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Original Research

Effectiveness of Early-stage Neurodevelopmental Treatment Following Brain Tumor Surgery

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Abstract

Objectives: This study aimed to examine the effectiveness of the early-stage neurodevelopmental treatment (NDT) concept after brain tumor surgery and compare the results with those of acute stroke patients.
Materials and Methods: This was a retrospective study that analyzed baseline hospitalization data and scores for motor function, activities of daily living (ADL), and cognitive status, recorded immediately after hospitalization and before discharge from acute stroke patients and patients with brain tumors undergoing surgery. An Early-stage NDT program was applied to both patient groups.
Results: 16 brain tumor patients matched with 16 acute stroke patients according to gender, and lesion sides. The length of stay in the rehabilitation of the patients with brain tumors was longer compared to the stroke patients. The within-group comparison revealed significant improvements in total The Stroke Rehabilitation Assessment of Movement Measure (STREAM), and STREAM subscales in the brain tumor group, and the stroke group ($p<0.05$). The median gains score between admission and discharge rehabilitation on the total STREAM, STREAM subscales, and the Functional Independence Measure was similar in the brain tumor group and stroke group ($p>0.05$). The median gain score in the Mini-Mental State Examination score between admission, and discharge rehabilitation was greater in the brain tumor group ($p<0.05$).
Conclusion: The early postoperative NDT approach to patients with brain tumors can improve ADL, motor, and cognitive functions, similar to results shown in stroke patients.

Keywords: *Brain Neoplasms, Function, Neuro-developmental treatment, Rehabilitation, Stroke.*

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Introduction

Primary brain tumors and stroke are major causes of morbidity and mortality. Intracranial tumors represent 1.8% of all cancers, and the prevalence of these tumors is increasing with each passing day (Ferlay et al., 2015; Landis et al., 1999; Prados et al., 1998). Stroke is the second most common cause of death after ischemic heart disease, from which around 6 million people die each year in the world (Mendis, 2013). More than two-thirds of surviving stroke patients, or patients who undergo surgery for brain tumors face functional impairments. In this sense, rehabilitation is an indispensable part of treatment following brain tumor surgery, and stroke (Buntin et al., 2010; Sherer et al., 1997).

Depending on the localization of the lesion, symptoms such as sensorimotor disorders, speech aphasia, ataxia, dysphagia, and decreased cognitive gain scores may occur in both patient groups (Geler-Kulcu et al., 2009). Mukand (Mukand et al., 2001) in their study conducted to identify common disorders in patients with brain tumors reported that patients suffer from disorders such as weakness (78%), sensory-perception disorders (53%), sensory loss (38%), and bladder-intestine incontinence (37%), and rarely cranial nerve paralysis, aphasia, ataxia, and diplopia are observed. In the study of Wee and Hopman (Wee & Hopman, 2005) conducted on acute stroke patients, balance disorders (100%), weakness (99%), sensory disorders (66%), aphasia (33%), dysarthria (35%), and cognitive disorders (15%) were observed in patients. Considering these studies that describe the functional losses of patients, a stroke and a brain tumor may present with similar symptoms. For the two disease groups, the importance of rehabilitation increases to treat similar functional deficiencies (Benito García et al., 2015; Kılınç et al., 2016; Mikołajewska, 2017).

Neurodevelopmental treatment (NDT) is a rehabilitation approach widely applied by physiotherapists for stroke patients, also known as Bobath Concept (Davidson & Waters, 2000). The content of the NDT concept includes functional training (functional active participation), quality, intensive exercise (non-recurring), patient-centered therapy, and holistic approach parameters. The NDT aims to identify and analyze problems within functional activities, and participation in everyday life as well as the analysis of movement components, and underlying impairments (Graham et al., 2009). Treatment sessions are planned for a certain function, and the patient's active participation is prompted as much as possible. According to the NDT approach, functional use of the affected side improves rehabilitation results (Vaughan-Graham et al., 2015).

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NDT is frequently used by physiotherapists working in the field of stroke, despite conflicting opinions about the effectiveness of program content (Lennon & Ashburn, 2000).

