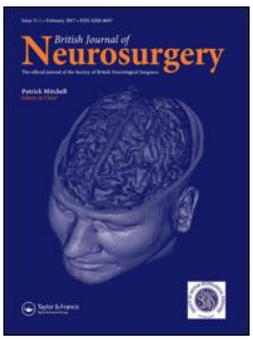

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ORIGINAL ARTICLE

Interesting different survival status of musicians with malignant cerebral tumors

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ABSTRACT

Introduction: The education of a musician may have an effect on the neuronal functions and organization of the brain, promote brain plasticity, resulting in functional and structural changes. A variety of malign cerebral tumors have affected the musician, instrumentalist or singer, at some time during their lives. No comprehensive investigation for musicians with malignant tumors has been performed yet. The aims of the study are to investigate if there is a relationship between the performed music style (classic or pop/rock) and the malignancy of the tumor.

Patients and methods: The key words were 'neurosurgery and music' and the names of composers. We used digital catalogs like 'Pubmed' as well as the libraries of universities. We investigated a list of people with brain tumors from the English Wikipedia. (https://en.wikipedia.org/wiki/List_of_people_with_brain_tumors).We divided musicians into two groups according to their performing of classic or rock-pop music, and their gender.

Results: We found 27 classic and rock/pop musicians who suffered from malign cerebral tumors. The median survival time estimations were 18 (mean 22.33, 95% CI ranged from 7.49 to 37.17) months for pop–rock musicians and 8 (mean 8.67, 95% CI ranged from 4.13 to 12.19) months for classical music performers. However, in Cox regression analysis, performed classical music type was associated with an increased risk of early death, lesser survival time age associated with an adjusted hazard ratio (aHR) of 1.06 [95% confidence interval (CI) 1.020 to 1.111; $p = .004$),

Conclusion: In musicians with malign cerebral tumors, music type performed by musician may affect the survival status, classical musicians have a worse outcome than rock–pop musicians.

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Neurosurgery; music; musicians; brain tumor; survival; gender

1. Introduction

Throughout history, science supported art and art supported science.[1] Music and neuroscience have been related for a long time.[2] Curiosity about music and the brain appears to have developed from a confluence of trends that began several centuries ago.[3] Musical training places high demands on the sensory, motor, and cognitive processing mechanisms.[4] Most musicians begin with their musical education at an early age. There is considerable evidence that the length of time an individual spends practicing plays an important role in the level of expertise attained on a musical instrument.[5] It is suggested that there is an amazing parallel between music and the brain, in terms of structure, organization, and function—anatomic, histologic, and associative.[6] The understanding of plastic cerebral alterations in response to musical practice is a recent interest.[7] Musicians with extensive music training and playing experience provide an excellent model for studying plasticity of the human brain.[8] In the history of medicine, there is an evidence that the surgical manipulation of the nervous system has been performed for more than 12,000 years.[9] As a general rule, our clinical practice is usually guided by scientific principles.[10,11] Neurosurgery is a rapidly evolving specialty and has often adopted new technologies.[12] Currently, neurosurgery is a highly developed medical field.[13] The high-level techniques and methods have been used in current neurosurgical practice.[14] Today, neurosurgeon use modern neuroimaging methods such as CT, MRI,[15,16] functional MRI, SPECT, PET.[17] major changes in the practice of neurosurgery have been observed[18] and cancer is still a leading cause of mortality in human. A variety of primary malign cerebral tumors have affected the musician, instrumentalist, or singer, at some time during their lives. The brain damage caused by the abnormal growth of malign tumors of musicians disrupts the functional music processing system, creating a unique opportunity to investigate the effect of this damage of the survival times of musicians, the brain plasticity of a musician with malign brain tumor may affect his/her survival rate, but to our knowledge, no previous studies have examined this subject.

2. Patient and methods

As the authors of this study, we followed the principles outlined in the 'World Medical Association Declaration of Helsinki: Research involving human subjects'.

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The key words were 'neurosurgery and music' and the names of composers. We used digital catalogs like 'PubMed' as well as the libraries of universities. The data of the study were obtained from Wikimedia Commons, the free media repository. For that reason, informed consent could not obtain from the patients (musicians).

