Effect of Mozart Music on Hippocampal Content of BDNF in Postnatal Rats

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Introduction: It has shown that listening to Mozart music can potentiate spatial tasks in human; and reduce seizure attacks in epileptic patients. A few studies have reported the effects of prenatal plus postpartum exposure of mice to the Mozart music on brain-drived neurotrophic factor (BDNF) in the hippocampus. Here we investigated the effect of postpartum exposure to The Mozart music on BDNF concentration in the hippocampus of rat.

Methods: Thirty male one day old newborn Wistar rats divided randomly in two equal experimental and control groups. Experimental group exposed to slow rhythm Mozart music (Mozart Sonata for two pianos KV 448, 6 hour per day; sound pressure levels, between 80 and 100 dB) for 60 successive days. The control group was kept in separate room with housing conditions like experimental group except music exposure. After 60 days the rats were euthanized and hippocampuses extracted; then the content of BDNF protein was measured using ELISA sandwich method.

Results: Data analysis revealed that rats exposed to Mozart Sonata music had significantly increased BDNF content in the hippocampus as compared to control rats (P±0.01). The concentrations of BDNF were 86.30±2.26 and 94.60 ±6.22 ng/g wet weight in control and music exposure groups respectively.

Discussion: Exposure to the Mozart music early in life can increase the BDNF concentration in the hippocampus in rats.

1. Introduction

Music generation and perception are two brain functions that developed well in humans. These two processes involve many cortical and subcortical structures, including; prefrontal, frontal, sensorimotor, visual, auditory, parahippocampal, and hippocampal cortices and also striatum, cerebellum, and thalamus (Levitin & Tirovolas, 2009; Platel et al., 1997; Tramo, 2001). On the other hand, listening to music also has considerable effects on brain functions, in both cognitive and emotional domains (Baumgartner, Lutz, Schmidt, & Jancke, 2006; Blood, Zatorre, Bermudez, & Evans, 1999; Koelsch, 2009; Samson, Dellacherie, & Platel, 2009; Thaut et al., 2009). There is general

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consensus that music has cardiovascular, respiratory, hormonal and behavioral effects (Kemper & Danhauer, 2005); and music therapy, as a complementary medicine, have been used successfully in some neurological, neuropsychological and cardiovascular disorders (Boso, Politi, Barale, & Enzo, 2006; Hillecke, Nickel, & Bolay, 2005; Kemper & Danhauer, 2005; Koelsch, 2009; Moradipanah, Mohammadi, & Mohammadil, 2009; Samson et al., 2009; Sarkamo et al., 2008; Suda, Morimoto, Obata, Koizumi, & Maki, 2008; Thaut et al., 2009).

The effects of music on brain functions seem to be carried out via the neural circuits in both limbic and neocortical regions of the brain (Levitin & Tirovolas, 2009; Menon & Levitin, 2005). It also has been shown that music can change the pattern of brain electrical activity in electroencephalography recordings (Iwaki, Hayashi, & Hori, 1997; Y. P. Lin, Jung, & Chen, 2009; Overman, Hoge, Dale, Cross, & Chien, 2003; Rideout & Laubach, 1996; Sarnthein et al., 1997; Shaw & Bodner, 1999; Yuan, Liu, Li, Wang, & Liu, 2000). Some studies have shown the effect of music on hippocampal content of brain derived neurotrophic factor (BDNF) in both prenatal plus postpartum and adult exposed animals (Angelucci et al., 2007; Chaudhury & Wadhwa, 2009; Li et al., 2010). BDNF is a growth factor that promotes neurogenesis and structural plasticity in hippocampus (Yamada & Nabeshima, 2003). Regarding the crucial roles of hippocampal formation in cognitive and emotional processing, these findings are important; especially the role of the hippocampus in regulation of hypothalamic control of endocrine and autonomic functions (Bratt et al., 2001).

