinical treatment decisions. Second, KPS clinical ratings should not be a proxy or substitute for capacity evaluations.

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