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Exploring the Impacts of Different Music Genres on Oxidative Stress in Rat Brain and Serum

Farklı Müzik Türlerinin Oksidatif Stres Üzerine Etkilerinin Rat Beyni ve Serumunda Araştırılması

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Abstract

Music reduces emotional stress, relieves anxiety, and is utilized while treating various diseases. The present study explored the impacts of various music genres at different decibels on the oxidation state in the brain tissue and serum. We carried out the study on 42 male Wistar Albino rats. The rats were randomized (*six rats in each cage*) as a control group and groups exposed to noise, rock music, and slow music at different decibels for 21 days and 4 hours a day. At the end of the experiment, we studied oxidant [malondialdehyde (MDA), nitric oxide, protein carbonyl (PC)] and antioxidant [superoxide dismutase (SOD), glutathione peroxidase (GSH-Px)] parameters in the cerebral cortex, cerebellum, and serum. In the cortex, while MDA levels were low in the 100 dB(A) slow music group, the 50 dB(A) noise and rock music groups had elevated SOD, GSH-Px, and MDA levels when compared to the control group and higher MDA and GSH-Px levels when compared to the 50 dB(A) slow music group. In the cerebellum, although SOD levels did not significantly change, we found MDA and GSH-Px to increase in the 50 dB(A) and 100 dB(A) rock music groups and the 50 dB(A) noise group. Finally, we determined MDA and PC levels to be low and SOD levels to be high in the 50 dB(A) slow music group. Overall, that high dB rock music created oxidative stress in cerebellar tissue, that low dB rock music and noise created oxidative stress in the cortex and cerebellum, and that high and low dB slow music may have positive impacts on oxidative stress.

Keywords: Music, Noise, Oxidative Stress, Brain, Decibel.

Özet

Müzik, emosyonel stresi azaltır, kaygıyı giderir ve çeşitli hastalıkların tedavisinde kullanılır. Bu çalışmada, farklı desibellerde çeşitli müzik türlerinin, beyin dokusu ve serumdaki oksidatif durum üzerine etkileri araştırıldı. Çalışma 42 adet erkek Wistar Albino cinsi rat üzerinde gerçekleştirildi. Ratlar her kafeste 6 adet olmak üzere 21 gün, günde 4 saat farklı desibel şiddetinde gürültü, rock müzik, *slow* müzik dinletilen ve kontrol grubu olmak üzere randomize edildi. Deney sonunda serebral korteks, serebellum ve serumdaki oksidan [malondialdehit (MDA), nitrik oksit, protein karbonil (PC)] ve antioksidan [süperoksit dismutaz (SOD), glutatyon peroksidaz (GSH-Px)] parametreler çalışıldı. Kortekste 100 dB (A) *slow* müzik grubunda MDA

düzeyleri düşük iken, 50 dB (A) gürültü ve rock müzik grubunda; kontrolle karşılaştırıldığında SOD, GSH-Px ve MDA düzeyleri, 50 dB (A) *slow* müzik grubuyla karşılaştırıldığında MDA ve GSH-Px düzeyleri yüksekti. Serebellumda 50 dB (A) ve 100 dB (A) rock müzik ve 50 dB(A) gürültü grubunda SOD düzeyleri değişmemişken, MDA ve GSH-Px düzeyleri artmıştı. Son olarak 50 dB(A) *slow* müzik grubunda MDA ve PC düzeylerinin düşük, SOD düzeylerinin yüksek olduğunu bulduk. Genel olarak, yüksek dB rock müzik serebellar dokuda ve düşük dB rock müzik ve gürültü korteks ve serebellumda oksidatif stres oluşturdu. Yüksek ve düşük dB *slow* müziğin ise oksidatif stres üzerine olumlu etkilerinin olabileceği gözlemlendi.

Anahtar Kelimeler: Müzik, Gürültü, Oksidatif Stres, Beyin, Desibel.