Although the symptoms seen in the acute phase in patients with brain tumors seem similar to those of stroke patients, there is no study evaluating the effectiveness of the "NDT" approach following brain tumor surgery. In addition, although the importance of rehabilitation treatment in brain tumor patients is emphasized in the literature, it is not yet known whether rehabilitation is meaningful or necessary if the survival rate is low and the recurrence rate is high. This study aims to examine the functional results of the NDT approach applied in the acute period following brain tumor surgery, in comparison with the reference values in patients with acute stroke. In addition to the limited number of studies proving the efficacy of NDT in the literature, the number of studies preferring NDT as the optimal treatment type is very few due to methodological limitations. However, the concept of NDT is the most widely used neurophysiological approach in Turkey. Since this study was conducted in Turkey, where most patients are normally offered NDT-based physiotherapy, it was not possible to have a control group without NDT. We hypothesized that patients with malignant or benign brain tumors would achieve similar functional gains to stroke patients from the acute NDT approach.

Material and Methods

Study Design

We retrospectively reviewed medical records maintained at two university hospitals (Hacettepe University Department of Neurosurgery, and Numune Education, and Research Hospital Department of Neurology), and identified patients with neurological impairment after brain tumor resection surgery, or stroke who were admitted for NDT based training between May 2013, and August 2017. This study proposal was approved by the Research Ethics Board of Hacettepe University (Decision Number: (GO 18/25-13). The study was registered in clinicaltrials.gov Identifier: NCT03574467. All participants signed the written informed consent form.

Participants

Fifty-nine patients with brain tumors who received rehabilitation service after tumor excision surgery and fifty-eight stroke patients who underwent rehabilitation in the acute period were included in the study. Brain tumors and stroke were defined as primary brain tumor and vascular lesion finding on brain imaging, computed tomography, or magnetic resonance imaging.

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Moderate functional loss (Modified Rankin Scale >2), being older than 18 years and having a Glasgow Coma Scale (GCS) score of at least 14 were determined as inclusion criteria for the study. Brain tumor patients undergoing multiple brain operations or adjuvant therapy during rehabilitation, and stroke patients with a history of recurrent cerebrovascular accidents were excluded from the study. Patients with brain tumors were divided into subgroups as defined by the World Health Organization. The lesion side was determined for both patient groups, the vascular distribution for stroke patients, and the major brain lobes affected for brain tumor patients (Huang et al., 1998).

Neurodevelopmental treatment

Individual NDT programs were applied to all patients by physiotherapists who have 13 years of experience in NDT (SB, İK, NK: Course information: Assessment, and treatment of adult hemiplegia – The Bobath concept. Trainer: Elia Panturin, Senior Instructor; International Bobath Instructors Training Association (April 15–22, 2006, and June 22–28, 2006), School of Physiotherapy and Rehabilitation, Hacettepe University, Ankara, Turkey). NDT programs were planned especially for each patient according to their needs. The treatment was administered five times a week, and each treatment session lasted for 60 min. Patients received NDT intervention until discharge. At any stage of treatment, compensation, poor-quality movements, and the negligence of the affected side was not allowed. During the treatment, external support (hand of a physiotherapist) was used to reach the targeted quality of movement. Starting with the first stage of the treatment, maximum sensory input, and correct positioning were ensured to prevent negligence in the patient. The patient was asked to participate actively and continuously repeat the exercises (if he/she could not repeat them, was asked to repeat them mentally).

NDT interventions are ranked from top to bottom in order of increasing difficulty (Tang et al., 2014):

- Selective movements of the hip, and/or knee
- Selective movements of foot/ankle
- Selective movement of the arm
- Stretching of the latissimus dorsi muscle
- Trunk mobilizations
- Rolling
- Bridging

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- Sitting
- Placing exercises to facilitate trunk extension in sitting
- Weight transfer to either side in sitting
- Anterior/posterior pelvic tilt in sitting
- Reaching to either side in sitting
- Weight-bearing through the affected arm
- Sit to stand
- Weight transfer with feet level in standing
- Walking

Educating patients and caregivers (stretching, walking, active or passive exercise)

Outcome Measure

Demographic and clinical data of patients such as sex, age, lesion side, onset-to-admission interval (OAI, time between injury onset, and admission to rehabilitation), length of stay in rehabilitation (LOS rehab), and GCS score were obtained from medical records. LOS rehab refers to the duration of the intervention that patients receive in the early period. Additional information, such as histological type, location of the tumor, and type of surgery, was collected from patients with brain tumors.

The Stroke Rehabilitation Assessment of Movement (STREAM) scores, Functional Independence Measure (FIM) motor scores, and Mini-Mental State Examination (MMSE) were collected at admission, and discharge from inpatient rehabilitation.