A. As classic musician, we rated musicians with following musicological criteria: 1. Musicians, who play classic orchestra instruments, 2. Musicians/composers, who were educated in classical music instrumental playing and/or composing on a music school or music conservatory, musicians/composers, who wrote music for classical orchestras and acoustic instruments, and compose music in classic movements, 3. Composers, who write modern music for classical instruments. 4. Singers, with a classical voice education, who sing operas, operettas, songs, and chanson in a classical singing technique.
B. As pop/rock musicians, we rated musicians with following musicological criteria: 1. Songwriters, composers, who write pop or rock music for pop- and rock instruments, as well as electronic instruments, or multi-media instruments. 2. Instrumentalist, who play characteristic pop- and rock instruments (e-guitars, drums, e-bass) and are educated in the special style of jazz, Pop/rock and musical. 3. Composers, producers who compose music for pop/rock bands, who mostly use electronic and pop-/rock instruments. 4. Composers, who write pop/rock music and who are not educated on a classical music school or conservatory. 5. Singers, who are not educated in classic voicing and who are not educated on a classical music school or conservatory. 6. Singers, who are specially educated in musical singing. 7. Drummers, percussionist, who play only percussion instruments and pop- and rock bands.

We investigated a list of people with brain tumors from the English Wikipedia. (https://en.wikipedia.org/wiki/List_of_people_with_brain_tumors), which contains a list of 52 classic and rock-/pop musicians who suffered from intracranial tumors. We divided musicians into groups as malign and nonmalignant tumors and made the statistical analysis. Statistical analysis was performed by SPSS.

2.1. Statistical analysis

The null hypothesis means that the median of a distribution is equal to some value. Under the null hypothesis, we would expect the distribution of the music type-related age and survival status differences to be approximately symmetric around zero and the distribution of positives and negatives to be distributed at random among the ranks. A non-parametric Mann–Whitney *U* and Chi-Square tests, Cox regression analysis were used. Means and medians for survival times were evaluated by Kaplan–Meier analysis.

3. Results

We found 27 cases of musicians with malign brain tumors in the Wikipedia list (https://en.wikipedia.org/wiki/List_of_people_with_brain_tumors). Fourteen musicians with the nonmalignant tumor such as low-grade gliomas, meningiomas, and benign pituitary tumors or unknown type were excluded from the study. We evaluated the cases of glioma grade III and IV/GBM). Of the 27 musicians with malignant tumors, 21 were Pop/Rock—or Jazz musicians–singers, composers, drummers, or other instrumentalists. Six were classic instrumentalists, composers, or classic educated opera or operetta singers (Table 1). The musicians with malignant tumors were shown in Table 1. Table 2 shows the gender distribution of musicians. There were 21 males and 6 female musicians. Chi-Square test showed that gender type is statistically different between groups ($p = .04$).

The median survival times were 18 (mean 22.33, 95% CI ranged from 7.49 to 37.17) months for pop-rock musicians, and 8 (mean 8.67, 95% CI ranged from 4.13 to 12.19) months for classical music performers (Table 3). Mean ages were 50.91 years for rock-pop performers (Group 1), 60.33 years for classical musicians (Group 2) (see Table 4). Mann–Whitney *U* test showed that there are no statistical differences for age and survival status in both groups (Table 5). In Cox Regression analysis, Exp(B) for music type is 3139, which is statistically significant with *p* values of .05 ($p = .026$) (Table 6).

4. Discussion

4.1. Key result

1. Although the median survival times were 18 (mean 22.33, 95% CI ranged from 7.49 to 37.17) months for pop–rock musicians and 8 (mean 8.67, 95% CI ranged from 4.13 to 12.19) months for classical music performers (Table 2). The difference was not statistically significant ($p > .05$). The less number of classical music performers may be the reason for this statistical result. This subject should be investigated in the future.
2. At present, neurosurgical practice is confronted by an explosion of technology[19,20] and neurosurgery has gone through moments of great renewal.[21] Despite this advancements, malign cerebral tumors continue to portend a dismal prognosis. Glioblastoma multiforme (GBM) is the most common and malignant primary brain tumor in adults.[22] Due to the aging of the population, diagnosis in the elderly is becoming more common.[22] Many investigations have been conducted to define the prognosis of malignant cerebral tumors. Musicians may have a different outcome and survival status. Previously, it was suggested that functional status is an important prognostic variable in the elderly.[23]In this study, the mean ages were 50.91 years for rock-pop performers (Group 1), 60.33 years for classical musicians (Group 2) (see Table 3). Mann–Whitney *U* test showed that there are no statistical differences for age and survival status in both groups (Table 4).
3. Cancers of the brain and CNS are more frequent among men than women. There is a gender-related difference in brain anatomy and function[24] because the female and the male brain develops differently.[24] Their action of the brain can be different in female and male musicians. In this study, there are 21 male and 6 female musicians (Table 2). The mean survey of the female musicians (16.00 months) and male musicians (20.09 months) was not statistically different.