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Introduction

Music therapy can be employed to treat various medical conditions from psychological disorders (e.g., depression, anxiety, learning disorders, and autistic disorders) to neurological diseases (e.g., stroke and dementia), from pain treatment to sleep disorders [1-3]. The previous research suggested substantial evidence for the positive impacts of music on the nervous, endocrine, and immune systems [1,4]. It was also shown that music contributes to the motor and behavioral symptoms ruined by neurological disorders (e.g., Parkinson's disease, multiple sclerosis, Alzheimer's disease, ataxia, and spasticity) [2,5,6]. Moreover, the relevant literature showed the desirable impacts of music therapy on behavioral and psychological symptoms and agitation in patients with dementia [7] and on electroencephalography (EEG) changes and seizure activity in patients with epilepsy [8].

The literature offers few studies on music and oxidative stress. Yet, in their study that created an atherosclerosis model on animals using music-modulated electric current (MMEC), Zubkova et al. [9] showed that the application of MMEC led to a decrease in lipid peroxidation in the cerebral cortex and myocardium tissue. In that study [9], the researchers highlighted the antistressor and antioxidant role of MMEC.

On the other hand, contrary to music, noise has negatively affected human health in recent years, in parallel with the increase in industrialization, population density, urbanization, technological developments and entertainment venues, causing both psychological and physical disorders. In addition, it is often shown at the pathological and biochemical levels that long-term exposure to high dB noise causes oxidative damage in the brain due to revealing excessive amounts of oxygen-free radicals [10].

At this point, it should be asked whether music characterized by its many mental and physical benefits exerts adverse impacts on the oxidation state. In this regard, Yamane et al. reported that loud rock and roll music disrupted the blood flow in the inner ear structures of guinea pigs, resulting in the emergence of oxidative products and damage [11]. In addition, other studies concluded that loud music causes hearing loss like noise [12-14].

The relevant literature seems to have missed uncovering the oxidation state in the brain and serum when listening to high and low dB rock music, slow Turkish reed flute (ney) sound known to provide mental and physical relaxation, and the noise proven to be harmful. Therefore, in this study, the effects of high and low decibel rock music, ney sound from slow music group, and noise on oxidative state in serum and cerebral tissue were investigated.

Material and Method

Gazi University Local Ethics Committee for Animal Experiments granted relevant approval for all procedures executed in the present study (dated 01.04.2011).

Experimental animals

We employed 42 Wistar Albino male rats (335±55 g). The ambient was kept between 22±2°C and illuminated to match the day/night cycle. We fed the rats with pellet feed and tap

water without any limitation. They were sheltered in groups of six in seven separate plastic cages of 40×55 cm^2 with sawdust.

Groups

Group 1: It was the control group exposed to no music and noise. Group 2: The rats were exposed to white noise at 100 dB(A) for 21 days, 4 hours/day. Group 3: The rats were exposed to rock music at 100 dB for 21 days, 4 hours/day. Group 4: The rats were exposed to slow music at 100 dB for 21 days, 4 hours/day. Group 5: The rats were exposed to white noise at 50 dB(A) for 21 days, 4 hours/day. Group 6: The rats were exposed to rock music at 50 dB for 21 days, 4 hours/day. Group 7: The rats were exposed to slow music at 50 dB for 21 days, 4 hours/day.

Music and noise exposure

We utilized "Solo Ney Taksimleri" (album) for slow music, "Iron Maiden" (album) for rock music, and a website (whitenoisemp3s.com/free-white-noise) for white noise. Slow music was exposed at 43-55 dB (low) and 85-105 dB (high), while rock music was played at 48-52 dB (low) and 82-103 dB (high). Besides, white noise was set to 50 dB(A) and 100 dB(A), respectively. Finally, we set the basal level of ambient noise to which the control group was exposed to 47 dB. We constantly measured the intensity of the music and noise via a sound meter (Sound Level Meter DT-8850, China). The device was set to "High" to measure high dB and "Low" to detect low dB. We placed the device in the middle of the cages to obtain precise sound measurements. We decided on the level of 100 dB(A) since one is likely to confront this level of sound in entertainment venues and many noisy workplaces.