STREAM, which measures the mobility of the patient in the acute period, is a valid and reliable scale (Ahmed et al., 2003). In this scale, which consists of six basic activities, each activity is scored between 1-6. STREAM evaluates 6 different activities including rolling in bed, coming to sit, sitting, standing up from sitting, standing, and walking. An increase in the score on the STREAM scale indicates an increased level of independence of the patient. The scores that can be obtained from the STREAM scale range from 6 to 36 (Daley et al., 1999).

FIM was created to improve upon previous independence measures that have been criticized for sensitivity and comprehensiveness. The items of the FIM are scored according to how much help the individual needs to carry out activities of daily living. FIM evaluates 6 different basic functions under 18 items. Items are divided into two areas motor (13 items) and cognitive (5 items). These areas are called Motor-FIM (eating, bathing, walking, etc.) and Cognitive-FIM

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(Expression, problem-solving, memory, etc.). The FIM is reported to take approximately 30-35 minutes to administer and score. Each item in the FIM is scored between 1 and 7 on a 7-point Likert scale. A score of 1 indicates full dependency, while 7 points indicate the maximum level of independence. After completing 18 items, the patient has a total score ranging from 18 to 126 (Linacre et al., 1994).

MMSE is a set of questions commonly used to screen cognitive function. This test can be used to indicate the presence of cognitive impairment after a head injury or neurological problems. The MMSE contains much more sensitive information in detecting cognitive impairment than the general observation of the patient by the healthcare professional. The test takes about 10 minutes but may not detect subtle memory deficits, especially in well-trained patients. When the scores obtained out of 30 are examined, 25-30 is considered normal, while 21-24' is classified as mild, 10-20 moderate, and <10 severe disorders (Norris et al., 2016).

Statistical Analysis

Descriptive statistics for continuous variables were expressed as mean, ± standard deviation, and median (Interquartile Range) values. For the categorical variables, the number, and percentage of frequencies were presented. Whether the data were normally distributed, or not was measured by the Shapiro Wilks test. Differences within the group were analyzed with the Wilcoxon signed-rank test. Between the groups, differences were compared using the Mann–Whitney U test. The p-values less than 0.05 (95% confidence interval) were determined to be statistically significant. All analyzes were performed with the IBM SPSS 25.0 program.

Results

Among the 59 brain tumor patients admitted to the rehabilitation program, 21 fulfilled the inclusion criteria. Among the 58 stroke patients admitted to the rehabilitation program, 23 fulfilled the inclusion criteria. 16 brain tumor patients matched with 16 acute stroke patients according to gender, and lesion sides (Figure 1). There were no between-group differences regarding the demographic characteristics ($p>0.05$), except the LOS rehab (Table 1). The LOS rehab of the patients with brain tumors was longer compared to the stroke patients ($p=0.001$). Of 16 brain tumor patients included in this study, 10 had benign tumors, and 6 had malignant tumors. There were no significant differences in tumor location, or surgery type between benign, and malignant tumor subgroups ($p>0.05$) (Table 2).

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Table 1. Demographic and clinical data of patients.

	Brain tumor n=16	**Stroke n=16**	**p**
Age (yr.) (X±SD)	58.31±7.19	63.38±9.38	0.113[a]
Gender (n (%))			
Male	9 (56.3)	9 (56.3)	1.000[b]
Female	7 (43.7)	7 (43.7)	
Lesion Side (n (%))			
Right	7 (43.7)	7 (43.7)	1.000[b]
Left	9 (56.3)	9 (56.3)	
Tumor etiology (WHO grade) (n (%))			
I (benign tumor)	2 (12.5)	NA	
II (benign tumor)	8 (50)		
III (malignant tumor)	3 (18.75)		
IV (malignant tumor)	3 (18.75)		
GCS ($\tilde{X}$ (Q1-Q3)	15 (14-15)	15 (14-15)	0.463[a]
OAI (days)	3.12±1.92	2.56±1.20	0.602[a]
LOS rehab (days)	9.88±7.26	4.25±1.43	**0.001[a]***

Values are presented as number (%) or mean±standart deviation or median (IQR); OAI: onset-to-interval (time between injury onset and admission to rehabilitation); LOS rehab: Length of stay in the rehabilitation; GCS:Glasgow Coma Scale; WHO: World Health Organization; NA: not applicable *p<0.05; [a] Mann-Whitney U Test; [b] Chi-Square Test

Median scores on admission, and discharge for STREAM, FIM, and MMSE as well as gain scores are displayed in Table 3. Statistically significant and similar improvements were observed in STREAM total, STREAM mobility, STREAM LE and FIM motor scores in patients with a brain tumor and stroke during the period from admission to rehabilitation to discharge ($p<0.05$). At the beginning of the rehabilitation process, STREAM Total ($p=0.024$), STREAM UE ($p=0.008$), and STREAM LE ($p=0.008$) scores were lower in brain tumors patients ($p <0.05$) (Table 3). The average baseline FIM and MMSE scores did not differ significantly between the groups ($p>0.05$) (Table 2).

