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Abstract: A number of studies have indicated that relaxing and pleasant melodies are useful for the treatment of patients with psychiatric disorders, including schizophrenia, depression, and dementia. However, few studies have investigated what constitutive elements of the music had an effect on brain activity. As Canon chord progression is one of critical elements for pleasant melodies, we sought to examine the effects of Canon chord progression and pitch-shifted Canon chord progression on brain activity using performance on the auditory oddball task during event-related potentials (ERPs) in 30 healthy subjects. Unexpectedly, we found no differences in ERP components between subjects listening to Canon chord progression (n=15) or pitchshifted Canon chord progression (n=15). Next, we divided participants into two groups: those who found the melody pleasant (n=17) and those who did not (n=13), for both Canon chord progression and pitch-shifted Canon chord progression. The average of P300 amplitude was higher at Fz in subjects found the music pleasant versus those finding it unpleasant. Moreover, subjects who found it pleasant exhibited higher motivation scores than those who felt it was unpleasant, whereas listening to Canon chord progression did not matter. These findings suggest that the effects of Canon chord progression on brain activity and motivation depend on subjective feelings, not the chord progression per se.

**Keywords:** music, Canon chord progression, motivation, event-related potential, subjective feelings

## Introduction

Today, music exists in a multitude of different genres around the world and has become indispensable as a manner of enhancing the quality of life of the listeners. Participation in karaoke and vocal music has been utilized as an instrument for eliminating stress and promoting health and, accordingly, music can be considered an important tool for maintaining psychological and physical health. Movies and television dramas differentiate between the use of upbeat and somber music to impart certain impressions to the viewer. In the area of sports, many people have experienced an entire stadium brimming with excitement as a rousing piece of music is played.<sup>1,2</sup> In such ways, music is thought to act strongly upon the psyche of the audience. In medicine, numerous studies have demonstrated the effectiveness of music therapy for mental disorders, including schizophrenia, depression, and dementia.<sup>3-6</sup>

Melodies unanimously considered enjoyable probably do not exist, but melodies that use Canon chord progression are considered to be pleasant by many people. Canon chord progression in the famous work by Johann Pachelbel, considered to be a founding father of the Canon, has the following form:  $D \to A \to Bm \to F\#m \to G \to Bm \to F\#m \to G$ 

Correspondence: Manabu Makinodan Department of Psychiatry, Nara Medical University School of Medicine, 840 Shijocho, Kashihara, Nara 634-8522, Japan Tel +81 744 22 3051 Fax +81 744 22 3854 Email mmm@naramed-u.ac.jp  $D \to G \to A$ , displaying slight periodic movement which is produced by the repeating chord sequence. In the present-day music scene, a variety of derived forms are used based on Canon chord progression. "Let it be," a representative work by the Beatles, also frequently uses the progression  $C \to G \to Am \to F$ . Although it cannot be categorically said that a musical work or melody that everyone would find enjoyable exists, and taking into consideration the fact that Canon chord progression is used in many hit songs, it is conceivable that Canon chord progression could have some direct effect on the brains of the listeners. However, few studies have investigated the neural effects of the constitutive elements of the Canon chord progression.

Event-related potentials (ERPs) are measured by electroencephalography and commonly used as a physiological measure of brain activity, because they are easily and noninvasively recorded. The components of ERPs are defined by positive and negative polarity, latency, region on the scalp, and their relation to experimental variables. Indeed, ERP measurement has enabled the investigation of neurophysiological mechanisms underlying motivation. Motivation is a psychological variable that can be manipulated by using reward to increase the value of a stimulus and the attention allocated to it. In the current study, we investigated the effects of Canon chord progression on physiological brain activity and motivation. We hypothesized that Canon chord progression would increase P300 amplitude and motivation.