4.2. Interpretation of the B and EXP(B) in Cox regression output in this study

The regression coefficient thus allows to quantify the log of the hazard in the survival status of both group (compared to the rock-pop or classical musician group), accounting for the covariates included in the model; it is interpreted as a relative risk (assuming no time-varying coefficients) (See Table 6).

Table 1. List of musicians with cerebral malign tumor.

Case number	Year	SS	Age	Gender	Music style (rock, pop or classic music)	Survey
1-BB	1965	12	39	Male	Rock and roll bass player; recorded with Elvis Presley during 1954–1958	His last tour in 1964. Less than 1 year
2-RB	2004	36	53	Male	Pop, Musician, comedian and voice actor	3 years
3-GB	1998	12	40	Male	Pop, Tap dancer and choreographer	Less than 1 year
4-CC	2002	12	77	Female	Pop, Cuban salsa singer, Afro-Cuban music	Less than 1 year
5-JF	1994	10	29	Male	Pop, Rock, Bassist of rock band The God Machine	Less than 1 year
6-SF	1989	8	63	Male	Classical singer, Italian-American tenor	9 month, August 03, 1989–May 1, 1990.
7-GG	1937	1	39	Male	Classic musician, Jazz and classical music composer; co-writer of stage musicals and film scores	Only less month
8-BH	1980	3	75	Male	Pop, Rock, Leader of one of the first rock and roll bands, The Comets	October 25, 1980–February 09, 1981; 3 month
9-SJ	1997	20	48	Male	Pop, Classic, Cross over music, Guitarist, composer and arranger; member of the Penguin Cafe Orchestra	Less than 2 years
10-JL	2005	18	59	Male	Pop, Sound engineer, record producer and founder of Southern Studios	18 month
11-JM	2006	9	78	Male	Classic, instrumentalist, Principal oboist with the Cleveland Orchestra Classicalmusician	Less than 1 year
12-BL	1989/90	29	38	Male	Pop, Musician, songwriter and music producer; member of the bands Chilliwack and The Headpins	2.5 years
13-JM	1975	12	66	Male	Pop, Songwriter and lyricist	1 year
14-EM	1984	10	75	Female	Pop, Classic, cross over, specialized on musical voice. Broadway singer and actress	10 month
15-RM	2005	4	71	Male	Pop, Inventor of the modern music synthesizer	4 month
16-TM	2001	7	54	Male	Pop, Singer, songwriter and musician who formed the band Ted Mulry Gang (TMG).	7 month
17-RP	1982	5	69	Male	Classic, Italian-born British singer, classical, famous for the 1982 Christmas number-one Save Your Love	5 month
18-JP	1971	1	39	Male	Pop, Blues singer	Less than 1 month
19-FP	1999	10	60	Male	Classically trained Irish tenor	10 month
20-RP	1996	20	45	Male	Pop, Guitarist, singer and songwriter	20 month
21-CS	1999	29	34	Male	Pop, Rock, Former guitarist and singer for the band Death; former guitarist for Control Denied; influential figure in the development of death metal	2 years + 5 month
22-TT	1967, 1970	30	25	Female	Pop, Rock, Soul/R&B/Motown Singer, duettist with Marvin Gaye on 'Ain't No Mountain High Enough' and other hit singles. Also toured with James Brown.	2 years + 6 month
23-SW	2005	11	47	Female	Pop, Rock, Musician, singer-songwriter and drummer	Less than 1 year
24-WY	2003	8	71	Male	Pop, Jazz trumpeter and cornetist	8 months
25-AA	1993	16	53	Female	Classic singer, American soprano	16 month
26-JF	2014	17	40	Female	Russian pop	17 months
27-DB	2010	168	44	Male	Jazz-pop	14 years

SS: survival status.

Table 2. Shows the gender distribution of musicians.