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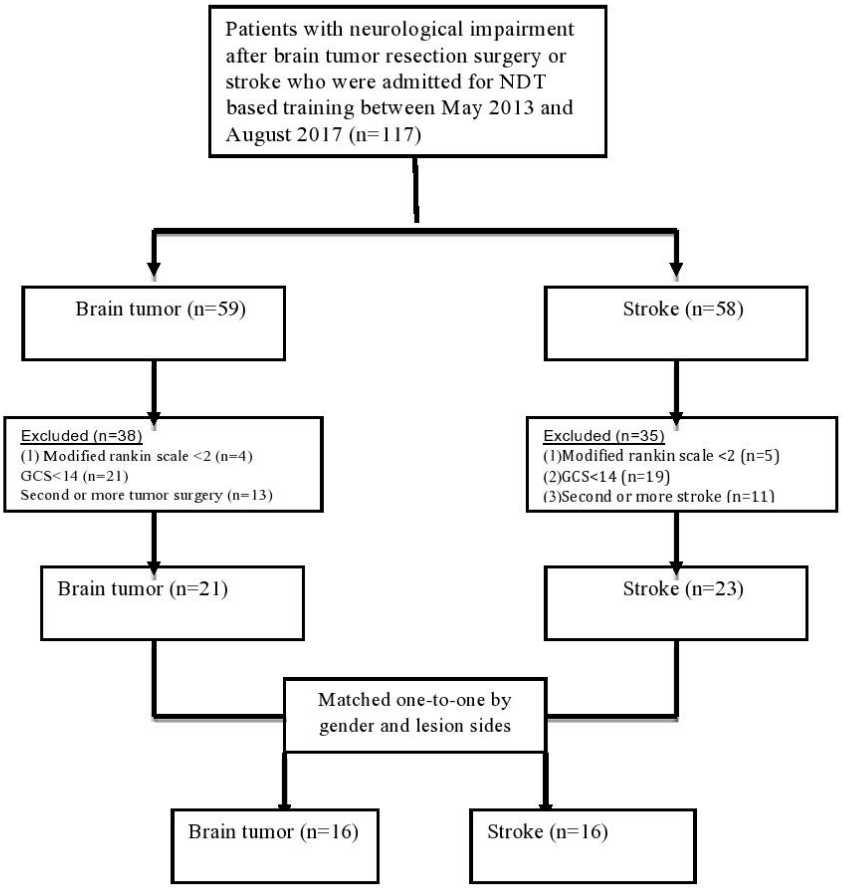

Figure 1. Flow chart of participants

From the beginning of rehabilitation to discharge, the gain score on the total and subscale scores of STREAM and FIM motor scales were similar in the brain tumor and stroke groups ($p>0.05$). In this process, the only difference between the stroke and brain tumor patient groups occurred in the MMSE score. The median gain score of the MMSE was higher in the brain tumor group than in the stroke group ($p=0.007$).

Discussion

In this study, we investigated (1) whether the NDT principles affect in functional, and cognitive abilities of patients with a brain tumor following surgery; (2) whether patients with brain tumors make functional gains similar to those of patients with stroke. The result of this study showed that early postoperative NDT approach to patients with brain tumors can improve ADL,

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motor, and cognitive functions, similar to results shown in stroke patients. The early postoperative NDT approach to patients with brain tumors can improve ADL, motor, and cognitive functions, similar to results shown in stroke patients.

Table 2. Brain tumor group characteristics.

	Malignant n=6	**Benign n=10**	**p**
Lesion Localization	**(n (%))**	**(n (%))**	
Temporal	1 (16.67%)	2 (20%)	
Parietal	2 (33.33%)	2 (20%)	0.477
Frontal	1 (16.67%)	5 (50%)	
Occipital	2 (33.33%)	1 (10%)	
Surgery type			
Subtotal	2 (33.33%)	2 (20%)	
Total	2 (33.33%)	6 (60%)	0.587
Gross-Total	2 (33.33%)	2 (20%)	

Values are presented as the number of patients (%), Chi-Square test.