Preparing and studying blood and tissue samples

The day after listening to music or noise for 4 hours a day for 21 days, the animals were anesthetized with ketamine 100 mg/kg and xylazine 4 mg/kg. In the next step, the animals were sacrificed after obtaining intracardiac blood. We quickly took brain tissue samples from the rats. The right side of each brain tissue was divided into two parts (cerebral cortex and cerebellum), wrapped in aluminum foil, and kept in a refrigerator at -80°C for biochemical examinations. We centrifuged the blood samples at 5.000 rpm for 5 minutes to obtain their serum and then placed and stored in the refrigerator at -20°C for further biochemical analyses.

For biochemical analyses, we took the brain tissue samples out of the refrigerator (-80°C) and dissolved them in Tris-HCl buffer (50 mM, pH 7.4) containing 0.50 ml of 1-1 Triton x-100 (1/5) for 2 minutes at 13.000 rpm (Homogenizer: Ultra Turrax T25 Basic, IKA Labortechnik, Germany). The supernatants of the tissues were obtained by centrifuging the homogenates at 5000xg for one hour. We stored the tissue and blood samples at +4°C throughout the entire procedure. We then spectrophotometrically determined superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), nitric oxide (NO), malondialdehyde (MDA), and protein carbonyl (PC) levels in serum samples, homogenates, and supernatants obtained to evaluate oxidative stress using standard chemicals (Sigma, St. Louis, USA).

Protein levels were calculated at a wavelength of 660 nm spectrophotometrically based on the method proposed by Lowry et al. [15]. All samples were tested twice.

SOD (EC 1.15.1.1) activity was studied using the method introduced by Sun et al. [16] and modification by Durak et al. [17]. SOD activity was demonstrated in tissue as unit/milligram (U/mg) tissue protein and in serum as unit/milliliter (U/ml).

GSH-Px activity were determined based on the method by Paglia et al. [18]. The GSH-Px activity was defined in tissue as unit/gram (U/g) tissue protein and in serum as unit/liter (U/L).

MDA levels were measured based on the method by Esterbauer [19]. The values obtained in the tissue were shown as nmol/gr wet tissue and in serum as μmol/L.

As NO measurement is rather challenging in biological specimens, tissue nitrite and nitrate are often considered an index of NO, according to the method introduced by Cortas et al. [20]. In this study, the values obtained were expressed as μmol/g in tissue and as μmol/L in serum.

The PC levels were calculated based on the method by Levine et al. [21]. PC values obtained in serum were expressed as nmol/ml and in tissue as nmol/mg protein.

Statistical analysis

We used the Kruskal Wallis-H test to compare the groups. Then, we performed the Mann-Whitney U test for pairwise comparisons of the parameters showing statistically significant differences. The data were presented as median (first and third quartiles). We performed the analyses on SPSS 22.0 (IBM Corp., Armonk, NY) and accepted a p-value <0.05 to be statistically significant.

Results

Cortex

We measured the highest SOD levels in the cerebral cortex in Group 6. When comparing the groups with the control group, in Group 6 yielded a difference (p=0.008). When comparing the groups exposed to the same genre of sound, SOD levels were found to be higher in the cerebral cortex in Group 6 than in Group 3 (p=0.006). Similarly, SOD levels were found to be higher, despite non-significant, in the cortex in Group 5 than Group 2. Comparing the groups exposed to sounds at the same dB, we discovered a difference between Group 6 and Group 7 by SOD level in the cortex (p=0.010) (Table 1).

The highest GSH-Px levels in the cerebral cortex were measured in Group 5. They were lower in the control group than in Group 3, Group 5, and Group 6 (p=0.004, p=0.004, p=0.004, respectively) and higher compared to Group 4 (p=0.025). When it comes to the groups exposed to the same type of sound, we found that GSH-Px levels in the cortex to be lower in Group 2 and Group 4 than Group 5 and Group 7 (p=0.004, p=0.025, respectively). Considering the groups by sounds at the same dB, GSH-Px levels in the cerebral cortex were found to be higher at high decibels in Group 3 compared to Group 2 and Group 4 (p=0.004, p=0.004, respectively). Besides, we discovered the GSH-Px levels in the cerebral cortex were lower in Group 7 at low decibels compared to Group 5 and Group 6 (p=0.004, p=0.004, respectively) (Table 1).

