Research on the Frontal lobe Activation Effect of Music Therapy — Effect of Listening Music on Frontal lobe Activation by Using Near-Infrared Spectroscopy —

Mayumi IKEUCHI¹,²*, Sachiko MORI², Hiromi JONO², Tomoko KUTSUZAWA²

¹ Department of Health Management, Tokai University
² Department of Nursing, Tokai University School of Health Sciences

[ABSTRACT]
This study used topographic near-infrared spectroscopy (NIRS) to characterize frontal lobe activation while individuals actively or passively listened to exciting or calm music. Participants were 22 healthy female volunteers (mean age, 21 ± 4.1 years). Initial analysis showed that oxy-Hb significantly decreased in many channels when subjects listened to calm music. In contrast, oxy-Hb significantly increased when subjects listened to lively music. In addition, after listening to calm music, cortisol, α-amylase, and immunoglobulin A significantly decreased. A subsequent analysis showed that oxy-Hb significantly increased when subjects listened to music while clapping to its rhythm compared with when subjects listened to music only. Our study suggests that calm music reduces levels of human stress and enables effective relaxation. In addition, our data suggests that clapping to the rhythm of music increases brain activation. Therefore, active music therapy may be more effective than passive music therapy with respect to brain activation. Such active therapy (i.e., playing rather than listening to music) may improve functional and psychological status, and cooperative abilities.

[Key words]
NIRS, Frontal lobe, exciting music and calm music, Active and passive musical listening, Music therapy

INTRODUCTION
Music in human culture produces pleasure and has reward value. The experience of music includes listening, seeing, feeling, memorizing, moving to music, and so on. When we experience music, various emotions and associated physical reactions may be engendered.

Accordingly, music therapy has been increasingly used in various clinical settings, such as rehabilitation, psychiatry, pediatrics, hospice care, and alternative and complementary medicine, to reduce stress and/or pain. By listening to music, patients with...
dementia and Alzheimer’s disease have shown improvements in categorical word fluency, memory for lyrics, and working memory. As described above, music therapy is used in medical and welfare fields, and a number of staff have commented how effective music therapy has been, but most of these are subjective reports. Therefore, there is not enough medical evidence regarding the effect of music therapy. For music therapy to be accepted as an alternative or complementary therapy, proof of its efficacy is required, using objective as well as subjective assessments. However, few studies have sought objective data regarding music therapy. A possible reason for this deficit is that music therapy includes numerous factors, which interact with each other in determining the therapy’s effectiveness. Such effects are difficult to evaluate objectively. In addition, music varies greatly in terms of genre, type, rhythm, and tempo, and listener-related factors can greatly affect outcomes. The latter includes psychological and physical aspects, such as age, a memory, prejudice, and musical taste. Moreover, music therapy may be passive or active. Passive music therapy is used to reduce stress, whereas active music therapy is used to energize and engender emotions, and improve functioning. Further, the emotions experienced when listening to music vary from person to person. When investigating the effect of music on emotions, it is necessary to consider separately the felt and the perceived emotion.

Brain imaging studies have been performed using functional magnetic resonance imaging (fMRI), xenon contrast computed tomography (Xe-CT), and positron emission tomography (PET). Recently, the development of near-infrared spectroscopy (NIRS) has enabled noninvasive, bedside measurements of regional cerebral blood volume changes in terms of the relative concentrations of oxy-hemoglobin (oxy-Hb), deoxy-hemoglobin (deoxy-Hb), and total hemoglobin (total-Hb), with high time resolution. NIRS has been used in a variety of studies of cognition, in fields including sensorimotor functioning, visual perception, language, development, and clinical studies. Here, we used a topographic NIRS system to investigate hemodynamic responses in the prefrontal area while listening to music. The purpose of this study is to examine the frontal lobe activation effect of music therapy on the human body and to make use of the results for nursing.

MATERIALS AND METHODS

1. Subjects
The volunteers were recruited via posters placed in various locations around Tokai University. Twenty-four healthy, right-handed adult women, aged 20–38 years old (mean age±SD, 21 ± 4.1 years) participated in this study. Informed consent was obtained prior to conducting the study, in compliance with the Declaration of Helsinki. The Ethical Review Board of Tokai University approved this study (No. 13-10).

