



The Impact of Stereotaxy on Cognitive Domains of Patients with Glioma

KEYWORDS

Stereotaxy, Cognitive domains, Glioma

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ABSTRACT

Introduction: This study tries to determine the impact of stereotaxy on cognitive domains of patients with glioma. **Methods and Materials:** It was a cross-sectional study performed on 42 glioma patients aged from 15 to 65 years old. All of the patients were examined by neurosurgeons, neurologists and psychiatrists and then 42 patients were referred to stereotaxy. Cognitive evaluations were done through Stroop, CPT, and TOL tests. **Results:** Based on the performance assessment of the patients before and after stereotaxy, a significant difference was observed between Stroop, CPT and TOL tests measures ($P < 0.05$).

Conclusion: The present study indicated that cognitive impairments could be found in patients with glioma after stereotaxy so that for survival, longevity and better life quality they need cognitive rehabilitation simultaneous with stereotaxy.

Introduction:

Since the brain tumor originates from brain tissues, it will cause complex changes in physiological and molecular condition of neural system and consequently will lead into cognitive impairments (19, 32, 36, 38, 55). It should be said that about 50% of patients with brain tumor are faced with these impairments (50). New studies which were made in the thirty recent years exhibit the growth of glioma disease and so the need of more cares for these patients. These patients have symptoms such as headache, anorexia, nausea and insomnia that may increase the severity of cognitive changes (17, 30). The damage location made by the tumor's placement is also of the other reasons that cause such impairments (9, 23). The cognitive impairments in patients with glioma can affect the quality of their lives (16, 27, 47); the surgery and stereotaxy is also of the intervening factors that can affect the cognitive condition (6). Coping with the cognitive challenges among patients with glioma is a demanding task (53). Several studies focus more on the cognitive aspects than mental aspects and some others emphasize on the effects of this disorder on patients quality of life (27, 54). These problems are seen at the phase of diagnosis, treatment and also survival (35). According to previous studies, cognitive changes were associated with reduced survival especially in patients with a low grade (24-26, 29, 33) and a high depression was along with low quality of life (14, 24). The quality of life has an important role in survival's rate increase and the patients are experiencing new treatments (48). Several researchers have examined the effects of different demographic factors on cognitive changes in these patients (57-59). The cognitive changes are complex processes which consisting a variety of cognitive domains. Executive function is referred to self-control behaviors and attention domain is a set of complex neural processes which are conducted by a distributed neural net with cortical and sub-cortical parts including frontal cortex and basal ganglia-thalamic-cerebellar connections (35). Sustained, selective attention and executive functions are considered among important cognitive domains that patients with glioma will have problem with them (27, 47, 59). The objective of the current study is to show that cognitive domains of attention and planning among glioma patients are influenced by the

trauma of surgery and stereotaxy. So, with a better evaluation of the cognitive impairments successful diagnosis and treatment management for these patients will be attained.

Materials and Methods:

This cross-sectional study was conducted on 42 patients with frontal lobe glioma during 10 months since 3.2.2011 until 20.12.2012 at neurosurgery department of Shohada Hospital, Tehran, Iran. The whole participants were selected through simple random sampling. Before entering the study it was necessary for the patients to fill the informed consent letter. They had to be examined first by the neurosurgeon, neurologist, and psychiatrist and later on be sent to perform MRI and CT for the final diagnosis. After being confirmed by the mentioned physicians they were referred to start the tests. Carrying out the cognitive tests was needed once prior stereotaxy and the other time in 24 to 72 hours post stereotaxy.

The inclusion criteria were as follows: the patients with frontal lobe glioma brain tumor, right handedness, inhabitant of Tehran, Persian language speaker, age range of 15-65 years, identified by WHO criteria, free from previous or current history of psychological and neurological disorders, surgery, stereotaxy, chemotherapy and radiotherapy before surgery. Exclusion criteria were as follows: having any kind of tumors except glioma, left handedness, not an inhabitant of Tehran, out of age range of 15-65 years, non-Persian language speaker, not identified based on WHO criteria, having previous or current history of psychological and neurological disorders, surgery, stereotaxy, chemotherapy and radiotherapy before surgery.

