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ARAŞTIRMA / RESEARCH

Effects of music on stress induced hormones and oxidative stress levels

Müziğin strese bağlı indüklenen hormonlar ve oksidatif stres üzerine etkisi

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Abstract

Purpose: Perinatal stress, anxiety, and depression have been thought having influences on the developmental period of organisms. In this study, we aimed to investigate the effects of different types of music exposure during perinatal period on depression-like behavior, serum levels of adrenocorticotropic hormone (ACTH), corticosterone (CORT) and parathyroid hormone (PTH) as well as serum oxidative stress index in rats.

Materials and Methods: Pregnant Wistar albino rats were randomly divided into four cages; the control group (no music exposure), the classical music group (Canon in D Major/ Johann Pachelbel, 60 dB), the traditional Sufi music group (Whirling Derwish/ Omar Faruk Tekbilek, 30 dB), and the rock music group (In Your Face/ Children of Bodom, 120 dB). Dams and pups in each music groups listened to their own music 1 hour/day from gestational day 10 to postnatal day 21.

Results: According to the results of tail suspension test, the longer duration of immobility which shows the level of depression was increased in the classical music group compared to the control group. At hormonal level, significant alterations were obtained only in serum ACTH levels. It was increased in the classical music group, while decreased in the sufi music group compared to the control group. In addition, a marked increase in oxidative stress index was found in the rock music group compared to the control group.

Conclusion: The sound intensity of music which is listened during the pregnancy has vital importance in the stress and depression level of offspring.

Keywords: Hypothalamic-pituitary-adrenal (HPA) axis, perinatal music, depression-like behavior, parathyroid hormone (PTH), oxidative stress index.

Öz

Amaç: Perinatal stresin, kaygı ve depresyonun organizmaların gelişim dönemini etkilediği düşünülmektedir. Bu çalışmada perinatal dönemde farklı müzik türlerine maruz kalmış sıçanların depresyon benzeri davranışları, adrenokortikotropik hormon (ACTH), kortikosteron (CORT) ve paratiroid hormon (PTH) serum düzeyleri ile serum oksidatif stres üzerindeki etkilerini araştırmayı amaçladık.

Gereç ve Yöntem: Gebe Wistar albino sıçanlar rastgele dört kafese ayrıldı; kontrol grubu (müzik yok), klasik müzik grubu (D Major'da Canon / Johann Pachelbel, 60 dB), geleneksel Sufi müzik grubu (Whirling Derwish / Omar Faruk Tekbilek, 30 dB) ve metal müzik grubu (In Your Face/ Children of Bodom, 120 dB). Her müzik grubundaki anneler ve yavrular, hamileliğin 10. gününden doğumdan sonra 21. güne kadar 1 saat / gün kendi müzik türlerine maruz bırakıldılar.

Bulgular: Kuyruktan asma testi sonuçlarına göre klasik müzik grubunda depresyon düzeyini gösteren hareketsizliğin kontrol grubuna göre arttığı gözlenmiştir. Hormonal düzeyde, sadece serum ACTH seviyelerinde önemli değişiklikler elde edilmiştir. Bu değer kontrol grubuna göre klasik müzik grubunda artarken, tasavvuf müzik grubunda azalmıştır. Ayrıca metal müzik grubunda kontrol grubuna göre oksidatif stres endeksinde belirgin bir artış saptanmıştır.

Sonuç: Hamilelik sırasında dinlenen müziğin ses yoğunluğu, yavruların ileri yaşamlarındaki stres ve depresyon düzeyinde hayati önem taşımaktadır.

Anahtar kelimeler: Hipotalamik-hipofiz-adrenal (HPA) ekseni, perinatal müzik, depresyon benzeri davranış, paratiroid hormone (PTH), oksidatif stres.

