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Comparative Assessment of Neuro-Cognitive Impairments Among Patients with Brain Tumor and Healthy Adults

Beyin Tümörlü ve Sağlıklı Yetişkinler Arasında Nörokognitif Bozuklukların Karşılaştırmalı Değerlendirmesi

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ABSTRACT

AIM: Most brain tumor patients encounter cognitive impairments. Coping with such challenges is intolerable for them. Objective: This study tries to determine the diagnostic role of cognitive tests, CPT, Stroop and TOL, in assessing neuro-cognitive impairments among patients with brain tumor and healthy participants.

MATERIAL and METHODS: A cross-sectional study was done on a sample of 15 to 65 years old of 84 brain tumor patients and 84 healthy Iranians. Participants of both groups were physically and mentally examined and approved by neurosurgeons, neurologists and psychiatrists. By completing the questionnaires, they all entered the study and were referred to the neuroscientist for performing the tests.

RESULTS: According to CPT, Stroop and TOL tests, the performance of both groups was significantly regarding about age, sex and education variables ($P<0.05$).

CONCLUSION: Brain tumor patients in comparison to healthy participants met more cognitive changes on sustained, selective attention and planning. Therefore, diagnosis and assessment of these cognitive changes before and after the surgery can help rehabilitating patients' brains and improve their lives quality.

KEYWORDS: Neuro-cognitive impairments, Brain tumor, Healthy adults

ÖZ

AMAÇ: Çoğu beyin tümörü hastası kognitif bozukluklar yaşar. Bu tür zorluklarla başa çıkmak bu hastalar için tolere edilemez bir durumdur. Bu çalışma, beyin tümörü olan hastalar ve sağlıklı kişiler arasında nörokognitif bozuklukları değerlendirmek için CPT, Stroop ve TOL kognitif testlerinin diagnostik rolünü belirlemeye çalışmaktadır.

YÖNTEM ve GEREÇLER: Bu çalışma, 15 - 65 yaşında 84 beyin tümörü hastası ve 84 sağlıklı İranlı üzerinde yapılmıştır. Her iki grubun katılımcıları beyin cerrahları, nörologlar ve psikiyatristler tarafından fiziksel ve zihinsel olarak incelenip onaylanmışlardır. Sonra soru formlarını doldurarak çalışmaya katılmış ve testlerin yapılması için bir nörolojik bilimler uzmanına gönderilmişlerdir.

BULGULAR: CPT, Stroop ve TOL testlerine göre iki grup arasında yaş, cinsiyet ve eğitim değişkenleri bakımından önemli performans farkı bulunmuştur ($P<0,05$).

SONUÇ: Sağlıklı katılımcılara göre beyin tümörü hastalarında uzun süreli ve seçici dikkat ve planlama konusunda daha fazla kognitif değişiklik bulunmuştur. Bu nedenle, cerrahi öncesinde ve sonrasında bu kognitif değişikliklere tanı koyma ve değerlendirme bu hastaların beyin rehabilitasyonuna ve yaşam kalitelerini arttırmaya yardımcı olabilir.