This study was approved in the ethic committee and research faculty of Shahid Beheshti University of Medical Sciences and was also verified and performed in Functional Neurosurgery Research Center (FNRC).

Computerized cognitive tests

Stroop test: This test was developed for the first time by Ridley Stroop in 1935 for evaluation of selective attention and

cognitive flexibility (28). This test was used for a variety of cognitive evaluations (1, 2, 11, 34, 44, 45, 58, 59). The test has two stages: the first stage is naming the colors in which the examinee is asked to click on the key of the same color of the 4 circles of red, blue, yellow, and green colors shown frequently. The goal of the first stage is training the test performance technique to the examinees and has no effect on the final result. The second stage of the test is its performance. In this stage 48 congruent words and 48 incongruent words are shown. The congruent words are those that their meaning is the same with word itself, for example the word Blue is having the blue color. The incongruent word is one that its color is different from its meaning for example the word Blue is shown with red color. There are 96 congruent and incongruent words in total which are shown randomly on the monitor and the examinee has to answer according to the color only and not the meaning. The presentation time of each stimulus on the monitor is 2 seconds and the interval between each two presentation is 800 milliseconds. The researchers do believe that in the second stage, the mental flexibility, interference and inhibition of response is measured (52). The interference measure is obtained by subtracting the score of correct incongruent number from the score of correct congruent words. In this stage, a circle shape is shown to the examinee in red, yellow, green and blue consecutively, so that s/he has to determine and press the defined color labeled keys with maximum speed. The examinee should also be explained that the color of the words could be unrelated to its meaning and the focus is on the color. The measured variables consist of congruent and incongruent error, congruent and incongruent Time reaction and Result tests of the participants (1, 11, 44, 45, 59).

CPT test: This test is used for surveying continuous attention in several studies (22, 49, 51, 57). In all types of CPT, the examinee has to pay attention to a set of relatively simple visual or auditory stimuli. In this study, only the visual stimuli are presented. The mentioned test is also designed with computer. At the appearance moment of the target stimulus, the examinee by clicking on a key provides his or her answer. The test has to be performed in a proper time and place and performance conditions of the test must be observed psychologically. The purpose is that each examinee applies his or her maximum ability to present the best performance with a proper speed. A total of 150 stimuli are presented in this test from which 20% are target stimuli (the stimulus that the examinee has to answer is depicted as stars, moon, and circles in white color). The presentation time of each stimulus is 200 milliseconds and the interval between each two presentation is 1 second. Before the initiation of the main test an experimental test is performed. On the onset of the experimental test the required explanations are given to the examinee. After the experimental part and report on readiness the test will start. The time for test including the time for experimental part is totally 200 seconds. By notifying the various tests and analyses derived from the CPT, in this study the variables are: Time test, Error01 (commission), No01 (omission), True01, Time reaction, Error02 (commission), No02 (omission), True02, Time reaction, Error03 (commission), No03 (omission), True03 and Time reaction (39, 51, 57, 59).

TOL test: This test was first introduced by Shallice in 1982 for planning ability measurement (41). This test was designed to assess two aspects of executive functions, planning and problem solving. The test was developed to evaluate these functions in various diseases such as brain trauma, Parkinson, Huntington chorea disease, hydrocephalus, depression, ADHD, autism and brain tumor (20, 31, 59). The method of this computerized test similar to all other types of TOL test consists of an experimental stage in which the examinee tries to learn the correct way of doing the test. On the left side of the monitor an example is designed and the examinee has to put the color rings on the beam on the right side in a similar fashion with the left side. During the test, by putting the colored rings (green, red, blue) on the correct position the points related to that example is received. By accomplishing each example, the examinee has only three tries, doing the example on the first try has 3 points, and the second has 2, and last has only 1. If the examinee did not succeed in doing the example after three tries, the point of this level will not be considered. The moves made in each level will be counted and if more than 3 moves are made, the test will stop and the points are calculated up to this example. The surveyed variables in this test consist of the Time Test, Time Late, Time Total, Result and Error (13, 28).