Table 1. Comparison of the groups by oxidant and antioxidant levels in the cortex.

Groups	SOD (U/mg protein) Median (Q)	GSH-Px (U/g protein) Median (Q)	MDA (nmol/G wet tissue) Median (Q)	NO (µmol/g wet tissue) Median (Q)	PC (nmol/mg protein) Median (Q)
G1-Control	0.06 (0.06-0.07)	1.75 (1.69-1.86)	53.74 (53.45-56.56)	2.13 (1.93-2.19)	10.61 (9.40-11.88)
G2-100 dB Noise	0.06 (0.06-0.07)	1.79 (1.70-2.08)	49.88 (47.82-61.53)	1.96 (1.74-2.05)	8.67 (8.10-9.26)
G3-100 dB Rock music	0.06 (0.06-0.07)	4.01 (3.98-4.41)	65.80 (59.81-71.36)	1.28 (1.23-1.95)	11.22 (9.65-11.95)
G4-100 dB Slow music	0.06 (0.06-0.06)	1.49 (1.48-1.57)	44.08 (42.70-45.22)	1.74 (1.66-1.96)	10.01 (8.41-10.05)
G5-50 dB Noise	0.07 (0.06-0.08)	6.04 (5.56-6.17)	83.09 (70.01-94.04)	1.38 (1.20-1.56)	13.02 (10.73-13.9)
G6-50 dB Rock music	0.08 (0.07-0.08)	5.44 (4.04-6.99)	69.26 (65.68-73.47)	1.53 (1.38-1.76)	9.69 (9.43-11.53)
G7-50 dB Slow music	0.07 (0.06-0.07)	1.71 (1.61-1.94)	53.19 (48.56-56.87)	1.92 (1.70-2.07)	10.13 (9.59-11.21)
G1-G3		0.004*		0.025*	
G1-G4		0.025*	0.006*		
G1-G5		0.004*	0.004*	0.005*	
G1-G6	0.008*	0.004*	0.004*	0.006*	
G2-G3		0.004*			
G2-G4			0.018*		
G2-G5		0.004*	0.037*	0.010*	
G3-G4		0.004*			
G3-G6	0.006*				
G4-G7		0.025*	0.011*		
G5-G7		0.004*	0.004*	0.016*	
G6-G7	0.010*	0.004*	0.004*		

Q; Quartiles. *p<0.05

We observed the highest MDA levels in the cerebral cortex in Group 5. They were found to be higher in Group 5 and Group 6 and lower in Group 4 than in the control group (p=0.004, p=0.004, p=0.006, respectively). We also compared the groups exposed to the same genre of sound and found that MDA levels in the cerebral cortex were lower in Group 4 and Group 2 than in Group 7 and Group 5 (p=0.01, p=0.037, respectively). When the groups were compared by sound at the same dB, the findings revealed that Group 7 had lower MDA levels in the cortex than Group 6 and Group 5 (p=0.004, p=0.004, respectively). Moreover, MDA levels in the cortex were found to be lower in Group 4 than Group 2 (p=0.018) (Table 1).

NO levels in the cortex were higher in the control group than in Group 3, Group 5, and Group 6 (p=0.025, p=0.005, p=0.006, respectively). Meanwhile, regarding the groups exposed to the same genre of sound, NO levels in the cortex were lower in Group 5 compared to Group 2 (p=0.010). Finally, comparing the groups exposed to sounds at the same dB, NO levels in the cortex were found to be higher in Group 7 compared to Group 5 (p=0.016). (Table 1).

The groups did not significantly differ by PC levels in the cerebral cortex (Table 1).

Cerebellum

Group 7 has the highest SOD levels in the cerebellum. In comparison with the control group, Group 7 yielded a significant difference (p=0.004). Considering the groups exposed to the same genre of sound, SOD levels in the cerebellum were found to be higher in Group 7 and Group 5 when compared to Group 4 and Group 2 (p=0.004, p=0.006, respectively). Comparing the groups by sound at the same dB, we found SOD levels in the cerebellum to be higher in Group 7 than in Group 5 and Group 6 (p=0.004, p=0.004, respectively). It was also the case between Group 3 and Group 2 (p=0.016) (Table 2).