ANAHTAR SÖZCÜKLER: Nörokognitif bozukluklar, Beyin tümörü, Sağlıklı yetişkinler

INTRODUCTION

Recent neuro-cognitive investigations stressed that the incidence of tumors has increased in the last 30 decades (23). Brain tumors are a group of neoplasm with unique biology, diagnosis and treatment. Cognitive impairments are noticeable amongst brain tumor patients as significant deficits which arise through complicated processes (41, 43); half of all brain tumor patients are faced with emotional and cognitive disorders at some stage of their disease (20, 37, 57). Coping with the emotional and cognitive challenges of brain tumors is a difficult task for patients with brain tumor. Some previous studies have underlined cognitive aspects over emotional ones (63); whereas others have focused on the quality of life, instead of emotional and cognitive aspects of brain tumor patients (29). In this regard, neurosurgeons, neurologists, psychiatrists and neuroscientists have tried to improve the patient's condition. Currently, researchers are of the view that the recognition and rehabilitation of cognitive impairments may possibly help to increase life expectancy and improve the lifestyle and quality of life of brain cancer patients (4, 19, 30, 60). The most prevalent cognitive impairments amongst brain tumor patients include disorders in attention, executive functions, visuo-spatial and constructional skills, sensory perceptual functions, language, memory and intellectual functions (35). Cognitive impairments depend on the location and type of tumor, as well as the treatment and other changes like fatigue and anxiety during sleep. (14, 65). These problems can occur during the cancer diagnosis and treatment period, and also during survival. Executive function attributed to self-control behaviors and attention is a set of complicated neural processes controlled by the dispersed neural net, including the cortical and sub-cortical regions such as the frontal cortex and basal ganglia–thalamic–cerebellar connections. (40). Some researchers have considered the effect of dependent demographic agents and medical variables on neuro-cognitive impairments and feel that sustained and selective attention, information processing rate and executive functions in brain tumor patients are reversible. Previous studies have reported that targeted therapies may delay cognitive decline; however, these results require confirmation in future studies. (28). Considering these issues, cognitive tests such as the Continuous Performance Test (CPT), Stroop and Tower of London (TOL) tests are quick and frequently used measures for assessing neuro-cognitive impairments in executive function and attention amongst patients and healthy individuals. CPT generates quantitative data relating to the participant's ability in sustaining attention for a period of time; and can be used to assess cognitive impairments in brain tumor patients. Studies in brain tumor patients and healthy individuals using different versions of the CPT have shown that the results of the CPT can be influenced by harm or impairments to brain function, which can be affected in various diseases (40). The Stroop test is a quick and commonly used measure for assessing dysfunction in selective attention and cognitive flexibility (48, 52). The response of participants to target stimuli, whether the distracting items exist or not, can be an appropriate method to assess selective attention. The Stroop test may also be useful to investigate cognitive inhibitory processes. The TOL test can recognize unexpected impairments to the planning processes of frontal lobe (27, 58). Although these three tests have been used to assess cognitive impairments in a variety of studies by many researchers, our current investigation has its own novelty (1, 9, 13, 25, 31-34, 38, 39, 42, 44, 45, 47, 50, 53, 55, 56, 61, 64). As previously discussed, patients with brain tumor are faced with dysfunctions in sustained and selective attention and planning, and therefore the computerized CPT, Stroop and TOL tests were regarded as trustworthy tools for assessing cognitive impairments in the present study. Comparison of cognitive disorders between brain tumor patients and healthy individuals can help to diagnose the patient's risks to prevent, cure, recognize and rehabilitate them (35). This study was accomplished through the goal of assessing neuro-cognitive impairments among patients with brain tumor and healthy participants comparatively based on the mentioned authentic and valid tests.

MATERIAL and METHODS

Subjects

A cross-sectional comparative assessment of neuro-cognitive impairments was conducted during 6 months of study from May to September 2010, among an Iranian study population of 84 brain tumor patients 15 to 65 years old and 84 healthy participants with a mean age of 46±3 years at the Neuroscience Department of Functional Neurosurgery Research Center (FNRC) of Shohada Hospital, Tehran, Iran. Healthy participants were referred to FNRC through a public recall. Brain tumor patients were from hospital in-patients who were all selected through simple random sampling. All participants were physically and mentally with the help of reliable neurosurgeons, neurologists and psychiatrists based on MRI, CT and stereotaxis to ensure the absence of any other diseases. The ongoing study was also approved by the Shahid Beheshti University. Before research participants enter the study, it was necessary to complete the informed consent and demographic questionnaire. Out of the total number of patients, 42 entered the study before and after surgery, and 42 before and after stereotaxis. Inclusion criteria were as follows: to be within the age range of 15 to 65 years, an inhabitant of Tehran, right-handed, Persian language speaker, lacking any history of neural and mental disease, surgery and medicine consumption. Exclusion criteria were not being in the age range of 15 to 65 years, not an inhabitant of Tehran, left-handedness, not Persian language speaker, having any history of neural and mental disease, and surgery and medicine consumption.