Music Type × Gender Type Cross tabulation

	Gender type		
Count	Male	Female	Total
Groups			
Group 1	16	5	21
Group 2	5	1	6
Total	21	6	27

The confidence interval (CI) tells us within which range (of 95% probability) we can expect this value to differ if we were to repeat this survey for an infinite number of times. Variables with positive coefficients (such as 1144 the B values in this study) are associated with increased hazard and decreased survival times, i.e. as the predictor increases the hazard of the event increases and the predicted survival duration decreases. Negative coefficients indicate decreased hazard and increased survival times. Exp(B) is the ratio of hazard rates that are one unit apart on the predictor. In this study, Exp(B) for music type is 3139. The hazard rate increases by 3.13 with each unit increase in survival times. The HR for music type is 3.13, so an increase in 1.0 will be associated with a 3.13-fold increase in the hazard. It is statistically significant with p values of .05 ($p = .026$).

The graph of Figure 1 shows the survival status among groups of musicians patients. An apparent difference is seen due solely to the effect of music type.

4.3. What can we learn from the results of this study?

Our result may be related to the effect of education of musicians. A number of different neural mechanisms of the embodiment are likely to be activated during the perception of human action, but a reasonable candidate network is the mirror neuron system which is in charge of imitated learning for such abilities in the human brain and the neuroplasticity in this network led to the introduction of genius learners with artistic capabilities.[25] The education of musician may have an effect on the neuronal functions and organization of the brain or the mirror neuron system because, with the demands it places on the nervous system, musical training promotes brain plasticity, resulting in functional and structural changes.[26] For that reason, musicians, because of their traditional and rich associations between auditory, somatic, and sensorial systems, are an excellent model to investigate[7] by neuroscientists. Reading music score, hearing,

Table 3. The median survival times were 18 (mean 22.33, 95% CI ranged from 7.49 to 37.17) months for pop-rock musicians, and 8 (mean 8.67, 95% CI ranged from 4.13 to 12.19) months of classical music performers.

Means and medians for survival time

	Mean[a]				Median			
			95% Confidence interval				95% Confidence interval	
Muztip	Estimate	Std. error	Lower bound	Upper bound	Estimate	Std. error	Lower bound	Upper bound
Rock Group	22.333	7.571	7.493	37.173	12.000	0.567	10.889	13.111
Clasiccal Group	8.167	2.056	4.137	12.197	8.000	2.449	3.199	12.801
Overall	19.185	5.984	7.456	30.914	12.000	1.004	10.033	13.967

[a]Estimation is limited to the largest survival time if it is censored.

Table 4. Mean ages were 50.91 years for rock–pop performers (group 1), 60.33 years for classical musicians (group 2).

Descriptives

					95% confidence interval for mean			
Age	*N*	Mean	Std. deviation	Std. error	Lower bound	Upper bound	Minimum	Maximum
Group 1	21	50.905	16.1056	3.5145	43.574	58.236	25.0	77.0
Group 2	6	60.333	13.4412	5.4874	46.228	74.439	39.0	78.0
Total	27	53.000	15.8187	3.0443	46.742	59.258	25.0	78.0

Table 5. Mann–Whitney *U* test showed that there are no statistical differences for age and survival status in both groups.

Test statistics[b]

	Music type	Age
Mann–Whitney *U*	31.000	41.500
Wilcoxon W	52.000	272.500
Z	−1.871	−1.255
Asymp. Sig. (two-tailed)	0.061	0.209
Exact Sig. [2*(one-tailed Sig.)]	0.065[a]	0.216[a]

[a]Not corrected for ties.
[b]Grouping variable: survival.

Table 6. In Cox regression analysis; exp(B) for music type is 3139, which is statistically significant with *p* values of .05 ($p = .026$).

Variables in the equation

							95% CI for Exp (B)	
	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Music type	1.144	0.514	4.948	1	0.026	3.139	1.146	8.602