2. Musical Stimuli
We selected four musical stimuli by asking 50 students to complete a questionnaire. Two exciting pieces of music were Japanese pop (Gakuentengoku) and a cinematic theme (Indiana Jones theme), whereas two selected pieces of calm music were classical (G line of Aria) and a traditional Japanese song (Whisper Little Stream). In addition, we included an environmental sound (the murmur of a brook).

Prior to the NIRS measurements, all subjects listened to each of the musical stimuli. The subjects sat in comfortable chairs and listened to the music using earphones. The listening room was soundproofed and held at 24°C with 45% humidity. The subjects were instructed to focus on a point in front of them while listening to the music.

3. Near-infrared Spectroscopy
NIRS measurements were performed using a multichannel instrument (FOIRE-3000, Shimadzu Co., Kyoto Japan). The system consists of an array of optodes comprising 8 light source and 8 detector fibers arranged for 22-channel simultaneous recording. Three wavelengths were used to determine hemoglobin concentrations (780, 805, and 830 nm). The system can detect changes in concentrations of oxygenated hemoglobin (oxy-Hb), deoxygenated hemoglobin (deoxy-Hb), and total hemoglobin in cortical regions of the brain. Inter-optode distances were set at 3.0 cm. The alignment of each fiber and channel are indicated in Figure 1. The optodes were brought firmly into contact with the head using a holder. The probes were placed on the subject’s frontal region and measured changes in the relative concentration of hemoglobin at 22 measurement points in a 14 × 11-cm area, with the lowest probe positioned along the Fp1-Fp2 line, according to the international 10/20 system of electro-encephalography (EEG), which was used for...
Influence of Music on Frontal lobe optode positioning. This optode array can create two-dimensional 14 × 11-cm Hb concentration images (i.e., topographies).

4. Study Design

All subjects were carried Experiment 1, 2 and 3. The study consisted of three experiments, each of which included the assessment of changes in oxy-Hb. Experiment 1 was a comparison of exciting and calm music. The study block design is shown in Figure 2. In Task A (3 min) the subject listened to calm music, and in Task B (3 min) the subject listened to exciting music. Tasks A and B were presented alternately (ABABA), using computer software. The subject was instructed to concentrate on listening to the A or B music.

Experiment 2 consisted of conditions comprising no sound, environmental sound, exciting music, and calm music. The study design is shown in Figure 3. In Task A (60 s), the subject was played no sounds. In Task B (60 s), the subject listened to environmental sounds. In Task C (60 s), the subject listened to calm music or exciting music.

Experiment 3 consisted of a comparison of active and passive musical listening. The study block design is shown in Figure 4. In Task A (20 s), the subject listened to exciting music. In Task B (20 s), the subject listened to exciting music while clapping her hands to the rhythm of the music. Tasks A B were alternated (ABABA), with the experimenter gesturing when the task changed.

Fig.1 Optical fiber alignment and channels. Circles show sources and detectors, and white boxes show channels, with numbers indicated.

Fig.2 NIRS experimental paradigm (Experiment 1). The comparative analysis between exciting music and calm music.

Fig.3 NIRS experimental paradigm (Experiment 2). The comparative analysis between no sound, environmental sound, exciting music and calm music.
5. Saliva Sampling

We collected saliva samples 4 times (Fig. 3), using a well-described technique. In short, a cotton-based neutral swab was used. Teeth were not brushed and no food was eaten within 2 hours of the sampling. Thereafter, saliva samples were centrifuged and frozen at -20 to -80°C until assayed. All samples were analyzed concurrently using commercial kits (Salimetrics Europe, Ltd. UK) to assess cortisol, α-amylase, and immunoglobulin A.