Statistical analysis:

After performing the Stroop, CPT and TOL tests, the data were entered the SPSS₁₈ software. By using descriptive statistical test, Pearson correlation coefficient, stepwise regression and paired T-test the analyses were done.

Results:

Table 1. Evaluation of demographic variables in patients with glioma

Age Vs. Sex		Age groups					TO-TAL	Value	df	Sig
		15-24	25-34	35-44	45-54	55-65				
Sex	Female	3	5	2	7	4	21	1.256	2	0.004
	Male	3	5	2	7	4	21			
TOTAL		6	10	4	14	8	42			
Age Vs. Education		15-24	25-34	35-44	45-54	55-65	Total	6.656	2	0.036
Education	Illiterate	3	2	1	1	2	9			
	Diploma	3	3	3	4	8	19			
	Associate of arts	1	3	1	3	2	10			
	Bachelor of art	1	0	1	1	1	4			
	Master of art	1	0	2	0	1	4			
TOTAL		15	12	13	18	26	84			

In table 1, considering the age groups of the participants in both sexes and the equal number of them a significant correlation (p=0.004) is seen and in comparison with the education, the age groups also were significant (p=0.036).

Table 2. Evaluation of the relationship between age, sex, education and the variables of STROOP, CPT, TOL tests among brain tumor patients

STROOP	Time01	Error01	No01	True01	Timerec01	Time02	Error02	No02	True02	Timerec02	Result test
CPT	No01	True01	Timerec01	Error02	No02	True02	Timerec02	Error03	No03	True03	Timerec03
TOL	Time test	Time late	Time total	Error	Result						
age	r=0.074	r=-0.052	r=0.053	r=0.046	r=0.046	r=0.072	r=-0.055	r=0.046	r=0.057	r=0.074	r=0.077
	p-val-ue=0.012	p-val-ue=0.042	p-val-ue=0.047	p-val-ue=0.055	p-val-ue=0.055	p-val-ue=0.026	p-val-ue=0.051	p-val-ue=0.06	p-val-ue=0.049	p-val-ue=0.041	p-val-ue=0.023
	r=0.054	r=-0.042	r=0.053	r=0.076	r=0.051	r=0.042	r=0.045	r=0.046	r=0.057	r=0.074	r=0.087
	p-val-ue=0.022	p-val-ue=0.048	p-val-ue=0.047	p-val-ue=0.045	p-val-ue=0.027	p-val-ue=0.026	p-val-ue=0.051	p-val-ue=0.06	p-val-ue=0.049	p-val-ue=0.041	p-val-ue=0.02
	r=0.045	r=0.046	r=0.027	r=-0.084	r=0.081						
	p-val-ue=0.051	p-val-ue=0.06	p-val-ue=0.049	p-val-ue=0.041	p-val-ue=0.023						

sex	r=.024	r=-.031	r=.022	r=.032	r=.045	r=.064	r=.072	r=-.083	r=-.034	r=-.036	r=.045
	p-value=.051	p-value=.061	p-value=.060	p-value=.060	p-value=.065	p-value=.054	p-value=.009	p-value=.021	p-value=.061	p-value=.061	p-value=.065
	r=.037	r=.036	r=.042	r=.034	r=.045	r=.064	r=.042	r=.084	r=.064	r=.045	r=.021
	p-value=.061	p-value=.071	p-value=.070	p-value=.061	p-value=.065	p-value=.054	p-value=.027	p-value=.021	p-value=.054	p-value=.051	p-value=.71
	r=.036	r=.087	r=-.064	r=.015	r=.014						
p-value=.061	p-value=.021	p-value=.010	p-value=.065	p-value=.061							
education	r=0.062	r=-0.052	r=0.043	r=0.086	r=0.061	r=0.052	r=-0.055	r=0.056	r=0.037	r=0.084	r=0.077
	p-value=0.022	p-value=0.042	p-value=0.047	p-value=0.045	p-value=0.027	p-value=0.026	p-value=0.051	p-value=0.06	p-value=0.049	p-value=0.041	p-value=0.023
	r=0.054	r=-0.042	r=0.053	r=0.076	r=0.051	r=0.042	r=-0.045	r=-0.046	r=0.027	r=0.074	r=0.087
	p-value=0.022	p-value=0.048	p-value=0.047	p-value=0.045	p-value=0.027	p-value=0.026	p-value=0.051	p-value=0.06	p-value=0.049	p-value=0.041	p-value=0.02
	r=0.072	r=0.025	r=0.046	r=-0.027	r=0.071						
p-value=0.026	p-value=0.051	p-value=0.06	p-value=0.049	p-value=0.041							