### **Methods**

# **Participants**

A group of 30 healthy medical students and interns were recruited as participants from Nara Medical University. The participants consisted of 22 men (mean±SD age, 25.6±3.0 years) and eight women (mean±SD age, 24.4±1.5 years). None of the participants reported a history of neurological disorder, a head injury, a serious medical condition, or a history of psychiatric disorder and substance abuse/dependence. All participants gave written informed consent for participation in the study, which was approved by the ethical committee of Nara Medical University School of Medicine. Participants were randomly assigned and listened to a Canon melody (n=15) or a pitch-shifted Canon melody (n=15) between ERP measurements. All participants were asked if they found the music to be pleasant or unpleasant. The participants were then divided into two groups: those who considered the music pleasant (n=17) and those who did not (n=13).

# Canon chord progression and pitchshifted Canon chord progression

The Canon chord progression and pitch-shifted Canon chord progression were of the form:  $C \to G/B \to Am \to G \to F \to Em \to F \to G$ . In this study, we set up C as the first chord because the key does not matter for the chord progression and the musical scale generally starts with the C chord. Pitch-shifted Canon chord progression was composed of the same sounds shifted by a semitone. Each progression had a duration of approximately 3 minutes. The progressions were played by an electronic device through headphones. All participants listened to each of the progressions twice.

# Intrinsic Motivation Inventory

The Intrinsic Motivation Inventory (IMI) is a questionnaire with several elements that shows qualitative information about the level and content of motivation that participants feel during an intervention. <sup>13,14</sup> Motivation is scored on a 7-point Likert scale ranging from "not at all true" to "very true". A neutral score on the IMI is 4, and a higher score indicates a more positive result in terms of motivation. All participants completed the IMI before and after each progression.

# Visual Analog Scale

The visual analog scale (VAS) is a simple questionnaire about motivation and affect. <sup>15</sup> Participants were instructed to express their motivation on a 10-cm long line ranging from 0 (not motivated at all) to 10 (extremely motivated). All participants completed the VAS before and after each progression.

### **ERPs Task**

We used an NEC Multi Stim II auditory stimulus system (NEC, Tokyo, Japan). We elicited P300 components using an auditory oddball task based on the guidelines for evoked potential measurements. 16 The P300 wave data were analyzed during the period between 200 ms pre-stimulus and 750 ms post-stimulus. Frequent non-target stimuli were presented as 1,000 Hz bursts (P=0.8), and infrequent target stimuli were presented as 2,000 Hz tone bursts (P=0.2). Both types of stimuli were presented for 50 ms at 1.5 s intervals and at an intensity of 80 dB, with rise/fall times of 10 ms. Both stimuli were randomly presented by headphones. All participants were instructed to keep their eyes open, to listen carefully for the target stimuli, and to press a response button as quickly as possible upon hearing each target stimulus. The duration of the auditory oddball task (P300) was 240 s. Infrequent and frequent stimuli were presented 30 and 120 times, respectively. The sample rate was 1,000 Hz.

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We used the same system to elicit mismatch negativity (MMN) components. MMN was analyzed during the period between 50 ms pre-stimulus and 360 ms post-stimulus. Standard stimuli were 1,000 Hz tone bursts (*P*=0.9) and deviant stimuli were 1,100 Hz bursts (*P*=0.1). Each stimulus was presented for 50 ms at 500 ms intervals at 80 dB intensities. Moreover, both stimuli were randomly presented by headphones. The MMN components were recorded while participants read books of their choice without paying particular attention to the auditory stimuli. The duration of the auditory oddball task (MMN) was 250 s. Infrequent and frequent stimuli were presented 50 and 450 times, respectively. The sample rate was 5,000 Hz. ERPs (P300 and MMN) were measured before and after listening to music for all participants.