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INTRODUCTION

Stress is a condition that disrupts homeostasis of the living organisms at the cellular, endocrinological, and behavioral levels[1]. The hypothalamic-pituitary-adrenal (HPA) axis is a central stress response system. Activation of HPA axis causes to release corticotropin-releasing hormone (CRH) that stimulates the secretion of adrenocorticotropic hormone (ACTH)[2]. In response, ACTH induces the synthesis and secretion of glucocorticoids (corticosterone (CORT) in rodents) from the adrenal cortex into the blood circulation[2,3]. Adaptive feedback mechanisms against to stress was stimulated by CORT-mediated activation of specific receptors[4]. Both a decrement in the intestinal calcium absorption and kidney calcium reabsorption by increasing parathormone/parathyroid hormone (PTH) secretion are among these feedback effects countered by the systemic effect of CORT[5]. In a previous study, PTH was considered a candidate for "stress" hormone because there was a correlation between an alteration in serum calcium level and PTH level of parathyroidectomized male rats after confinement / ultra-high frequency stress[6]. In addition, we have recently found that PTH levels were shown to negatively correlate with plasma CORT levels in rats received acute restraint stress[7].

Musical stimuli might have influences on cognitive and emotional components of the stress response in both humans and animals. According to the physiological effects of music on organisms, the parameters that help to determine whether a musical piece has arousing or relaxing effects were determined[8]. Several experimental studies showed that music exposure improved the ability of spatial tasks, increased neuroplasticity, reduced anxiety, lowered blood pressure, and increased immune function[9-14]. On the other hand, most studies investigating the effects of different types of music yielded different results because the musical factors like tone, harmony, or melody can be important in exerting its effects on the body of the living organism[15,16].

In the light of aforementioned evidence, our previous findings on the possible role of PTH against the stress response have been shifted our attention to whether musical stimuli have an effect on PTH signaling associated with the HPA axis. Due to the limited studies in literature consisting the effects of music on stress-induced hormones along with PTH, in this study, we hypothesized to investigate the long-term behavioral and molecular effects of different pieces of music exposure on rats through the measurements of serum hormones level of ACTH, CORT, PTH and serum level of oxidative stress index.

MATERIALS AND METHODS

All procedures were designed in accordance with generally accepted ethical standards for animal experimentation and the guidelines established by National Institutes of Health for the care and use of laboratory animals and the local scientific Ethical Committee of Bezmialem Vakif University (Approval date:29/01/2015, Approval number: 2015/30).

Animals and music exposure

Adult female and male Wistar albino rats were housed under standard (21°C; 12-hour light/dark cycle) and stress-free environmental conditions having free access to food and water. Female rats were individually placed in transparent Plexiglas cages, and one male rat was placed for each female cage for mating. Until day 10, female rats were controlled for presence of vaginal plug as an evidence of fertilization. The day of existence of vaginal plug was admitted as gestational day 0 (GD0)[17]. In GD0, pregnant female rats were randomly divided into four cages; control group (no music exposure) (n=3), classical (Canon in D Major/ Johann Pachelbel, 60 dB) (n=4), traditional Sufi (Whirling Derwish/ Omar Faruk Tekbilek, 30 dB) (n=4), and rock (In Your Face/ Children of Bodom, 120 dB) (n=4) music groups. Dams (n=12) and pups (n=34) in each music groups listened to their own music one hour per day from GD10 to postnatal day 21. The dams (n=3) and the pups (n=12) in the control group stayed undisturbed in their home cage.

Measures

Tail suspension test (TST)

All animals were subjected to tail suspension test in order to measure despair in rats. A horizontal bar was put to a place 50 cm above from the ground. In the experimental procedure, rat was placed to the bar from their tail by adhesive tape. The time of being immobile was measured for a 5-minute testing period. The observers were blinded to the groups.

Enzyme-linked immunosorbent assay

The animals were decapitated when the behavioral

experiment was completed. Heart blood samples of all rats were collected into serum separator tubes immediately after sacrification. Blood serum was obtained by centrifugation at 3,500 rpm for 10 minutes, and stored at -80°C. Serum levels of ACTH (Intra assay CV%: 10 sensitivity: 2.49 ng/L, Shanghai YeHua Biological Technology Co., Ltd., China), CORT (Intra assay CV%:5 sensitivity: ~0.3 ng/ml, Abcam, UK), and iPTH (Intra assay CV%: 10 sensitivity: 0.51 ng/L, Shanghai YeHua Biological Technology Co., Ltd., China) in all groups were measured using commercially available ELISA kits according to the manufacturer's instructions.