6. Data analyses

Here, we primarily used the oxy-Hb results because we consider oxy-Hb to be the most sensitive index of the brain hemodynamic response [9, 16, 20]. We calculated activation indices (AI) as follows for Experiments 1 and 3:

\[
AI = \frac{\text{average of task B} - \text{average of task A}}{\text{average of task B} + \text{average of task A}} \times 100
\]

Whereas the index for Experiment 2 was

\[
AI = \frac{\text{average of task B [environmental music]} - \text{average of task A [no sound]}}{\text{average of task B} + \text{average of task A}} \times 100
\]

and

\[
AI = \frac{\text{average of task C [exciting music or calm music]} - \text{average of task A [environmental sounds]}}{\text{average of task C} + \text{average of task A}} \times 100
\]

AI becomes zero when there is no difference between Task A and Task B or between Task B and Task C. The significance of hemodynamic changes was determined using repeated measures analysis of variance (ANOVA) and Bonferroni-corrected post-hoc tests. Comparisons of salivary cortisol, α-amylase, and immunoglobulin A between before and after listening to music were assessed using t-tests. We considered \( p < 0.05 \) to be statistically significant.

RESULTS

1. Experiment 1

The analysis of Experiment 1 consisted of a comparison of exciting and calm music. Figure 5 shows AI calculated using the full set of oxy-Hb data for the block design. When the subjects listened to exciting music, oxy-Hb increased in all channels. Significant oxy-Hb increases in channel numbers 8, 9, 13, 18, 19, 20, 21, and 22 were observed when subjects listened to exciting music as compared to calm music.

2. Experiment 2

Experiment 2 compared responses to no sound, environmental sound, exciting music, and calm music. Figure 6 shows AI values calculated using Task B (environmental music) responses and Task A (no sound) responses. Significantly decreased oxy-Hb was found in channel numbers 6, 19, 20, and 21 when subjects listened to environmental sound. However, there was a less AI change.

Figure 7 shows AI for Task C (exciting music or calm music) versus Task A (no sound). Significantly decreased oxy-Hb occurred in many channels when subjects listened to calm music. In contrast, oxy-Hb significantly increased when subjects listened to exciting music.

Figure 8 shows AI calculated for Task C (exciting music or calm music) versus Task B (environmental music). Similar to the above results, oxy-Hb significantly decreased in many channels when subjects listened to calm music, and significantly increased when subjects listened to exciting music.

Figure 9 shows cortisol, α-amylase, and immunoglobulin A values. After listening to calm music, cortisol, α-amylase, and immunoglobulin A significantly decreased. After listening to exciting music, the salivary data tended toward lower values as compared to that before listening, but the difference was not statistically significant.
Influence of Music on Frontal lobe

Fig. 5 The comparative analysis between exciting music and calm music (Experiment 1).
The data expressed as an activation index (AI), AI = (average of task B: exciting music) – (average of task A: calm music) / (average of task B + average of task A) × 100. Each value represents mean ±SD. *, p < 0.05.
In the upper right figure, the black circle showed the channels which Oxy-Hb increased significantly.

Fig. 6 The comparative analysis between no sound and environmental sound.
The data expressed as an activation index (AI), AI = (average of task B: environmental sound) – (average of task A: no sound) / (average of task B + average of task A) × 100. Each value represents mean ±SD. *, p < 0.05.
In the upper right figure, the white circle showed the channels which Oxy-Hb decreased significantly.
Fig. 7 The comparative analysis between without sound vs exciting music or calm music.

The data expressed as an activation index (AI).

\[
AI = \frac{\text{average of task B: exciting music or calm music} - \text{average of task A: without sound}}{\text{average of task B} + \text{average of task A}} \times 100
\]

Each value represents mean ±SD. *, p < 0.05.

In the right upper figure, white circle showed the channels which Oxy-Hb decreased significantly. In right lower figure, the black circle showed the channels which Oxy-Hb increased significantly.

Fig. 8 The comparative analysis between environmental sound vs exciting music or calm music.

The data expressed as an activation index (AI).

\[
AI = \frac{\text{average of task B: exciting music or calm music} - \text{average of task A: environmental}}{\text{average of task B} + \text{average of task A}} \times 100
\]

Each value represents mean ±SD. *, p < 0.05.

In the right upper figure, white circle showed the channels which Oxy-Hb decreased significantly. In right lower figure, the black circle showed the channels which Oxy-Hb increased significantly.
3. Experiment 3
Experiment 3 compared active and passive musical listening. Figure 10 shows AI for Task B (listening to exciting music plus clapping) versus Task A (only listening to exciting music). When subjects listened to music while clapping oxy-Hb was significantly increased as compared to that when subjects only listened to the music.