playing, performing motor skills, and social interacting with other musicians requires a high development of neuronal networks. (See Figure 2(A)) Learning and performing music may alter the anatomic structures of the brain. (See Figure 1(B)). Today is different from past.[27] Currently, high technology has been used in the medical practice.[28,29] In the last decade, some researchers have investigated the neural processes underlying music structure,[30] and the relationship between brain structure and musical experience. It was found that some anatomic structures of the brain between musicians and non-musicians have been reported.[26] Figure 3 shows a summary of these differences. The classic instrumental technique requires the highly specialized development of basal ganglia pathways. Performance is determined by the written work of the composer. The performance of rock pop music musician is characterized by rhythm, improvisation, and elements of athletic motion like singing, dancing and body movement. Sound and light effects create the background. An increased grey matter volume may be seen in a musician,[31] her/his outstanding musical ability is associated with increased leftward asymmetry of cortex subserving music-related functions.[31] The planum temporale is larger on the left side of the brain than on the right in humans generally, and this appears to be more the case in musicians compared to nonmusicians.[32,33] The corpus callosum tends to be thicker in musicians who begin their training at an early age, including in regions of the CC that connect the motor and premotor cortices across the hemispheres[33,34] (Figure 2).

4.4. Neuroplasticity and brain

Emerging research over the last 20 years has shown that long-term music training and the associated sensorimotor skill learning can be a strong stimulus for neuroplastic changes.[8] The brain has the capacity to reorganize itself.[35] Neuroplasticity is a remodeling of neuro-synaptic maps, to optimize the functioning of cerebral networks.[35,36] The conventional approach of neurosurgeons and oncologists are generally to investigate the tumor, its responses to surgery or radio and chemotherapy with very few considerations regarding the brain plasticity itself. Strong relationships seem to exist between music and plastic potential.[36] In string players, the increased cortical representation of the digits has been demonstrated,[37] suggesting that complex spontaneous musical performance involves a wider neural network.[36] Classical music performance: playing classic orchestra instruments needs early music education and long training in instrumental technique and of fine motor skills.

4.5. Importance of the present study

The first craniotomy of a musician with a malignant cerebral tumor was performed in 1937.[20,38] The remarkable consequences of craniotomies, neurosurgical interventions for the quality, and outcomes of musicians lives as well as their musical activities have been reported in the literature.[17,38–40,41,42,43] One of the key novel findings in some of these craniotomies is the fast recovery of the musician after surgery. After the damage to the cerebral structure, with functional reshaping underlying a partial or complete clinical recovery was known as; 'post-lesional plasticity'.[44] This plasticity may have an effect on the outcome. Geographic

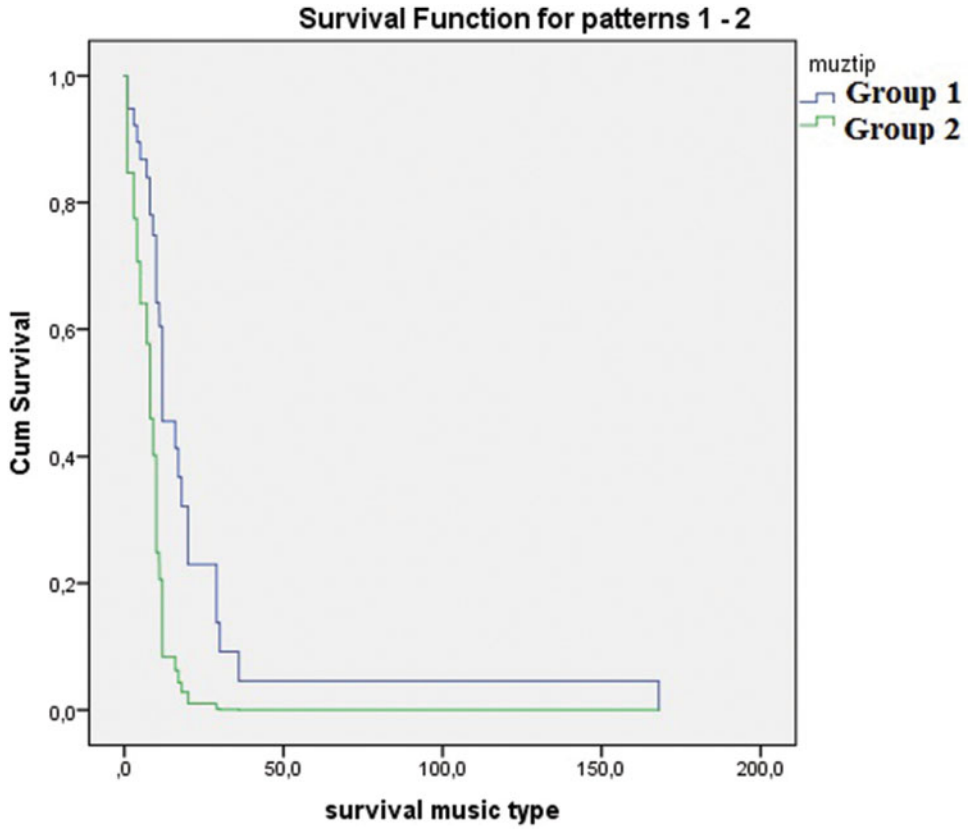

Figure 1. The survival status among groups of musician patients are seen; An apparent difference is due solely to the effect of music type.