Measurement of total antioxidant and oxidant status

The total antioxidant status (TAS) and the total oxidant status (TOS) of serum samples were determined spectrophotometrically by a microplate reader (Thermo Scientific, MultiSkan GO Microplate Spectrophotometer). Briefly, in the measurement of TAS and TOS, the synthesized hydroxyl radical and oxidized molecules, were measured after incubation with prochromogen solution (Rel Assay Diagnostics, #RL0024, #RL0017, Gaziantep/TURKEY). Data were determined at 660 nm for TAS and at 530 nm for TOS using a microplate reader (MultiskanTM GO, Thermo Fisher Scientific, USA). Oxidative stress index (OSI) was calculated from TAS and TOS values for each sample. OSI was calculated using the following formula:

OSI (arbitrary units) = [((TOS)/(TAS*1000)) ×100][18].

Statistical analysis

All data were presented as mean ± S.E.M. Statistical differences for immobility time in tail suspension test, levels of both hormone and oxidative stress among four music groups were analyzed by One-Way ANOVA test (treatment as independent factor) (SPSS for Windows, version 18.0, Chicago, IL, USA). Fisher's Least significant difference (LSD) results were evaluated for pairwise comparison. $p<0.05$ was considered as statistically significant.

RESULTS

The depression-like behavior was evaluated by TST (Figure 1). According to the One-way ANOVA results, there was a significant treatment effect among groups ($F_{(3:45)}=5.855$, $p=0.002$). TST revealed that immobility duration in rats which were exposed to classical music was significantly longer than that of the other groups (the rock music group ($p=0.041$), the sufi music group ($p=0.001$), and the control group ($p=0.002$)). However, compared to the control group, the level of depression-like behavior was not affected in the both rock and sufi music group ($p > 0.05$) (Figure 1).

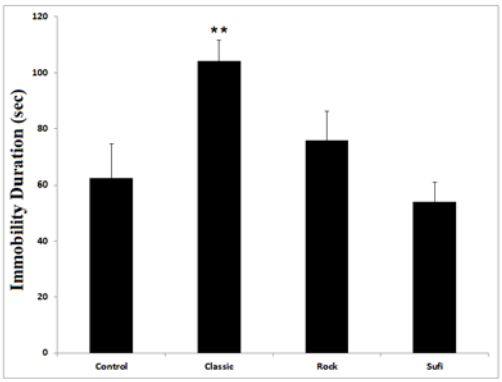

Figure 1. Effect of music on depressive like behavior in 30-day old rats.

The immobility durations of rats in the Control, Classic, Rock, and Sufi groups. The degree of significance was denoted as * for $p \leq 0.05$. Error bars indicate SEM (standard error of mean)

Music induced changes in the levels of serum ACTH, CORT, and iPTH were measured by ELISA method (Figure 2). There were statistically remarkable differences in serum ACTH levels among groups ($F_{(3:38)}= 9.016$, $p\leq0.001$). Serum levels of ACTH in rats of the classic music group was significantly higher than that of the control level ($p=0.045$). In addition, the level of ACTH was significantly lowered in the sufi music group compared to the control group ($p=0.008$) (Figure 2A). However, serum CORT levels did not change in response to the exposure of different music types ($F_{(3:44)}=0.286$, $p=0.835$) (Figure 2B). Similarly, there was no change in the serum iPTH levels among groups ($F_{(3:39)}=0.698$, $p=0.559$) (Figure 2C).

According to the One-way ANOVA, the perinatal music exposure did not change the TAS levels ($F_{(3:36)}=0.745$, $p=0.533$) (Figure 3A). On the other hand, the TOS levels of rats were significantly affected from the perinatal music exposure ($F_{(3:36)}=6.279$, $p=0.002$). According to the post hoc analysis, the levels of TOS in the rock music group was significantly higher than the TOS levels of the control group ($p\leq0.001$) (Figure 3B). In addition, TOS levels in the rock music group significantly increased compared to that of the classic group ($p=0.002$) and sufi group ($p=0.004$)

(Figure 3B). Furthermore, it was recorded that the OSI levels of rats was also significantly altered in response to the perinatal music exposure ($F_{(3:35)}$=6.174, p=0.002). In parallel to the TOS levels, the OSI values in the rock music group was significantly higher than the that of the other groups (the control group ($p \leq 0.001$), the classic music group (p=0.002), and the sufi music group (p=0.026)) (Figure 3C).