DISCUSSION
We used NIRS to investigate the hemodynamic response in prefrontal areas while listening to music. To the best of our knowledge, this is the first NIRS study evaluating brain activation for exciting music versus calm music, and for active versus passive musical listening.

We first compared exciting music and calm music using a block design. When the subjects listened to exciting music, oxy-Hb increased in all channels. Activity in the left prefrontal cortex (channel numbers 8, 9, 13, 18, 19, 20, 21, and 22) was significantly increased when subjects listened to exciting music as compared to calm music (Fig. 5).

In our second experiment, we investigated environmental sounds and without sound. Although oxy-Hb in some channels significantly decreased when subjects listened to environmental sounds, there was a less AI change. In general, in order to relax

Fig.9 Effects of salivary cortisol, α-amylase and Immunogloblin A on listening music.
Each value represents mean ± SD. **, p < 0.01 before vs after music listening.

Fig.10 The comparative analysis between active and passive musical listening.
The data expressed as an activation index (AI). AI = (average of task B: listening to exciting music plus hand clapping) – average of task A: only listening to exciting music) / (average of task B + average of task A) × 100. Each value represents mean ±SD. *, p < 0.05.
In the right figure, the black circle showed the channels which Oxy-Hb increased significantly.
many people use environmental music. In previous research, the total Hb and oxy-Hb concentrations were significantly lower when forest scenery was viewed than when urban scenery was viewed, which indicates that forest environments have physiological and psychological relaxing effects compared to urban environments. In the current study, effects were not as pronounced when listening to environmental music. This shows that the brain activity was not suppressed in without sound period. Additionally, subjects listening to the music for only a short period of time.

Further, we compared exciting music, calm music, no sound conditions. Significant decreases in oxy-Hb occurred in many channels when subjects listened to calm music. In contrast, oxy-Hb significantly increased when subjects listened to exciting music (Fig. 7). A lower concentration of total Hb and oxy-Hb indicates that the quantity of oxygen transmitted to the prefrontal cortex tissue is small. That is, prefrontal cortex activity is relatively low while listening to calm music versus exciting music. This result is consistent with a previous study that showed low total-Hb concentration indicates a depression of brain functions. In addition, our results showed that after listening to calm music, cortisol, α-amylase, and immunoglobulin A were significantly decreased as compared to before. Many previous studies have shown that lower levels of stress results in lower concentrations of cortisol, α-amylase, and immunoglobulin A. When listening to exciting music, salivary cortisol, α-amylase, and immunoglobulin A were not significantly altered.

Therefore, our results support the interpretation that calm music reduces human stress levels and enables effective relaxation. Neuroimaging studies have noted a relationship between brain activity in response to music and emotion. Specifically, when subjects assessed the emotions they felt while listening to music, activity occurred in the prefrontal area, ventral striatum, midbrain, and amygdala. Our result that oxy-Hb significantly increased when subjects listened exciting music as compared to calm music suggests that the former may have some positive emotional effects.

In our third experiment, we compared active and passive musical listening. We investigated listening to exciting music plus clapping to its rhythm and listening to exciting music without clapping. The oxy-Hb changed to a greater extent when subjects listened to music while clapping as compared to listening to music only. In a previous study, we used to NIRS to investigate the effect of clapping on brain activation. The premotor cortex was activated, but the prefrontal cortex area was not. However, in the current study, clapping hands in time to the music activated the prefrontal cortex. This suggests that although hand clapping per se does not activate the prefrontal cortex, hand clapping to musical rhythm leads to brain activation of the attention related region. Therefore, active music therapy may more effective than passive music therapy, with respect to brain activation.