Few clinical trials have been conducted to evaluate the effect of the early NDT approach on acute stroke patients. Tang et al. reported that the early Bobath approach was beneficial for stroke patients because it increases balance, motor function of the lower extremity, and basic mobility of these individuals. They observed an increase of more than 30 in the STREAM scores after rehabilitation, which they applied for 50 min five days a week, for eight weeks in the early period in stroke patients (Tang et al., 2014). Langhammer and Stanghelle observed that the Bobath approach, which they applied for two weeks in the early period in patients with acute first-ever stroke, provided the improvement in motor function, and activity daily living (ADL) (Langhammer & Stanghelle, 2000). Xu et al. reported that early rehabilitation (especially the Bobath approach) can effectively improve stroke patients' ADL especially in eating, bed-chair transfer, and short distance walking activities (Xu et al., 2004). Functional gains, also showed in these studies, after the NDT approach in patients with stroke has supported the results of the present study.

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Table 3. Functional and cognitive outcomes of patients with a brain tumor and stroke.

		Brain Tumor n=16	**Stroke n=16**	
	Values	**X̃ (Q1-Q3)**	**X̃ (Q1-Q3)**	**p[b]**
STREAM -Total	Pre-treatment	25.0 (14.0-27.5)	36.5 (20.3-53.0)	**0.024***
	Post-treatment	29.0 (20.0-34.3)	55.5 (29.0-62.8)	**0.008***
	p[a]	**0.001***	**<0.001***	
	Gain score (Δ)	5 (4.0-6.3)	6.5 (4.0-12.0)	0.238
STREAM -Mobility	Pre-treatment	8.0 (4.0-15.0)	10.0 (5.0-12.8)	0.343
	Post-treatment	10.0 (5.0-12.8)	21 (13.0-31.5)	**0.008***
	p[a]	**0.004***	**0.002***	
	Gain score (Δ)	2.0 (1.0-3.0)	2.5 (1.0-5.8)	0.687
STREAM -UE	Pre-treatment	6.5 (2.5-6.3)	12.0 (6.5-18.3)	**0.008***
	Post-treatment	6.5 (3.5-8.0)	15.5 (8.5-20.0)	**0.004***
	p[a]	0.976	**0.032***	
	Gain score (Δ)	1.0 (0.0-2.0)	1.0 (0.5-2.3)	0.128
STREAM -LE	Pre-treatment	7.0 (5.5-8.5)	12.0 (7.5-17.0)	**0.008***
	Post-treatment	8.5 (6.0-9.5)	16.0 (11.5-19.0)	**0.001***
	p[a]	**0.004***	**0.004***	
	Gain score (Δ)	2.0 (0.0-2.0)	2.5 (1.3-4.1)	0.343
FIM-MOTOR	Pre-treatment	56.0 (41.0-66.8)	67.5 (49.5-85.0)	0.126
	Post-treatment	69.5 (47.0-74.3)	82.5 (56.5-91.0)	0.108
	p[a]	**0.001***	**<0.001***	
	Gain score (Δ)	5.0 (3.3-14.3)	4.0 (4.0-8.0)	0.687
MMSE	Pre-treatment	18.0 (13.3-27.3)	27.5 (15.3-30.0)	0.128
	Post-treatment	21.5 (14.5-29.5)	28.0 (14.5-30.0)	0.287
	p[a]	**0.004***	0.680	
	Gain score (Δ)	2 (0.0-3.0)	0 (0-0)	**0.007***

p[a] = within-group differences, Wilcoxon Signed Rank Test, p[b]= between-group differences, Mann-Whitney U Test, *= statistically significant p-value, Δ= Differences between baseline and last assessment, Q: Quartile, UE: Upper Extremity, LE: Lower Extremity, MMSE: Mini-Mental State Exam

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No studies have been found evaluating the efficiency of the NDT approach following brain tumor surgery. This study's results demonstrated that early-stage NDT provided an improvement in motor function and mobility in patients with brain tumors similar to those of patients with stroke. However, the significant improvement in patients with stroke, and brain tumors remained at a lower level in terms of clinical significance compared with the above-mentioned studies. This can be attributed to the fact that the rehabilitation length, which is an average of 10 days for patients with brain tumors, and four days for stroke patients, is shorter than the other studies. Considering these results, it is thought that the rehabilitation length, as well as the rehabilitation applied in the early period, may be effective in the functional gains.