# Recording and analyses

ERPs were recorded with an MEB 2200 evoked potential measuring system (Nihon Kohden, Tokyo, Japan). Electroencephalography (EEG) was recorded at Fz, Cz, Pz, C3, and C4 positions on the scalp using disk electrodes. The impedance of the electrodes was set at  $\leq 5 \text{ k}\Omega$ , through all electrodes that were re-referenced off-line to the average of two mastoid electrodes. Artifact-free responses to the stimuli were added and averaged after excluding trials with EEG amplitudes ≥100 µV. Trials with artifacts due to muscular activity and complex eye movement were excluded during a first visual inspection of the raw data by an experienced scientific researcher. Finally, data were corrected for eye movement artifacts.<sup>17</sup> To prevent participants from becoming tired, each trial was conducted only once. In relation to P300, we averaged 30 responses to infrequent target stimuli. The P300 was identified as a negative wave with a peak latency occurring between 250 and 550 ms, and its mean latency and amplitude were calculated. Next, in relation to MMN, 450 responses to the frequent standard stimuli and the 50 responses to the infrequent deviant stimuli were averaged separately, and a waveform was calculated as the difference between the averaged waveforms (frequent minus infrequent). MMN was identified from the difference waveform as a negative wave with a peak latency between 100 and 250 ms, and its latency and amplitude were recorded. We have previously reported similar methods for examining ERPs in several psychiatric disorders. 18,19

# Statistical analyses

We conducted a statistical comparison of participant characteristics between the two groups using a Student's *t*-test.

Additionally, differences in whether participants found Canon melody pleasant or unpleasant were analyzed using a Chi-squared test for categorical variables. Moreover, analyses of variance were performed to examine groups (two levels: participants who found the Canon melody pleasant or unpleasant) × ERP measurements (two levels: before and after listening to the Canon melody, regardless of whether it was the conventional and pitch-shifted Canon), and Tukey's post hoc test was used to analyze continuous variables. We used PASW Statistics 18.0 J for Windows (IBM Corp., Armonk, NY, USA) for the statistical analyses. Statistical significance was obtained when *P* value was <0.05.

### Results

# ERPs before and after Canon chord progression or pitch-shifted Canon chord progression

We hypothesized that Canon chord progression leads ERP measurements in a better direction; on the other hand, pitch-shifted Canon chord progression leads ERPs measurements for the worse outcomes. However, we found no differences in the grand average of the MMN and P300 either before or after Canon chord progression and pitch-shifted Canon chord progression (Figures 1 and 2).

# ERPs before and after each melody

We noticed that some participants found Canon chord progression and pitched-shifted Canon chord progression pleasant, whereas others found the melodies unpleasant. Therefore, ERP changes might be, at least in part, due to their preference for each melody. To investigate this issue, we assembled a new experimental plan dividing the participants into two groups: one group included those who found each melody pleasant and the other group included those who found them unpleasant (Figures 3 and 4).

We found that the grand average wave of the P300 amplitude in the group that found each melody pleasant was higher at Fz ( $F_{1,28}$  =5.772, P=0.23) after listening to the melody (Figure 5). We found no differences in the P300 latency and MMN amplitude/latency after listening to the melody compared with baseline.

# Motivation evaluation before and after melody

We found no differences in motivation scores such as IMI and VAS between Canon chord progression and pitch-shifted Canon chord progression. Furthermore, several previous studies reported correlations between the P300 amplitude

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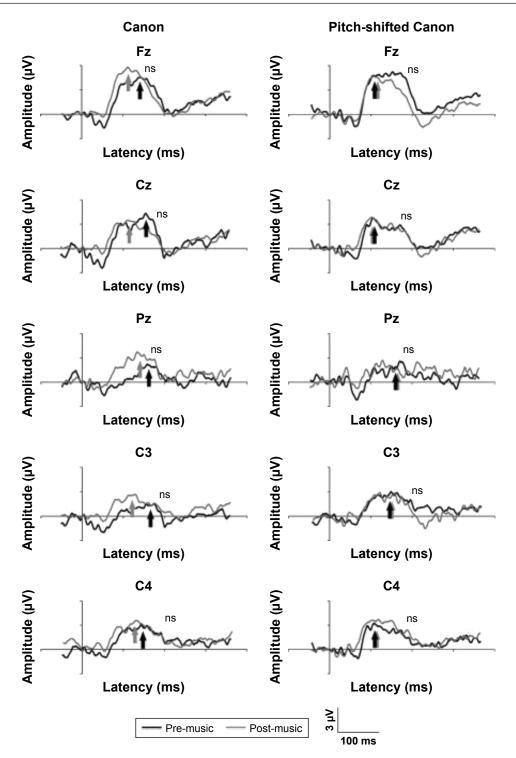


Figure I Grand mean MMN waveforms before and after listening to Canon melody or pitch-shifted Canon melody.