Procedure

In the current study, sustained, selective attention and planning were evaluated through CPT, Stroop and TOL tests, respectively. In all forms of the CPT test, the examinee has to pay attention to a set of quite simple stimuli, visual or

auditory (only visual stimulus is present in this test). Then, at the appearance time of the target stimulus, the subject presses a button to provide the answer. This test should occur in a suitable place. Also, the performance conditions of the test must be observed psychologically. The purpose is that the examinee applies his maximum capacity and performs with the best speed. In this test, totally 150 stimuli are presented; among which 20% are target stimuli (stimulus which is appeared in the form of star, moon or circle on the screen and the examinee has to select it). The presentation time of each stimulus is 200 milliseconds and the interval between them is 1-second. After entering the personal information of the examinee in the profile section, the test is administered. Before the main test, the experimental (sample test) will be performed. At the beginning, necessary explanations are presented on the screen and the examiner should explain them for the examinee. The test gets started when the examinee is ready. The test time by considering the experimental test is entirely 200 seconds. According to the various forms and the obtained analyses of test, designed computerized CPT in this study is based on the comparison of response rate, commission, omission, reaction time and interference of participant's response (5, 6, 15, 36, 59).

The computerized Stroop task was produced by Ridley Stroop in 1935 for the first time to measure selective attention and cognitive flexibility (50). This test has been used in different studies of various clinical groups to assess the ability of response inhibition, selective attention, cognitive variability and flexibility. It consists of two stages. In the first stage, color naming, the examinee is asked to discover the intended color of the appeared shape on the screen from among a determined collection of colors (red, blue, yellow and green). This stage purpose is just training and familiarizing the colors and places of keys on the keyboard which has no impact on the final result. The second stage is the main Stroop test performance. At this stage, 48 congruent and 48 incongruent colorful words are shown randomly and consecutively to the examinee in red, blue, yellow and green. Congruence is referred to the words which are similar in color and meaning in Persian language, for instance the word blue which has a blue color too. Congruent words are those which their color and meaning is different, for example the word green which is displayed in red, blue or yellow. The task of examinee is to find out the apparent color regardless of the word's meaning. The presentation time of each stimulus on the screen is 2 seconds and the interval between each presentation is 800 milliseconds. Researchers believe that the color-word task (the second stage) can assess mental flexibility, interference and response inhibition (62). The interference measure will be obtained by subtracting the number of correct incongruent score from the score of correct congruent words. Here, a circle shape is shown for the examinee in red, yellow, green and blue consecutively. They have to press the defined keys to determine the correct color by maximum speed. Congruent and incongruent error (error01 and erroe02), congruent and incongruent Time reaction (timerec01 and timrec02) and Result tests of the participants are the investigating measures of the Stroop test.

The ability of planning in order to predict events and monitoring to access the goal in most problem solving activities is known as a main cognitive component. The Tower of London task was first introduced by Shallice in 1982 (24). This task has been developed to evaluate at least two aspects of problem solving and executive actions which means strategic planning. Recently, researchers have tried to apply this test in assessing dysfunction of the frontal lobe in different clinical populations including Parkinson's disease, depression, schizophrenia, Huntington's chorea disease, failure attention deficits with hyperactivity, learning disorder, autism, hydrocephalus and other diseases such as brain tumor (51). After entering the personal information of the examinee in the profile section, the test starts. During the test, the sample should get fixed with minimum necessary movements by moving the color pages (green, blue and red) and putting them in the right place. It should be noted that only the upper pages can be moved and in long column 3 pages, in the middle column 2 pages and in short column 1-page can be placed. Then, the examinee is asked to solve the example. The examinee is permitted to solve the problem in 3 tries and s/he has to follow the instructions with minimal necessary movements. After each stage of success (and if after three attempts, the problem is still not resolved) the next stage will be given to the examinee. The computerized TOL test is based on comparison of Time test, Time late, Time total, Result, Error, reaction time and Response interference measures.