Table 2. Comparison of the groups by oxidant and antioxidant levels in the cerebellum.

Groups	SOD (U/mg protein) Median (Q)	GSH-Px (U/g protein) Median (Q)	MDA (nmol/G wet tissue) Median (Q)	NO (µmol/g wet tissue) Median (Q)	PC (nmol/mg protein) Median (Q)
G1-Control	0.05 (0.05-0.07)	3.03 (2.20-3.44)	62.02 (58.74-67.15)	4.14 (3.73-5.07)	11.75 (10.08-12.79)
G2-100 dB Noise	0.07 (0.07-0.07)	2.47 (1.88-2.82)	78.71 (54.40-88.10)	4.30 (3.33-4.55)	11.90 (11.05-12.32)
G3-100 dB Rock music	0.08 (0.07-0.08)	6.55 (6.03-8.32)	108.82 (74.28-218.45)	2.09 (1.86-2.35)	14.42 (13.46-18.06)
G4-100 dB Slow music	0.08 (0.07-0.09)	2.99 (2.63-3.34)	70.87 (62.71-77.29)	3.93 (3.25-4.02)	11.53 (9.99-12.56)
G5-50 dB Noise	0.09 (0.08-0.09)	7.36 (5.98-8.31)	99.48 (86.79-115.43)	2.85 (2.69-3.28)	12.43 (11.88-15.78)
G6-50 dB Rock music	0.08 (0.08-0.08)	6.48 (6.33-7.24)	116.73 (107.85-130.61)	2.68 (2.28-2.94)	12.79 (10.89-16.59)
G7-50 dB Slow music	0.10 (0.10-0.11)	2.36 (1.92-2.89)	55.55 (52.87-60.36)	3.77 (3.72-3.98)	9.45 (9.18-10.91)
G1-G3		0.004*	0.010*	0.006*	0.016*
G1-G5		0.016*	0.004*	0.010*	
G1-G6		0.004*	0.004*	0.004*	
G1-G7	0.004*				
G2-G3	0.016*	0.004*		0.010*	
G2-G5	0.006*	0.004*		0.016*	
G3-G4		0.004*		0.010*	0.016*
G4-G7	0.004*		0.010*		
G5-G7	0.004*	0.006*	0.004*	0.037*	0.004*
G6-G7	0.004*	0.004*	0.004*	0.006*	0.037*

Q; Quartiles. *p<0.05

We measured the highest GSH-Px levels in the cerebellum in Group 5. They were higher in Groups 3, 5, and 6 when compared to the control group (p=0.004, p=0.016, p=0.004, respectively). In the comparison of the groups exposed to the same genre of sound, Group 5 was found to have higher GSH-Px levels in the cerebellum than Group 2 (p=0.004). Besides, when the groups

were compared by sound at the same dB, Group 3 had higher GSH-Px levels in the cerebellum than Group 2 and Group 4 (p=0.004, p=0.004, respectively). At low dB, Group 7 yielded lower measurements than Group 5 and Group 6 (p=0.006, p=0.004, respectively) (Table 2).

The lowest MDA levels in the cerebellum were measured in Group 7. The control group was found to have lower MDA levels in the cerebellum than Groups 3, 5, and 6 (p=0.010, p=0.004, p=0.004, respectively). Among the groups exposed to the same genre of sound, MDA levels in the cerebellum were higher in Group 4 compared to Group 7 (p=0.010). Regarding those exposed to sounds at the same dB, Group 7 was found to have lower MDA levels in the cerebellum than Group 5 and Group 6 (p=0.004, p=0.004, respectively) (Table 2).

The control group had higher NO levels than Groups 3, 5, and 6 (p=0.006, p=0.010, p=0.004, respectively). Regarding the groups exposed to the same genre of sound, we found that Group 2 had higher NO levels than Group 5 (p=0.016). Considering exposure to sounds at the same dB, NO levels in the cerebellum were found to be higher in Group 2 and Group 4 compared to Group 3 (p=0.01, p=0.01, respectively). Regarding the groups exposed to low dB sound, NO levels were higher in Group 7 when compared to Groups 5 and 6 (p=0.037, p=0.006, respectively) (Table 2).