Notes: The left side represents participants listening to Canon melody, whereas the right side represents those listening to pitch-shifted Canon melody. The MMN measured before listening to the melody is represented by the black line, and MMN measured after listening to the melody is represented by the gray line. MMN is indicated by arrows.

Abbreviations: MMN, mismatch negativity; ns, not significant.

and motivation. <sup>10,11</sup> Thus, we considered the possibility that the higher P300 amplitude after participants heard the melody they found pleasant might be related to higher motivation. Therefore, we investigated motivation both before and after

listening to the melody in the two groups, using IMI and VAS. We found that those who found the melody pleasant after listening to the melody exhibited higher changes of IMI total scale relative to those who found it unpleasant

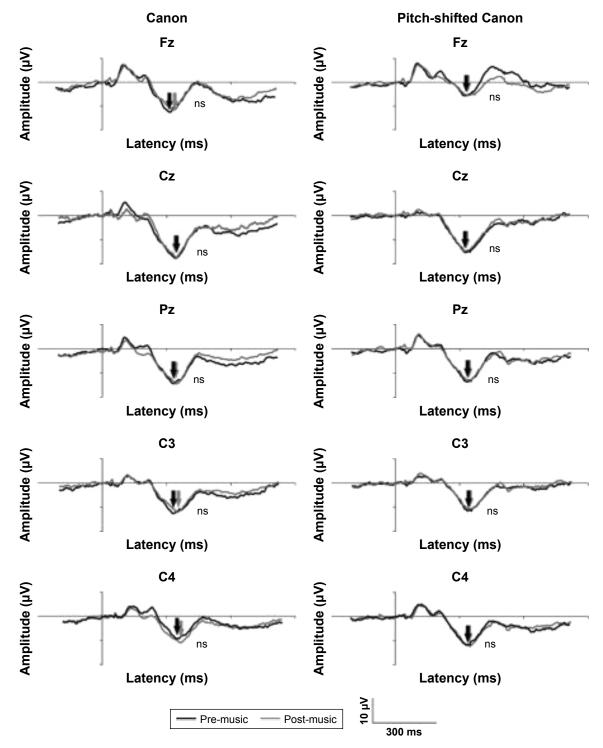


Figure 2 Grand mean P300 waveform before and after listening to Canon melody or pitch-shifted Canon.

**Notes:** The left side represents participants listening to Canon melody, whereas the right side represents those listening to pitch-shifted Canon melody. The P300 measured before listening to the melody is represented by the gray line. The P300 is indicated by arrows.

Abbreviation: ns, not significant.

 $(F_{1,28}=6.005, P=0.21; Figure 6)$ . Moreover, those who found it pleasant after listening to the melody exhibited higher changes of scores on the VAS scale relative to those who found it unpleasant  $(F_{1,28}=6.001, P=0.16; Figure 6)$ .

### **Discussion**

This study is the first investigation comparing the effect on brain functions – ERPs and motivation – of Canon chord progression, which is a type of chord progression that

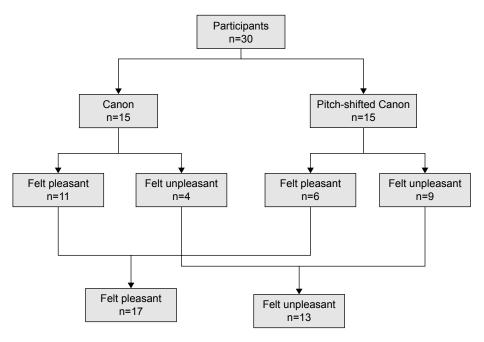


Figure 3 The flowchart of participant assignment based on whether they found the melody pleasant or unpleasant.

configures a variety of popular and pleasant music, as well as a pitch-shifted Canon chord progression, with notes transposed to a semitone from the Canon chord progression.