In table 2, a significant relationship was observed between the Time01, Error01, No01, Time02, True02, Timerec02 and Result test measures of STROOP test and age and education variables (p<0.05). Sex variable also had a significant relationship with Error02 and No02 (p<0.05). Regarding CPT, there is a significant relationship (p<0.05) between nine measures of this test, No01, True01, Timerec01, Error02, No02, True02, No03, True03 and Timerec03 and variables of age and education (p<0.05). Relationship of sex variable was significant with Timerec02 and Error02 measures in this test (p<0.05). In TOL test, age variable had a significant relationship (p<0.05) with Time total, Error and Result measures, sex variable was significantly related (p<0.05) with Time late and Time total measures and education variable also had a significant relationship (p<0.05) with Time late, Error and Result measures.

Table 3. Comparison of mean and mean differences before and after stereotaxy in STROOP test

Group of variables	M ±SD Before	M ±SD After	M difference ±SD N=42	t	P-value
Time01	68.95±13.58	71.3±13.89	-2.33±3.2	-4.63	0.00
Error01	2.45±3.54	5.38±3.89	-9.2±2.6	-7.27	0.00
No01	14.26±14.45	17.07±14.71	-2.8±2.5	-22.7	0.00
True01	26.31±28.16	74.28±31.15	52.2±8.2	65/5	0.00
Timerec01	19.1279±84.216	64.1265±45.194	35.1±32.1	664.0	0.511
Time02	86.71±53.13	43.76±64.13	-57.4±47.2	-99.11	0.00
Error02	55.7±83.12	12.12±65.12	-57.4±47.2	-99.11	0.00
No02	16±26.15	57.20±51.15	-57.4±47.2	-99.11	0.00
True02	71.24±75.17	62.20±06.17	-95.4±47.2	658.9	0.00
Timerec02	1.1320±22.273	64.1324±61.272	-57.4±55.2	-58.11	0.00
Resulttest	5.6±65.12	12.8±04.13	-57.1±81.3	-67.2	0.011

In Table 3, there is a significant difference between the mean data before and after stereotaxy. The only exception is Timerec01.

Table 4. Comparison of mean and mean differences before and after stereotaxy in CPT test

Group of variables	M ±SD Before	M ±SD After	M difference ±SD N=42	t	P-value
Error01	14.4±4.2	24.1±68.1	-78.2±78.2	-47.6	0.00
No01	57.4±16.3	02.2±7.2	-54.2±77.2	-94.5	0.00
True01	35.43±5.4	17.47±75.3	8.3±9.3	24.6	0.00
Timerec01	4.490±9.139	05.477±75.157	-33.1±5.191	-452.0	654.0
Error02	62.5±7.2	738.0±964.0	-88.4±4.2	-173.13	0.00

No02	1.7±5.3	2.2±93.2	-88.4±4.2	-173.13	0.00
True02	19.42±01.4	07.47±3.3	88.4±4.2	173.13	0.00
Timerec02	4.506±02.142	5.501±7.141	-58.4±4.2	-87.12	0.00
Error03	57.5±9.2	69.0±29.1	-88.4±4.2	-173.13	0.00
No03	38.7±82.3	5.2±12.3	-88.4±4.2	-173.13	0.00
True03	92.41±45.4	81.47±67.3	88.4±4.2	173.13	0.00
Timerec03	38.517±3.194	5.512±5.194	-88.4±4.2	-173.13	0.00

Regarding CPT test Table 4, before and after stereotaxy significant differences were seen between mean data of the CPT test measures. Timerec01 was the only exception.