Statistical analysis

It is hypothesized that the neuro-cognitive tests of CPT, Stroop and TOL could assess and diagnose attention and executive functions of brain tumor patients and the healthy group for the study's goal. In doing so, a comparative assessment of all three test's variables was initially done separately on both 2 groups. Spearman correlation tables with significance level of 0.05 were used for this purpose and the corresponding P-value amounts were examined. Then, the tests were reviewed. By using the Fischer test, in the case that the samples were independent of one another the P-value amount of each sample was gained. Statistical analysis was performed with the SPSS 18 software. As the tables suggest in the results, the healthy subjects and brain tumor patients differ more significantly from one another in age, sex and education than the rest of variables.

RESULTS

Descriptive statistics for both 2 groups of brain tumor patients and healthy ones who performed the neuro-cognitive tests, CPT, Stroop and TOL are presented in 3 separate tables. These were analyzed through Pearson correlation coefficient and t-test statistical methods. At first, the variables which may affect the performance of these three tests were determined, including age, sex and education.

Data presented in Table I indicate there was a significant difference ($p<0.05$) in all measures of the CPT test between brain tumor patients and healthy participants in the whole age groups of the study. In other words, brain tumor patients face more sustained attention impairments than healthy ones in all age groups.

A significant difference ($p<0.05$) was also observed between brain tumor patients and healthy participants with any educational degree for the education variable in all measures of the CPT test. It means that in all educational levels, patients with brain tumor have more sustained attention impairments than healthy participants.

Considering the equal number of males and females in both groups of healthy and patients, it should be noted that sex variable was not an important factor in distinguishing sustained attention difference. As a result, the sustained attention scale was alike in both sexes (Table II).

Similar to the previous table, performance of the Stroop test in all measures was significantly different ($p<0.05$) among patients and healthy participants in all age groups. Based on the education variable, the only exception in which the difference of test's performance of both groups was not significant was the timerec02 measure (incongruent time reaction) (timerec02=6, p-value>0.05). Therefore, brain tumor patients are confronted with more selective attention impairments than healthy participants in all age groups and educational levels except in the mentioned measure.

The row related to sex variable shows there is no significant difference between males and females in both groups of healthy and patients due to the equal number of both sexes

The statistical results of TOL test are presented in Table III which indicates that at any age groups of patients and healthy participants with any kind of education level, the difference of both 2 groups of participant's performance was significant ($p<0.05$) without any exception in any measures of the test. In other words, brain tumor patients in all age groups and with any education levels had more impairment in planning ability than healthy ones.

Regarding the sex variable, as mentioned before, the number of males and females was equal in both groups of healthy and patients. Consequently, there was no significant difference between these 2 groups and they did not differ in planning ability scale. It is clear that this variable is not considered as an important factor in showing the different performance of the groups.