One of the well known effects of music that introduced to the literature was the effects of Mozart music on cognition (Rauscher, Shaw, & Ky, 1993). It was shown that Mozart music (Sonata for two pianos KV 448) can potentiate spatial tasks in human for a limited time after exposure(Rauscher et al., 1993). After this preliminary report, many studies investigated this effect and their results were controversial (Bangerter & Heath, 2004; Chabris, 1999; Fudin & Lembessis, 2004; Hughes, 2001, 2002; Hughes & Fino, 2000; Jenkins, 2001; Roth & Smith, 2008; Twomey & Esgate, 2002). However, there is a general agreement with the effect of Mozart music KV 448 on brain activity, specially on spatial-temporal functions and electroencephalogram activity(Jenkins, 2001). Earlier studies revealed the effect of Mozart music on seizure episodes in epileptic patients (Hughes, Daaboul, Fino, & Shaw, 1998; Hughes, Fino, & Melyn, 1999; L. C. Lin et al., 2010; L. C. Lin et al., 2011). However, the neurophysiologic mechanisms underlying these effects are not understood.

Previous study by chikahisa et al.(Chikahisa et al., 2006) had shown the effect of Muzart music on BDNF signaling in hippocampus of mice, but the time of exposure was prenatal plus postpartum and the results were decreased BDNF concentration in cortex and no significant change in hippocampus. Regarding the different pattern of BDNF expression during brain development (Silhol, Bonnichon, Rage, & Tapia-Arancibia, 2005) in the current study we investigated the effects of postnatal exposure on hippocampal content of BDNF. It was hypothesized that exposure to Mozart music postnatally would change the content of the hippocampal BDNF.

2. Methods

2.1. Animals

Thirty newborn male Wistar rats were used. One day old rats divided randomly in two equal experimental and control groups. Rats of each group and their mothers (for three weeks) housed in two 40×60 cm clear polycarbonated cages with sawdust bedding and free access to food and water, ad libitum. After 3 weeks pups were separated from their mothers. The temperature was kept about 23±2 °C. Dark/light cycles were 12 hours and lights were on at 6:00 AM. The experiments were according to the rules of ethical committee for animal experiments in Tehran University of Medical Sciences. All efforts were made to minimize the animal pain or discomfort.

2.2. Music Exposure

In order to understand the impacts of music on hippocampal BDNF content we exposed newborn male rats of music group to slow rhythm Mozart music (Mozart Sonata for two pianos KV 448, 6 hour per day; sound pressure levels, between 80 and 100 dB) for 60 consecutive days. Cages were placed at 30 cm distance from the speaker. Since animals are nocturnal, the music was played during the night hours. To avoid sleep disturbances, Music was played continuously for 6 hour starting from 6.00 p.m. to 12.00 p.m. The control group rats were kept in a separate room with similar housing conditions except music exposure.

2.3. BDNF ELISA Assay

After 60 day all 30 rats were sacrificed following an overdose of Isofluran. Hippocampal tissues was ex-

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Figure 1. figure shows the BDNF concentration of the hippocampus in control and experimental (Music-exposed) groups (n: 15/group). Music exposure significantly increased BDNF concentration. Bars represent Mean± SD (nanograms per gram wet weight of hippocampus). (*p < 0.001)

tracted and stored at - 80° C until BDNF protein measurement using ELISA sandwich method. For ELISA procedure hippocampal tissues was homogenized in cold extraction buffer containing 137 mM NaCl, 20 mM Tris (pH 8.0), 1% NP-40, 10% glycerol, 0.75 mg/ml phenyl methyl sulfonyl fluoride, 0.61 mg/ml sodium metavanadate, 0.1 mg/ml aprotinin, and 9.4 µg/ml leupeptin. The homogenates were acidified to pH ≤ 3 with 1N HCl, vortexed and incubated for 15 min at room temperature, followed by neutralization to pH ≈8 with 1N NaOH. Then the homogenates were centrifuged for 10 min at 3500 G, and the supernatant was assayed for BDNF with commercially available sandwich ELISA (R&D Systems).

3. Results

The hippocampal BDNF content in music-exposed and control groups was compared using independent T test. Data analysis revealed that rats exposed to the Mozart Sonata music had significantly increased BDNF content in the hippocampus as compared to control rats [t(28)=4.857, P=0.0001] (Fig.1).The concentration of BDNF (nanograms per gram wet weight of hippocampus) for control group was 86.30±2.26 and for the music-exposed group was 94.60 ±6.22.