Table 5. Comparison of mean and mean differences before and after stereotaxy in TOL test

Group of variables	M ±SD Before	M ±SD After	M difference ±SD N=42	t	P-value
Time test	33.188±01.178	83.194±07.180	-5.6±6.9	-095.6	0.00
Time late	52.123±39.99	26.127±01.100	-47.3±7.3	-57.6	0.00
Time total	86.311±66.250	31.316±74.250	-45.4±40.4	-136.7	0.00
Error	31.7±43.7	97.10±97.6	-76.3±8.3	-25.6	0.00
Result	05.27±23.9	31.25±25.9	23.2±5.2	135.6	0.00

Table 5 indicates that before and after stereotaxy, significant differences can be observed between the mean data of the whole TOL test measures without any exception.

Discussion:

Studies show that attention may be decreased due to the brain tumors. This attention reduction under the influence of various factors including therapeutic interventions such as surgery, stereotaxy, medicinal and chemotherapy may cause some cognitive problems for these patients (10). Despite the treatments presented, attention and planning impairments still exist among patients with brain tumor. As it seems treatments provided were not able to reduce these problems even in some cases made the cognitive performance more worsening among glioma patients. In many of the patients with glioma, impairment of attention and planning often is observed at the time of diagnosis (7, 8, 10, 16). The present study sought to assess the impact of stereotaxy on attention and planning domains in 1 to 3 days after operation. Availability of patients was assured and so it was possible to assess the mentioned hypothesis in this period. The findings on the comparative evaluation of the mean data differences of patients performance in STROOP test was significant in all measures except Timerec01 both before and after stereotaxy (Table 3). About CPT test, Timerec01 was also the only exception in mean data of CPT test which its difference was not significant before and after stereotaxy (Table 4). Patients' performance shows that the mean difference between all

measures of TOL test is significant both before and after stereotaxy with no exception (Table 5). Therefore, the hypothesis of the study is approved by the use of cognitive tests in 1 to 3 days after recovery according to which trauma of the stereotaxy does have effect on attention and planning domains of glioma patients.

These findings that confirm the attention and planning impairments in these patients declare these tests as a mean for cognitive evaluation and therefore lead the treatment and rehabilitation measures to have a more effective result and future studies to better approaches for this subject. Despite the defects in attention inhibition among patients with glioma, the evaluations of these impairments through the related tests are validated (3). These findings are in contrast with the previous studies which had shown no disorders (40, 43) and in the present test patients have exhibited impairments in sustained, selective attention and planning and this is another confirmation on the capacity of the mentioned tests in evaluation of attention and planning domains. The cognitive functions in patients with glioma in different scales of Stroop, CPT and TOL tests before and after stereotaxy indicate a significant difference. The statistical and quantitative analyses show that the diagnostic criteria of these tests are verified with an acceptable percentage of the patients with

glioma and this represents contrasts with previous studies (56) which verifies the novelty of the present study. In this study, the cognitive impairments were significantly associated to each other before and after surgery and stereotaxy and this relationship was also evinced in other studies. The relationship between these impairments can have a negative effect on survival and the quality of life in patients (13, 21). In the previous evaluated studies which were done on same patients, cognitive impairments had been noticed (5, 12, 18, 37, 42). Although the cognitive defects in these patients are due to various causes (59) the management, treatment, and rehabilitation of these impairments can have a positive role in survival and quality of life in these patients (15).

To sum up, the current study showed that stereotaxy has affected cognitive domains of attention and planning which their measures were significantly different before and after stereotaxy. These findings along with an explicit and precise diagnosis of disorders in these patients can help therapeutic recommendations and lead to better strategies for future studies. Cognitive impairments driven from stereotaxy under the influence of various cognitive intervening factors can change patient's life style and quality of life. Hence, rehabilitation of these impairments can have a significant role in promotion of survival and life quality in these patients.

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