In a study comparing the functional outcomes of brain tumors patients, and stroke patients, Han et al. studied functional, and cognitive outcomes of patients who underwent rehabilitation for four weeks at an early stage with the MMSE, and Barthel Index. Both groups showed significant improvements but there was no difference between the groups cognitively, and functionally (Han et al., 2015). Similarly, Greenberg et al. monitored the cognitive, and functional improvement of the patients with brain tumors, and stroke patients who were rehabilitated for an average of 19.4 days by the FIM score, and improvement was observed in both groups after rehabilitation when compared to the period before rehabilitation (Greenberg et al., 2006). However, there was no difference determined in functional, and cognitive improvement between the two groups. In the present study, differently from other studies, it was observed that patients with brain tumors had a higher improvement in the MMSE parameter related to cognitive gains compared to stroke patients. There are studies in the literature showing that the cognitive level is generally higher in stroke patients than in patients with brain tumors (Barker-Collo & Feigin, 2006; Geler-Kulcu et al., 2009). In these studies, patients were not included in any rehabilitation program. Furthermore, in the studies in which these two groups were included in rehabilitation, it was observed that although the LOS rehabilitation length was different, there was no difference in terms of cognitive gains (Greenberg et al., 2006; Huang et al., 1998). We think that the Bobath (NDT) concept (the quality of movement, patient-centered approach, functional training) that we use in our study may have increased the cognitive participation of the patient in rehabilitation, and may have led to higher cognitive gains in cognitive-poor brain tumor patients. The rehabilitation approaches (PNF, Brunnstrom, stretching exercises, resistance exercises, strengthening training, etc.) applied in other studies may not adequately involve the patient in rehabilitation from a cognitive aspect. In the

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Bobath concept, the therapist aims to utilize maximum afferent input to re-educate the individual's internal reference systems (Mikołajewska, 2017). It assists the patient in problem-solving and enables him, or her to experience the patterns of movement and success in achieving the task. In addition, Bobath advocated a 24-hour, holistic approach that involved the whole patient, their sensory, perceptual, and adaptive behavior as well as their motor problems. When the individual, family, all professionals, and other caregivers have insight into the problems and work together for the same goals, these goals are usually accomplished. All this intense sensory input can lead to the healing of the perceptual process as well as the motor process.

In our study, we worked with patients, families, and other health care professionals to ensure continuity of treatment in the acute stage. It was aimed to give continuous sensory input to the patient (to eat food from the hemiparesis side, or to contact with the patient from that side), to repeat the targeted exercise, and to ensure the active participation of the patients in each function (such as eating, turning, sitting, or walking). In this study, the NDT approach seems to have a beneficial effect on brain tumor patients improving cognitive ability. Our results suggest that the NDT approach should be more widely used for brain tumor patients following surgery.

In this study, the LOS rehabs of the two groups were different. The average LOS for patients with brain tumors was 10 days longer than acute stroke patients. Our present the majority of tumors were glial tumors. Because of the complicated surgical procedure, and risk of subsequent complications, brain tumor patients' LOS rehabs are longer than those for acute stroke patients. In recent years, the LOS hospital in our departments has decreased due to the department's policy. Our present LOS for patients with brain tumors was 10 days, and in past years LOS was found to be longer when examined by our departmental computerized database. The LOS rehab that is in the text for stroke patients is the average for the last year.

This study has several limitations: First, the small number of subjects, and the shorter rehabilitation period. Further research with larger samples and a longer rehabilitation duration is needed to define better the functional, and cognitive effect of the NDT approach in brain tumor patients. However, this study encourages rehabilitation specialists to use the NDT approach in the acute stage. To ensure the application of neurodevelopmental treatment in the acute stage that can help brain tumor patients improve in functional, and cognitive level, clinical training, and education in the acute stage related to NDT should be given to rehabilitation specialists. This study did not include a true control group (i.e., patients who did not receive Bobath training after brain

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tumor surgery). Thus, we could not confirm whether the improvement in neurological function was due to natural recovery, or rehabilitation. Finally, we found that arterial problems in the stroke group were quite heterogeneous (Anterior cerebral artery, middle cerebral artery, posterior cerebral artery, communicating arteries, etc.) and multiple. The lack of any standardization in this group is also a limitation.

Conclusion

Early postoperative NDT approach to patients with brain tumors can improve ADL, motor, and cognitive functions, similar to results shown in stroke patients. The early postoperative NDT approach to patients with brain tumors can improve ADL, motor, and cognitive functions, similar to results shown in stroke patients. These findings suggest that the early-stage NDT approach should be widely used in the rehabilitation of acute brain tumor patients following surgery.

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Conflict of interest

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