Substantial music studies examined brain function affected by listening to music in animal models and humans.<sup>20</sup> For example, Rauscher et al reported that when rats listened to Mozart's music and the music of another composer, the rats that had listened to Mozart exhibited increased spatial memory ability.21 In these studies, the effect of each component of music, such as chord progression, has not

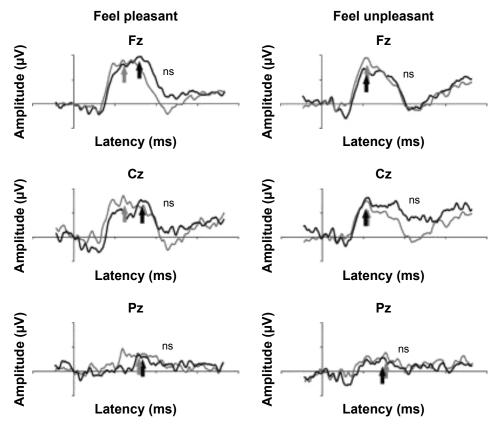


Figure 4 (Continued)

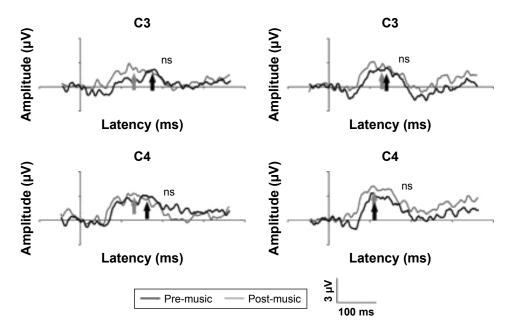


Figure 4 Grand mean MMN waveforms before and after listening to the melody based on whether participants found the melody pleasant or unpleasant.

Notes: The left side represents participants that found the melody pleasant, whereas the right side represents those who found it unpleasant. The MMN measured before listening to the melody is represented by the black line, and MMN measured after listening to the melody is represented by the gray line. MMN is shown by arrows.

Abbreviations: MMN, mismatch negativity; ns, not significant.

been dissected. Other studies have revealed that music changes mental function<sup>3–6</sup> and a number of those have measured and studied biological indicators, such as ERPs, report that listening to music does result in altered brain activity.

Arikan et al reported that listening to well-known music promotes attention and increases the P300 amplitude of ERPs.<sup>22</sup> Moreover, Guo et al showed that, by listening to music that can cause subjective relaxation, there is a decrease

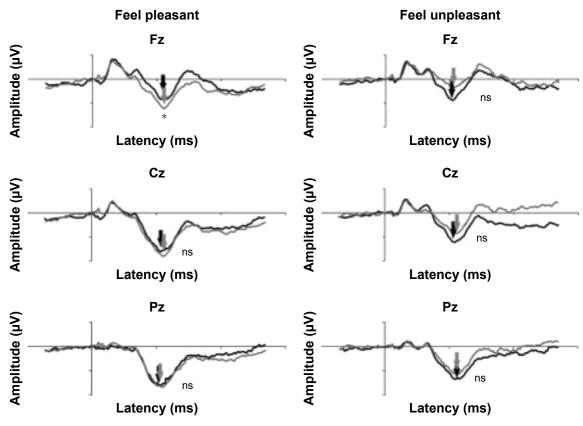


Figure 5 (Continued)

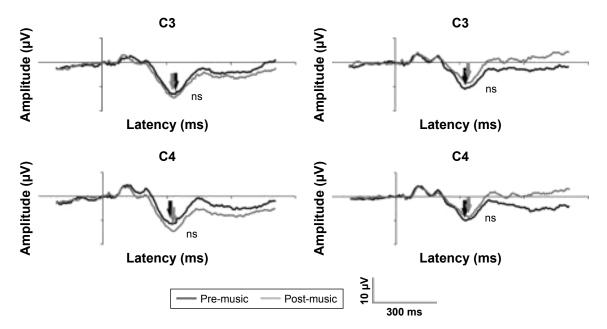


Figure 5 Grand mean P300 waveforms before and after listening to the melody based on whether participants found the melody pleasant or unpleasant.