We discovered that only Group 3 had higher PC levels in the cerebellum than the control group (p=0.016). Considering the groups exposed to sounds at the same dB, PC levels in the cerebellum were found to be lower in Group 7 compared to Groups 5 and 6 (p=0.004, p=0.037, respectively). They were also found to be higher in Group 3 than in Group 4 (p=0.016) (Table 2).

Serum

Serum SOD levels did not significantly differ between the control group and other groups. In the comparison of the groups exposed to the same genre of sound, we found serum SOD levels to be higher in Groups 5 and 6 than in Groups 2 and 3 (p=0.03, p=0.013, respectively). Among the groups exposed to sounds at the same dB, serum SOD levels were lower in Group 7 than in Groups 5 and 6 (p=0.01, p=0.024, respectively) (Table 3).

Table 3. Comparison of the groups by serum oxidant and antioxidant levels.

Groups	SOD (U/mL) Median (Q)	GSH-Px (U/L) Median (Q)	MDA (µmol/L) Median (Q)	NO (mmol/L) Median (Q)	PC (nmol/ml) Median (Q)
G1-Control	9.33 (8.68-9.41)	1831.60 (1735.20-2072.60)	2.66 (2.61-2.69)	70.96 (65.99-75.94)	744.00 (727.60-773.50)
G2-100 dB Noise	9.20 (8.58-9.35)	1783.40 (1614.70-1903.90)	2.64 (2.58-2.84)	68.26 (65.99-81.36)	759.30 (700.40-762.50)
G3-100 dB Rock music	8.97 (8.48-9.30)	2012.35 (1928.00-2313.60)	2.89 (2.76-2.97)	145.55 (130.18-159.10)	761.45 (725.50-781.10)
G4-100 dB Slow music	8.45 (8.27-8.79)	1735.20 (1470.10-2000.30)	2.80 (2.66-2.86)	73.23 (72.32-75.94)	741.85 (701.50-775.60)
G5-50 dB Noise	9.87 (9.56-10.03)	1855.70 (1590.60-1976.20)	2.71 (2.71-2.76)	80.46 (76.84-84.07)	699.25 (693.80-752.70)
G6-50 dB Rock music	9.56 (9.46-9.66)	2000.30 (1903.90-2024.40)	2.79 (2.76-2.79)	67.80 (62.38-68.70)	770.20 (703.60-810.50)
G7-50 dB Slow music	8.94 (8.94-8.94)	1542.40 (1542.40-1542.40)	2.76 (2.61-2.86)	78.65 (72.32-80.46)	665.50 (648.00-691.60)
G1-G3				0.004*	
G1-G5				0.030*	
G1-G7		0.004*			
G2-G3		0.019*		0.030*	
G2-G5	0.030*				
G3-G4				0.004*	
G3-G6	0.013*			0.004*	
G5-G6				0.010*	
G5-G7	0.010*	0.015*			
G6-G7	0.024*	0.004*		0.045*	

Q; Quartiles. *p<0.05

The lowest GSH-Px levels in serum were measured in Group 7, and we found them to be lower in Group 7 than in the control group (p=0.004). Comparing the groups exposed to sounds at the same dB, serum GSH-Px levels were lower in Group 7 than in Group 5 and 6 (p=0.015, p=0.004, respectively), but higher in Group 3 than in Group 2 (p=0.019) (Table 3).

We measured the highest serum NO levels in Group 3, and they were found to be lower in the control group than in Groups 3 and 5 (p=0.004, p=0.03, respectively). Considering the groups exposed to the same genre of sound, Group 3 had higher serum NO levels than Group 6 (p=0.004). In the comparison of groups exposed to sounds at the same dB, we realized serum NO levels to be higher in Group 3 than in Groups 2 and 4 (p=0.030, p=0.004, respectively), but lower in Group 6 than in Group 5 and Group 7 (p=0.01, p=0.045, respectively) (Table 3).