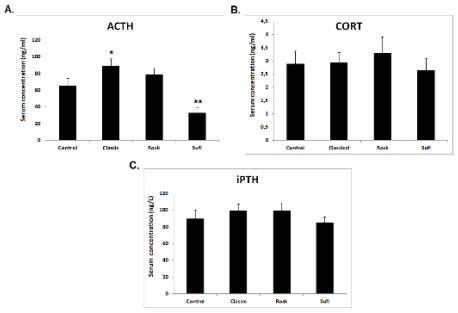

Figure 2. Effect of music on serum levels of A) Adrenocorticotropic hormone (ACTH), B) Corticosterone (CORT), C) Parathormone (iPTH) hormones in 30-day old rats in the Control, Classic, Rock, and Sufi groups.

The degree of significance was denoted as * for $p \leq 0.05$. Error bars indicate SEM (standard error of mean).

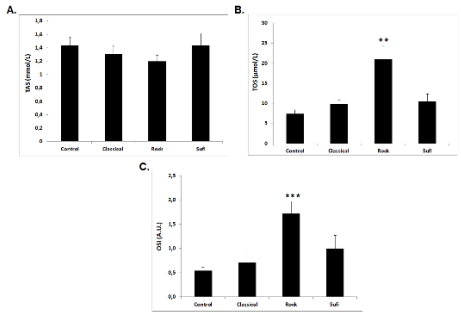

Figure 3. Effect of music on serum level of A) Total antioxidant status (TAS) B) Total oxidant status (TOS) C) Oxidative stress index (OSI) in 30-day old rat in the Control, Classic, Rock, and Sufi groups.

The degree of significance was denoted as * for $p \leq 0.05$. Error bars indicate SEM (standard error of mean).

DISCUSSION

In the present study, we explored the effects of different music types exposure on rats during their perinatal period on the alterations in the depression-like behavior in relation with the expression of HPA axis hormones and the level of oxidative stress.

Interestingly, we observed a significant increase in the depression level of the rats which were exposed to classical music during their perinatal period. In a study, sub-chronic exposure (100 Db; 4h/day for 15 days) to noise produced increase in immobility time indicating a depression like behavior in rats [19]. However, there are also previous studies showing that music can ameliorate depression-like behavior in experimental animal[20]. On the other hand, they observed that depressive behavior had opposite levels at the juvenile age and at the adult age [20]. In addition, most of the studies which investigated the effects of classical music showed an amelioration on the structure of brain cells and neurochemistry following an improved behavior like enhanced spatial memory or decreased anxiety. In parallel to the increase in the depression, the level of ACTH also increased in the rats that exposed to the classical music during their perinatal period while there was no change in the CORT and PTH levels which are related with the animals' stress level. In another study, when animals were exposed to Mozart's music, their anxiety behavior reversed, and their ACTH levels reduced after application of stress[21]. Although, it is well known that music could sound differently to rats and they might perceive a different sound, our contrary results to the literature pointed that the classic music might have been perceived as noise, because noise stress activated HPA axis[22] and depression-like behavior[19]. The reason why rats perceived classical music possibly as noise stressor rather than relaxing stimulation in our study might be that classical music could not have been exposed uniformly in order to be adapted by animals[23,24]. On the other hand, it was here evidenced, for the first time, to be lowered ACTH level in rats exposed to more relaxing music which was sufi music (30 dB; 1h/day) with a lower sound pressure. One of the previous studies showed that relaxing music can decrease the ACTH levels while high sound music can increase the levels of ACTH[25].

Noise exposure is one of the stressors that increases oxidative stress. In the both human and animal experiments, it was noted that exposure to noise increases peroxidation of lipids and alters the antioxidant enzyme levels[26]. In an animal study, it was also found that the oxidative stress indicator increased as a result of exposure to a noisy environment[27]. Supporting to these evidences, we observed a significant increase in the oxidative stress level in the rats exposed to the rock music.

To sum up, perinatal exposure of the classical music can increase the stress level of rat pups to produce a depression-like behavior whereas relaxing traditional music can reduce the stress level by decreasing the ACTH in the blood. In addition, the music type that have high sound intensity such as rock music may increase in the oxidative stress which harms the organism in different aspects. Besides, the fact that different hearing frequency of rat results a different perception of music type than human may be an important limitation for our study. Taking all into consideration, the sound intensity of music which is listened during the pregnancy has vital importance in the stress and depression level of offsprings.

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