DISCUSSION

The hypothesis of this investigation was to confirm the role and the impact of neuro-cognitive tests in diagnosing and assessing sustained, selective attention and planning of brain tumor patients. It can therefore be concluded that the aim of the study was accomplished through the current findings. The performance of brain tumor patients was compared with healthy participants for various measures of CPT, Stroop and TOL tests. It showed a significant difference ($p<0.05$) to a great extent. With regard to different aspects of attention and executive functions, sustained, selective attention and planning were evaluated through CPT, Stroop and TOL tests respectively. According to the obtained results, these cognitive impairments were more observed among brain tumor patients than healthy ones which can prove the diagnostic role of the neuro-cognitive tests. In situations where error reduction, speed and efficiency are considered, these tests can be well used (11). It is also worth noting that these neuro-cognitive tests are applied as a sensitive tool for vast range of clinical conditions relevant to cognitive impairments (17). The statistical and quantitative analyses indicate that the diagnostic criteria of these tests are verified with an acceptable percentage of the patients with brain tumor (66). Previous researches also have approved that having this kind of impairments make these patients disabled to learn and adjust to the environment, workplace and community condition in contrast to healthy participants (12). Reviewing different cognitive aspects can help better understanding of the involving factors in creating problems for these patients. The mentioned impairments can lead to failure in maintaining job opportunities for brain tumor patients. Developing dependence to others in performing basic activities at workplace and even daily personal ones is another problem (2, 3, 7). Attention impairments and executive dysfunctions still are considered as the most common complaints among patients with brain tumor. Finding these impairments in cognitive domains of brain tumor patients represents that the current study is in line with previous ones (46, 49). In studies including cognitive reviews, existence of attention and planning impairments have been affirmed in patients with brain tumor. It shows the variation of attention impairments level, the induced executive function related to the disease, treatment factors and also assessment tools (10, 18). Based on some studies, despite the treatments provided, attention and planning impairments still exist among brain tumor patients and these treatments were not effective in reducing the problems. They even occasionally led to worsening of the cognitive performance in brain tumor patients (21, 22, 26, 54). Several researches point to the rehabilitation role through other neural techniques (67). Finally, additional evidences can be derived from all these surveys for the purpose of diagnosing and assessing the aforementioned impairments of brain tumors. These findings along with a clarified diagnosis of impairments present in brain tumor patients can assist in therapeutic recommendations. It also leads further researches into greater guidelines of this issue (16).

The current study exhibited that the cognitive impairments of patients with brain tumor are approved with the new cognitive tests. It is suggested that the future comparisons with various mental and cognitive tests prior and after the treatment and rehabilitation can have a substantial role in promotion of treatment, survival and life quality among these patients.

Table I: Comparative Assessment of Sustained Attention Measure among Healthy and Patient Subjects Through Computerized CPT Task Based on Age, Sex and Education

		no01	true01	timerec01	error02	no02	true02	timerec02	error03	no03	true03	timerec03
Age	Healthy	r=.024 p-value=.051	r-.031 p-value=.061	r=.022 p-value=.060	r=-.024 p-value=.061	r=.042 p-value=.064	r=.045 p-value=.065	r=-.071 p-value=.009	r=.084 p-value=.021	r=.064 p-value=.054	r=.045 p-value=.051	r=.021 p-value=.71
	Patient	r=.054 p-value=.022	r=-.042 p-value=.048	r=.053 p-value=.047	r=.076 p-value=.045	r=.051 p-value=.027	r=.042 p-value=.026	r=.045 p-value=.051	r=.046 p-value=.06	r=.057 p-value=.049	r=.074 p-value=.041	r=.087 p-value=.023
	Difference p-value	.015	.010	.022	.018	.020	.008	.009	.03	.001	.002	.002
Sex	Healthy	r=.035 p-value=.056	r=.036 p-value=.061	r=.032 p-value=.060	r=-.034 p-value=.061	r=.042 p-value=.064	r=.045 p-value=.065	r=.071 p-value=.009	r=-.084 p-value=.021	r=.064 p-value=.054	r=.055 p-value=.051	r=.021 p-value=.71
	Patient	r=.037 p-value=.061	r=.036 P-value=.071	r=.042 p-value=.070	r=.034 p-value=.061	r=.045 p-value=.065	r=.064 p-value=.054	r =.042 p-value=.027	r=.084 p-value=.021	r=.064 p-value=.054	r=.045 p-value=.051	r=.021 p-value=.71
Education	Healthy	r=.026 p-value=.051	r=-.026 p-value=.061	r=.032 p-value=.060	r=.034 p-value=.061	r=.042 p-value=.064	r=.045 p-value=.065	r=.071 p-value=.009	r=-.084 p-value=.021	r=.064 p-value=.054	r=.055 p-value=.051	r=.021 p-value=.71
	Patient	r=.054 p-value=.022	r=-.042 p-value=.048	r=.053 p-value=.047	r=.076 p-value=.045	r=.051 p-value=.027	r=.042 p-value=.026	r-.045 p-value=.051	r=-.046 p-value=.06	r=.027 p-value=.049	r=.074 p-value=.041	r=.087 p-value=.023
	Difference p-value	.012	.016	.032	.038	.019	.028	.019	.012	.011	.012	.011