4. Discussion

Previous studies have shown the effect of music exposure on BDNF expression in rodents, and the correlation between music-induced BDNF expression and behavioral consequences in mice and rats (Angelucci et al., 2007; Chikahisa et al., 2006; Li et al., 2010). However, there is no study to show the effect of postnatal exposure to the

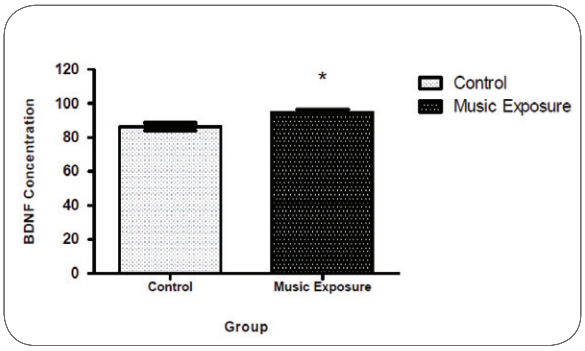

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Figure 2. figure show the BDNF concentration of hippocampus in control and experimental (Music exposure) groups (n: 15/group). Music exposure increased BDNF concentration. Bars represent Mean± SD (nanograms per gram wet weight of hippocampus). (*p < 0.0001)

Mozart music on BDNF expression. This study showed that exposure to the Mozart music from early in life also increases significantly BDNF content in hippocampus in rats. This finding is different from Chikahisa et al. study that had shown no significant change in BDNF concentration of hippocampus in mice exposed prenatally plus postnatally (Chikahisa et al., 2006). The cause may be related to age- dependent pattern of BDNF expression in rat brain (Silhol et al., 2005).

BDNF is one of the downstream molecules that its expression is mainly controlled by cyclic AMP response element binding protein (CREB) following protein kinase A (PKA) activation(Carlezon, Duman, & Nestler, 2005).

Some of monoamines especially dopamine via the activation of D1 like receptors can increase cAMP and consequently activate PKA in neural cells (Nijholt, Blank, Ahi, & Spiess, 2002). The effect of music on dopamine transmission in the brain has been suggested (Menon & Levitin, 2005), There may be a correlation between increased dopamine transmission in one hand and increased BDNF expression in hippocampus following Mozart music exposure on the other hand. However more studies are needed to clarify this hypothesis.

Considering the crucial role of BDNF in neural survival, differentiation and organization during development and even in adult brain, The observed effect of the Mozart music on BDNF in hipocampus is important. One of the well known effects of BDNF is its role in synaptic formation and activity, especially in hippocampus (Lee & Son, 2009; Monteggia et al., 2004; Rossi et al., 2006), where it acts as a booster of learning and memory process (Arancio & Chao, 2007). Previous studies have shown the effects of Mozart music on learning and memory and spatial-temporal tasks (Aoun, Jones, Shaw, & Bodner, 2005; Bodner, Muftuler, Nalcioglu, & Shaw, 2001; Johnson, Cotman, Tasaki, & Shaw, 1998; Lints & Gadbois, 2003; Rauscher, Shaw, & Ky, 1995). Although not assessed in this study, it seems that increasing BDNF expression in hippocampus may have a role in memory related tasks.

The correlation between BDNF in hippocampus and seizure in epileptic patients has been studied (Hughes et al., 1998; Hughes et al., 1999; Jenkins, 2001; L. C. Lin et al., 2010; L. C. Lin et al., 2011). It also has been shown that BDNF have antiepileptic properties (Kuramoto et al., 2011). Increased BDNF in the hippocampus following the Mozart music exposure may be beneficial for epileptic.

The effect of music on mood disorders is well known and music therapy as a complementary medicine has been implicated in the treatment of depression and anxiety (Hsu & Lai, 2004; A. Maratos, Crawford, & Procter, ; A. S. Maratos, Gold, Wang, & Crawford, 2008; Moradipanah et al., 2009; "Music therapy may help depression," 2008). It has been shown that BDNF concentrations of ventral striatum and hippocampus in depression were also changed (Angelucci, Brene, & Mathe, 2005; Covington, Vialou, & Nestler). It is possible that increased BDNF concentration in hippocampus following the Mozart music exposure may also have beneficial effects in depression and other mental disorders.

In conclusion, exposure to Mozart music early in life can increase the BDNF concentration in the hippocampus in rat. This finding may have a correlation with known effects of Mozart music on spatial-temporal tasks and epilepsy; and suggests the study of possible beneficial effect of Mozart music on mood disorders.

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