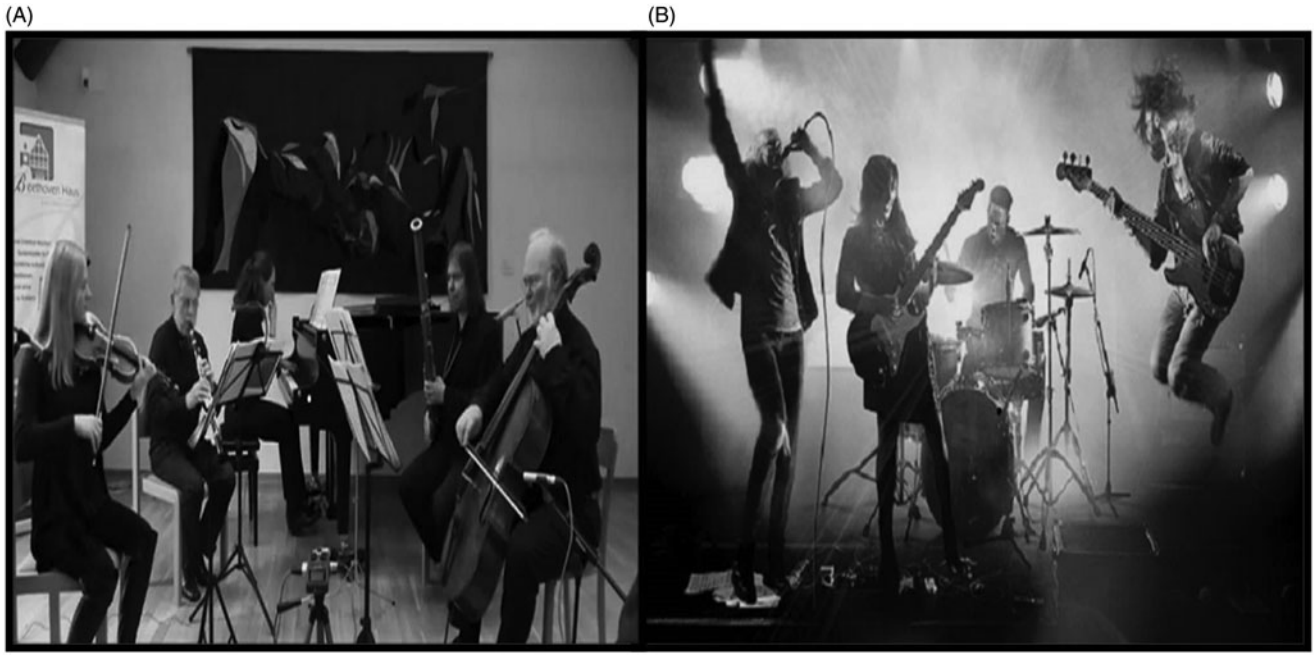

Figure 2. (A) Classical music performance: playing classic orchestra instruments needs early music education and long training in instrumental technique and of fine motor skills. The classic instrumental technique requires the highly specialized development of basal ganglia pathways. Performance is determined by the written work of the composer. Reading music score, hearing, playing, performing motor skills, and social interacting with other musicians requires a high development of neuronal networks. (B) Performance of Rock-/Pop music: Performance is characterized by rhythm, improvisation, and elements of athletic motion like singing, dancing, and body movement. Sound and light effects create the background. Social interacting and musical communications occur on an athletic level. Loudness, light, and physical exhaustion stress the nervous system.

variation and sex disparity in brain and CNS tumors have been observed.[45] Epidemiological studies in different parts of the world have shown that males have a higher risk of malignant brain and CNS tumors than females.[45] In this study, Table 2 shows the gender distribution of musicians. There were 21 males and 6 female musicians. Chi-Square test showed that gender type is