Table II: Comparative Assessment of Selective Attention Measure among Healthy and Patient Subjects Through Computerized Stroop Task Based on Age, Sex and Education

		time01	error01	no01	true01	timerec01	time02	error02	no02	true02	timerec02	Result test
Age	health	r=.037 p-value=.061	r=.036 p-value=.071	r=.042 p-value=.070	r=.034 p-value=.061	r =.042 p-value=.027	r=.045 p-value=.065	r=-.071 p-value=.009	r=.084 p-value=.021	r=.064 p-value=.054	r=.045 p-value=.051	r=.021 p-value=.71
	Patient	r=.074 p-value=.012	r=-.052 p-value=.048	r=.053 p-value=.047	r=.046 p-value=.055	r=.046 p-value=.055	r=.072 p-value=.026	r=-.055 p-value=.051	r=.046 p-value=.06	r=.057 p-value=.049	r=.074 p-value=.041	r=.077 p-value=.023
	Difference p-value	.002	.006	.04	.039	.039	.008	.009	.002	.010	.002	.001
Sex	health	r=.024 p-value=.051	r-.031 p-value=.061	r=.022 p-value=.060	r=.032 p-value=.060	r=.045 p-value=.065	r=.064 p-value=.054	r=.072 p-value=.009	r=-.083 p-value=.021	r=-.034 p-value=.061	r=-.036 p-value=.061	r=.045 p-value=.065
	Patient	r=.024 p-value=.051	r=.031 p-value=.061	r=.022 p-value=.060	r=.032 p-value=.060	r=.045 p-value=.065	r=.064 p-value=.054	r=.072 p-value=.009	r=-.083 p-value=.021	r=-.034 p-value=.061	r=-.036 p-value=.061	r=.045 p-value=.065
Education	health	r=.047 p-value=.051	r=-.036 p-value=.061	r=.012 p-value=.060	r=.014 p-value=.061	r=.022 p-value=.064	r=.015 p-value=.065	r=-.061 p-value=.009	r=.074 p-value=.021	r=.063 p-value=.054	r=.052 p-value=.051	r=.022 p-value=.71
	Patient	r=.062 p-value=.022	r=-.052 p-value=.048	r=.043 p-value=.047	r=.086 p-value=.045	r=.061 p-value=.027	r=.052 p-value=.026	r=-.055 p-value=.051	r=.056 p-value=.06	r=.037 p-value=.049	r=.084 p-value=.041	r=.077 p-value=.023
	Difference p-value	.016	.015	.037	.048	.029	.028	.029	.022	.021	6	.010

Table III: Comparative Assessment of Planning Measure among Healthy and Patient Subjects Through Computerized TOL Task Based on Age, Sex and Education

		Time test	Time late	Time total	Error	Result
Age	healthy	r=.074 p-value=.009	r=.087 p-value=.021	r=.065 p-value=.054	r=-.054 p-value=.051	r=.022 p-value=.71
	Patient	r=.045 p-value=.051	r=.046 p-value=.06	r=.027 p-value=.049	r=-.084 p-value=.041	r=.081 p-value=.023
	Difference p-value	.009	.011	.010	.009	.011
Sex	healthy	r=.036 p-value=.061	r=.087 p-value=.021	r=-.064 p-value=.010	r=.015 p-value=.065	r=.014 p-value=.061
	Patient	r=.036 p-value=.061	r=.087 p-value=.021	r=-.064 p-value=.010	r=.015 p-value=.065	r=.014 p-value=.061
Education	healthy	r=.015 p-value=.065	r=.074 p-value=.009	r=.089 p-value=.021	r=-.064 p-value=.054	r=.059 p-value=.051
	Patient	r=.072 p-value=.026	r=.025 p-value=.051	r=.046 p-value=.06	r=-.027 p-value=.049	r=.071 p-value=.041
	Difference p-value	.028	.019	.012	.011	.012

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