Notes: The left side represents participants that found the melody pleasant, whereas the right side represents those who found it unpleasant. The P300 measured before listening to the melody is represented by the black line, and the P300 performed after listening to the melody is represented by the gray line. The P300 is shown by arrows. \*P<0.05.

Abbreviation: ns, not significant.

in the performance deficit resulting from mental fatigue during work that applies cognitive exercise and an increase in the P300 amplitude in ERPs.<sup>23</sup> Although these studies have indicated the definite result that the cognitive exercise

function is promoted by listening to music that is well-known or is relaxing, there has been no discussion on whether increased ERP amplitude results from a direct physical effect of music, or whether it is a secondary effect of changes in

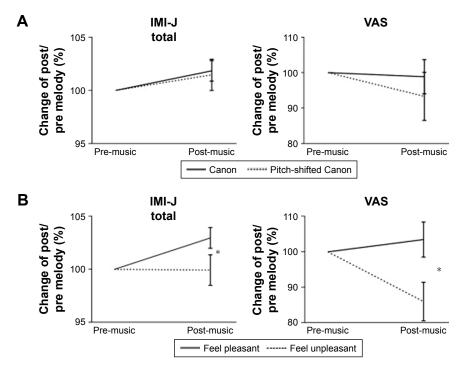


Figure 6 Assessment of motivation scores before and after listening to the melody.

Notes: (A) The black line represents participants listening to Canon melody, whereas the dotted line represents participants listening to pitch-shifted Canon melody. There were no differences in IMI and VAS between subjects who listened to Canon melody and those who listened to pitch-shifted Canon melody. (B) The black line represents participants who found the Canon melody pleasant, whereas the dotted line represents those who found it unpleasant. For those who found the melody pleasant, IMI total and VAS scores showed a significant improvement relative to those who found it unpleasant (IMI; F<sub>1,28</sub> =8.062, P=0.006, VAS; F<sub>1,28</sub> =6.533, P=0.01). \*P<0.05.

Abbreviations: IMI, Intrinsic Motivation Inventory; VAS, visual analog scale.

subjective mental activity (eg, comfort). Our study showed that increased P300 amplitude and motivation were not due to listening to a Canon chord progression in itself, but rather were correlated with a subjective feeling of appreciation when listening to the music, regardless of the Canon chord progression. In other words, we revealed that there is no direct physical effect from the Canon chord progression, but changes in subjective mental activity from a sensation of appreciation is important for changing the P300 amplitude and increasing motivation.

It has been known that musical affect expression depends on a combination of universal and culture-specific factors.<sup>24</sup> In particular, experiences during a young period have a large effect on later mental function and even brain structure,<sup>25–27</sup> and such experiences also have a strong influence on musical perception.<sup>28</sup> In addition, it has been shown that a critical period exists in early childhood for determining musical preferences.<sup>29</sup> In fact, some participants in this study experienced an unpleasant feeling after listening to music with Canon chord progression, which is thought to be universally pleasure inducing. Thus, there is no universal melody that causes brain activation, but rather, listening to music that is compatible with brain structure, as formed by experiences in early childhood, could cause a reaction in the brain and promote motivation.

Patients with schizophrenia, depression, and dementia are prone to decreased motivation and apathy,<sup>30,31</sup> but music therapy is said to ameliorate those symptoms.<sup>3–6</sup> Our results may suggest that it is important to use music that each individual finds enjoyable, rather than uniformly using music by Mozart or music with Canon chord progression, which are generally considered to be pleasant, in order to treat patients as described earlier.

A limitation of this study was the small sample size, with a relatively high ratio of male subjects comprising medical students and residents. In the future, it will be important to conduct a study with a larger sample size and using a greater diversity of subjects.

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### **Disclosure**

The authors report no conflicts of interest in this work.

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