The groups did not significantly differ by serum MDA or PC levels (Table 3)

Discussion

Oxidative stress, emerging for various reasons, occurs in all tissues and as an important disease factor. It affects brain tissue more than any other organ [22,23]. It has been proven that noise stress increases the formation of reactive oxygen species (ROS) and RNS, which may break down lipid and protein molecules and damage DNA, thereby triggering loss of function after exposure to noise and leading to cell death [10,24]. Yamane et al. [11] also found that high dB rock-'n-roll music increases ROS in the marginal cells of the stria vascularis. The body develops antioxidant mechanisms to scavenge the increased superoxide radicals, and the most important enzymes in these antioxidant mechanisms can be considered SOD, CAT, and GSH-Px [25]. Oxidative stress occurs as a result of an imbalance between antioxidants and the rate of formation of free radicals, which causes oxidative harm to molecules, especially proteins, lipids, and DNA, leading to disruption of cell metabolism and death of the cell [23]. PC levels due to protein oxidation and MDA levels due to lipid peroxidation increase in the tissue, helping to determine oxidative damage [19,26].

The literature hosts conflicting findings regarding the increase in free oxygen radicals and the corresponding increase in SOD activity. Manikandan et al. [27] found that SOD levels increased in the acute period but started decreasing despite being high in the chronic period. In the same study, while GSH-Px levels decreased in the chronic period, they discovered a relative decrease in MDA levels. In two other studies, it was found that SOD activity increased, GSH-Px values decreased, and lipid peroxidation increased in different brain tissues as a result of chronic noise exposure [10,28]. In another study, as a result of chronic noise stress, SOD levels increasing in some parts of the brain in the acute period returned to normal in the chronic period, while GSH-Px and MDA levels did not change [29]. In our study, SOD, MDA, PC, NO, and GSH-Px levels in the cortex, cerebellum, and serum did not change at the end of 21 days of 100 dB(A) chronic noise exposure. Noise exposure may lead to a temporary or permanent threshold shift (TTS-PTS); the type of threshold shift is highly affected by the intensity and duration of exposure [30, 31]. Mills reported that an octave noise band centered on the mid-frequency range and presented as low as 65-70 dB Sound Pressure Levels (SPL) may cause temporary hearing loss in humans [31]. The report of Bohne and Harding stated that there may be a hearing threshold shift as a result of constant noise exposure [32]. Samson et al. [29] stated that such a shift may cause decreased neuronal excitation and a corresponding reduction in the production of free oxygen radicals, which may bring SOD levels back to normal. These results suggested that chronic exposure to high dB noise may cause a hearing threshold shift, and this shift may lead to decreased neuronal stimulation - thus, a decrease in the production of free oxygen radicals - and may bring SOD levels, which we think to increase in the acute period, to normal in the chronic period. In our study, oxidant MDA, NO, and PC levels and antioxidant GSH-Px levels remained the same in the same groups compared to the control group may also support this hypothesis.

Based on the fact that the type of noise-induced threshold shift will be designated by the intensity and duration of the exposure [30,31], it

can be asserted that exposure to a low dB sound may be less likely to cause a hearing threshold shift compared to exposure to a high dB sound. In our study, SOD levels increased in the cortex in the groups exposed to 50 dB noise and rock music. In the same groups, we also found an increase in oxidant MDA and antioxidant GSH-Px levels. These results suggested that neuronal stimulation, thus the production of free oxygen radicals, continues, due to exposure to low decibel sound and antioxidant circuits emerge.

Another striking point in our study was that MDA levels in the cortex were significantly lower in the 100 dB slow music group than in the 100 dB(A) noise group and the control group. This finding may imply that slow music, albeit at high dB, leads to a decrease in lipid peroxidation compared to 100 dB(A) noise. Considering such a fact, low GSH-Px levels in the mentioned group can be explained by less oxidation, less hydrogen peroxide accumulation, and less need for the GSH-Px enzyme.