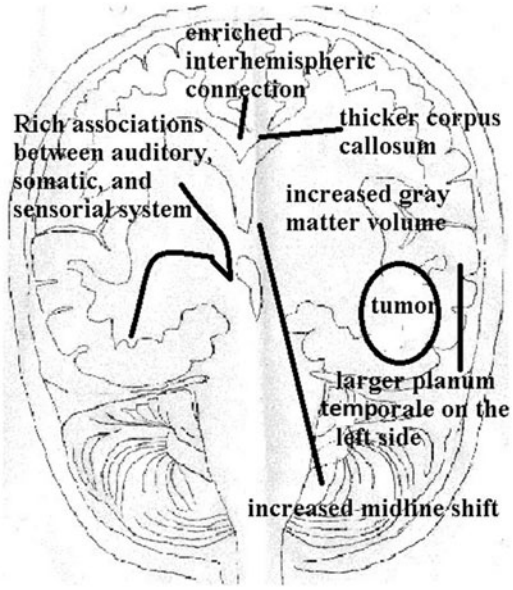

Figure 3. There are some differences in cerebral anatomic structures in musicians.

statistically different between groups ($p = .04$). In the Cox regression analysis of the study, Exp(B) for music type is 3139. The hazard rate increases by 3.13 with each unit increase in survival times. The HR for music type is 3.13, so an increase in 1.0 will be associated with a 3.13-fold increase in the hazard. It is statistically significant with p values of .05 ($p = .026$). This finding is the first time reporting of this case. If one is the first to report something, that something is of value.[46,47]

5. Limitations

In this study, we could only be reached a record of 27 musicians. The information of the musicians' group is based on a Wikipedia list and the data provided regarding diagnosis, survival, etc. are extracted from media reports, the quality and heterogeneity of data is a major concern in this study. The number of classical music musician is very lower than pop music musician. Twenty-one were Pop/Rock—or Jazz musicians–singers, composers, drummers or other instrumentalists. Six were classic instrumentalists, composers or classic-educated opera or operetta singers. Interestingly, only six records of classical music musician could be found. This is an important question that may be arisen from this study, why the low number of classic music performers with malignant cerebral tumors appeared in Wikipedia? The cause of this should be investigated. Is it association or causality? Another most important limitation of this study, our data depends on appearing the malignant cerebral disease musicians in Wikipedia. There might be more musicians number than the number that we studied here. This could not be published or appeared in Wikipedia. So, the reporting rate of the musician may be underestimated, especially by histological type, given the high percentage of unspecified malignant incident neoplasms. Another weakness of the study can come from comparing the pop musicians with classical musicians without considering the type of tumor and treatment received. In this study, a heterogeneous group from the musician with different age, ethnicity, gender was analyzed for survival times. This heterogeneous nature of musician is another limitation. In addition, common management of cerebral malignant tumors is resection to the maximum extent possible, followed by radio and chemo-radiotherapy. In this study, we do not know the surgical volume reduction of these musicians. In summary, it is important to note that other clinical, genetic, neurological, and medical factors (isocitrate dehydrogenase status, O^6-methylguanine-DNA methyltransferase methylation status, surgical or medical management of this musicians may have an effect their outcomes. It was not possible to consider these factors in this study. Geographic economic differences may reflect differences in the quality of medical care, the availability of diagnostic facilities, and the level of organization of registries for data collection and coding.[48]

6. Conclusion

This study, on a prospective basis, would act as a good stimulus to look into this issue amongst neuro-oncologists and neurosurgeons. In this article, we gathered from the internet information on 27 musicians who had malignant intracranial tumors and analyzed their survival times in relation to the type of musical specialty. The HR for music type is 3.13 for classical music performers, so an increase in 1.0 will be associated with a 3.13-fold increase in the hazard. It is statistically significant with p values of .05 ($p = .026$). Malignant tumors in musician may contribute to post-lesional functional changes in the brain. A better understanding of the differences in the survival of musicians with malign cerebral tumors will enable us to guide the cerebral plastic potential of musicians. Such linkage and its mechanisms underlying cerebral plasticity will open a large field of new perspectives on patients with cerebral malign tumors. Neurosurgeons should pay more attention to the cerebral functional networks of musicians with malignant cerebral tumors. We can have something to learn from the music type-related different survival times of musicians with malign intracranial tumors. As the first pilot study, there no doubt that our study will lead to performing more studies on this subject.

Disclosure statement

No potential conflict of interest was reported by the authors.

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