Suto et al. reported that oxy-Hb elevations in patients with major depressive disorder were smaller than in control subjects during a word fluency task. Most previous NIRS studies of such patients have used finger tapping and word fluency tasks. Such studies have reported decreased oxy-Hb activation in depression, consistent with decreased cerebral blood flow and metabolism in the dorsolateral prefrontal cortex in the resting state. This has been observed in functional neuroimaging studies using other methodologies, such as PET, SPECT, and fMRI. Moreover, the decreased cerebral blood flow activation during the cognitive task in these studies indicates that the cerebral cortex of patients with depression cannot obtain a sufficient increase in blood supply to compensate for increased oxygen consumption, unlike healthy control subjects. The continued lack of adequate blood supply could result in a decrease of neuronal activity in the cerebral cortex, resulting in the diagnosis of depression. In general, oxy-Hb activation in patients with depression and dementia appears suppressed relative to healthy people. Satoh et al. reported that physical exercise combined with music produced more positive effects on cognitive function in elderly people than exercise alone. In the current results, oxy-Hb changed to a greater extent when subjects listened to music while clapping versus when subjects listened to the music without clapping. In our previous studies, the following factors affected the change of oxy-Hb in the frontal lobe. (1) whether it's their favorite music, (2) music connected to memories, (3) whether they are enjoying the music, in addition, whether they are listening to the music passively or actively concentrating. The strongest response was experienced when listeners engaged with the music by clapping, dancing, moving their body etc. In many cases music encouraged physical exercise. Rehabilitation of patients requires more “active” therapies like this. Music therapy has been used in a variety of ways improve the functioning of those with
depression, dementia, and intractable neurological diseases. With respect to such diseases, the results we report here suggest that active music therapy may be more effective than passive music therapy.

This study has several limitations. First, the NIRS technique only permits one to measure hemodynamic changes on the cortical surface. A major criticism of prefrontal cortex NIRS data is that task-evoked changes may occur due to forehead skin perfusion. As such, one must interpret prefrontal cortex activity with caution. Second, activation was examined only in the frontal lobe but not in other cerebral cortices or deep brain structures. Third, this study used a block design, which does not permit the analysis of events as they would be experienced in real life. Event-related paradigms exist, but their use in NIRS studies is currently limited. Finally, we investigated a modest number of subjects. Further study with a large subject population is advised.

**CONCLUSION**

We compared exciting music, calm music and no sound conditions. Significant decreases in oxy-Hb occurred in many channels when subjects listened to calm music. In contrast, oxy-Hb significantly increased when subjects listened to exciting music. In addition, after listening to calm music, salivary cortisol, α-amylase, and immunoglobulin A significantly decreased. Results suggest that calm music reduces levels of human stress and enables effective relaxation. In addition, hand clapping by itself does not improve brain activation, but clapping to a musical rhythm leads to brain activation. Therefore, active music therapy may be more effective than passive music therapy for brain activation. Rehabilitation of patients requires more “active” therapies. Along with improvement of functional status and mental status, the patients’ ability to cooperate increases and they may participate in more active therapies (playing rather than listening to music). Furthermore, it is necessary to separate these types of exciting music and calm music in addition to separating active and passive music therapy. We also need to select the music therapy program according to the condition of the patient.

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要 旨

音楽療法の脳機能に関する研究
―近赤外分光法を用いた音楽聴取時の脳活動の評価―

池内眞弓1,2, 森 祥子2, 城生弘美2, 首澤智子2

1 東海大学健康学部 健康マネジメント学科
2 東海大学健康科学部 看護学科

本研究は、近赤外分光光度計を用い能動的音楽聴取と受動的音楽聴取および活性曲と鎮静曲聴取時の前頭葉のOxy-Hbの違いを評価した。健常女性（平均年齢22±4.1）22名を対象とした。鎮静曲聴取時、前頭葉のOxy-Hbは、多くのチャンネルで有意に低下し、活性曲聴取時はOxy-Hbは有意に増加した。また鎮静曲聴取後の唾液中コルチゾール、α-アミラーゼ、IgAは聴取前と比較し、有意に低下した。さらに能動的音楽聴取（音楽に合わせリズムを取り拍手をする）と受動的音楽聴取（音楽聴取のみ）時のOxy-Hbの違いを評価した。能動的音楽聴取時は、受動的音楽聴取時と比較し、Oxy-Hbが有意に増加した。以上の結果より、鎮静曲聴取は、ストレスの低減およびリラクス効果を有する事が示唆された。また能動的音楽聴取は受動的音楽聴取時と比較し前頭葉の賦活化が認められた。音楽聴取のみよりも音楽に合わせリズムを取り身体を動かす事により脳機能の活性化や心理状態の改善などに繋がる事が示唆された。

キーワード：NIRS、前頭葉、活性曲と鎮静曲、能動的および受動的音楽聴取、音楽療法

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