In a study on animals with atherosclerosis, Zubkova et al. [9] concluded a reduction in lipid peroxidation in the cortex and myocardial tissue in the group in which MMEA was applied and highlighted the antioxidant role of MMEA. In our study, we did not change in SOD, MDA, GSH-Px, and PC levels in the cortex in the low dB slow music group when compared to the control group. On the contrary, MDA and GSH-Px levels were lower in the slow music group compared to the same dB rock music and noise groups, which may also be due to less lipid peroxidation, less oxidation, less hydrogen peroxide accumulation, and less need for the GSH-Px enzyme. Our findings suggested that low dB slow music may not cause oxidative damage but instead provides oxidative balance.

Mandavilli and Rao [33] reported that the cerebellum is less vulnerable to oxidative damage than the cortex. In our study, 100 dB(A) noise exposure demonstrated the same impacts on the cerebellum and cortex in the groups compared to the control group. In chronic exposure to low and high dB rock music and low dB noise, SOD levels in the cerebellar tissue did not differ from in the control group, but MDA, GSH-Px, and NO levels were found to be increased. Exposure to low dB slow music compared to the control group, on the other hand, decreased MDA and PC levels in the cerebellum, albeit insignificant, and significantly increased SOD levels. Compared to the groups exposed to low dB rock music and noise, the group above had a similarly significant reduction in MDA and PC levels and increased SOD levels in the cerebellum. Thus, we may suggest that low dB slow music increases antioxidant mechanisms in the cerebellum and does not create oxidative stress.

NO is among the reactive nitrogen oxide species with free-radical properties, and a significant portion of NO is synthesized from L-arginine by inducible nitric oxide synthase (iNOS). While taking part in essential physiological functions at low concentrations, it has radical properties at high concentrations [34]. In their study, Shi et al. [35] observed iNOS activity in cochlear tissues as a result of exposure to high dB noise. The scholars linked noise-induced hearing loss to damage to hair cells as a result of NO production due to iNOS activity. In our study, NO levels in the serum, cortex, and cerebellum in the group exposed to 100 dB(A) noise were similar to those measured in the control group. While NO level increased in some studies in the literature, it did not change in others [25,36]. In our study, NO levels in the cortex and cerebellum were found to be low in the groups exposed to 100 dB rock music, 50 dB(A) noise, and 50 dB rock music. High MDA levels in the cortex and cerebellum in the groups exposed to 50 dB(A) noise and 50 dB rock music, and high MDA levels in the cerebellum in the group exposed to 100 dB(A) rock music may be a robust indicator of the presence of oxidative stress. It is well-known that glucocorticoid levels increase in the presence of any stress, including noise [28]. Besides, the iNOS enzyme is inhibited by glucocorticoids [37]. Although we did not check glucocorticoid levels in our study, low NO levels in our groups may be because of the inability to synthesize NO linked with iNOS inhibition. It may also explain the reason for high GSH-PX levels in the cortex and cerebellum in these groups. In cases of overproduced NO and increased superoxide levels, peroxynitrite formed as a result of the reaction between NO and superoxide causes antioxidant enzymes (e.g., GSH-Px) to be

depleted [38,39]. Since peroxynitrite cannot be formed at low levels of NO, GSH-Px values may be high in these groups.

The weakness of this study is that we did not measure the presence of hearing threshold shift in our study. In addition, another limitation is that the sound levels cannot be kept at a constant decibel intensity, as in the noise groups, due to the rhythmicity of the music that increases and decreases in music groups.

Conclusion

In this study, we concluded that high decibel noise provides oxidative balance in the cerebral cortex, cerebellum, and serum in repetitive exposures. In addition, our findings revealed that high dB rock music may create oxidative stress in the cerebellar tissue, while low dB rock music and noise cause oxidative stress in the cerebral cortex and cerebellum. On the other hand, we observed that high and low decibel slow music does not cause oxidative stress but may have positive effects against oxidative stress. The findings give rise to the thought that rock music may cause oxidative stress, while slow music may have an antioxidant role in the brain tissue.

Conflict of interest: The authors declare that there is no conflict of interest. The authors alone are responsible for the content and writing of the paper. **Financial disclosure:** The article is derived from a thesis study.

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