INTRODUCTION

Investigation of music from a neuroscience perspective may be a valuable way to probe a variety of complex cognitive functions and their neural substrate. Using recently developed neuroimaging techniques, such as fMRI [1], transcranial magnetic stimulation (TMS) [2] and MEG [3], many findings have been reported on the musician’s brain, concerning the functional plasticity, anatomical differences, audio-motor integration and maladaptive plasticity of the musician’s brain [4]. Absolute pitch (AP), the ability to identify any tones without reference (labeling) [5], is a useful example of highly specific cognitive skill that is unevenly distributed in the population. The prevalence of absolute pitch is estimated to be 0.1% of the general population [6]. However, the prevalence of absolute pitch among professional musicians is in the range 10–15% and, it is markedly higher among Asian music students at 32.1–47.5% [7,8]. In addition to the educational influence, familial aggregations and genetic predisposition have also been reported [8,9]. Absolute pitch ability is a good model for understanding the influence of genes and development on neural and cognitive function [10].

An auditory evoked field (AEF) component, N100m, the magnetic counterpart of the electrophysiological N100, represents the most prominent and stable peak of the AEF, which appears at about 100 ms after the stimulus onset. The source of the N100m was considered to be located around the auditory cortices along the bilateral superior temporal gyri (STG) [11,12].

There have been several neuroimaging studies on absolute pitch possessors. Pantev et al. [13] recorded a left N100m from musicians with absolute pitch, musicians without absolute pitch and non-musicians without absolute pitch. They reported that in the musicians, the dipole moments of the left N100m for piano tones were about 25% greater than those for pure tones and suggested that there was a plasticity in the auditory cortex, which was attributable to musical training but not to the absolute pitch possession itself. Hirata et al. [14] showed that the dipole of the left N100m of the absolute pitch musicians was significantly deviated posteriorly, compared with those of the non-musicians. They suggested distinct neural activities in the left auditory cortex of musicians, which may be the result of cortical plasticity [15]. Zatorre et al. [16] measured the cerebral blood flow during the presentation of musical tones to absolute pitch possessors. They showed that not only the superior temporal gyrus but also several other areas, e.g. left dorsolateral frontal region, played important roles in pitch perception in the absolute pitch possessors. Ohnishi et al. [17] reported in their fMRI study that the absolute pitch musicians showed left dominant secondary auditory areas and the left posterior dorsolateral prefrontal cortex during a passive music listening task, whereas non-musicians demonstrated right dominant secondary auditory areas. Concerning event-related potentials, Klein et al. [18] reported that the P300 in the absolute pitch possessors was smaller than that in the non-absolute pitch possessors in an auditory oddball task with 1000 and 1100 Hz pure tones. Hirose et al. [19], however, showed that the absolute pitch possessors exhibited similar P300 as the non-absolute pitch possessors in an auditory oddball task with 1000 Hz pure tones. Schlaug et al. [15] and Keenan et al. [20] showed an increased leftward asymmetry of the planum temporale (PT) in absolute pitch musicians from volumetric MRI studies. They suggested that there was a functional asymmetry in the brain of the absolute pitch possessors, especially in the superior temporal planes [15,20]. Keenan [20] also reported that the pruning of the
right PT rather than expansion of the left PT underlined the increased PT asymmetry in the absolute pitch musicians. These studies were, however, all performed in adult absolute pitch possessors. Hirose et al. [21] recorded N100m from the child absolute pitch possessors and non-absolute pitch possessors and reported the correlation between the age, the kinds of the tasks, the possession of the absolute pitch and the appearance rate of N100m.

There have been several studies on human pitch perception in non-absolute pitch possessors [22]. It was shown that the right auditory cortex had an important role in the pitch perception. Their tasks, however, exclusively required the relative pitch ability, and the absolute pitch ability was not necessary. There have been only a few physiological studies on absolute pitch, especially with respect to the mechanism of labeling, which was the core component of absolute pitch. Thus, physiological mechanism in absolute pitch possessors remains to be clarified. In the present study, we recorded, for the first time, MEG responses from adult absolute pitch possessors while they were labeling musical tones. We also recorded MEG responses while they were hearing pure tones inattentively. Our hypothesis was that the N100m increased when the absolute pitch possessors were labeling. We also hypothesized that the right auditory cortex had an important role in the absolute pitch perception of the absolute pitch possessors.

MATERIALS AND METHODS
Ten Japanese adult absolute pitch possessors (three males and seven females, age 22–31 years, average 27.4 ± 3.2 years) participated. They all received early musical education and started to play piano at the age of 3–4 years. For comparison, seven Japanese adult non-absolute pitch possessors (four males and three females, age 28–45 years, average 33.9 ± 6.0 years) participated. Before the measurements, a randomized sequence of 60 pure tones between C2 (65.5Hz) and C6 (1048Hz) was presented to the subjects. A subject was labeled as an absolute pitch possessor if 95% of the tones were correctly identified. The mean rate of correct responses in absolute pitch possessors was 97.7%. None of the non-absolute pitch possessors were able to perform the test above chance level. No subject had a history of neurological or audiological disorders and they were all right-handed. The entire study was approved by the Ethics Board of the University of Tokyo. Written informed consent was obtained from each subject.

The magnetic fields were recorded under the following two conditions. (1) Single tone session consisted of one kind of pure tone (1000 Hz) and subjects were requested to hear the tones inattentively. The subjects were instructed to stare firmly at a certain black point (diameter 1.5 cm) on the wall 2 m ahead of them and requested not to pay attention to the tones. At this stage, because they had not been informed of the following labeling session beforehand we considered their intentional process for labeling the tones was absent or minimal. (2) Labeling session consisted of eight different pure tones (\( p = 0.125 \)) ranging from C4 to C5 (262–524 Hz, averaged pitch) and subjects were requested to listen to the tones attentively and label each tone. Each session consisted of 200 sequential tones and the two sessions were conducted in that order in all subjects. The tones were generated using a personal computer (Physio-Tech Co., Ltd., Japan) and were presented binaurally with randomized interstimulus intervals of 1.00 ± 0.1 s. The duration of each tone was 200 ms including a 10 ms rise and fall time and its intensity was 90 dB sound pressure level (SPL). The tones were sine curve tones without overtones.

Each subject sat in a chair in a magnetically shielded room during the recording with a 204-channel whole head neuromagnetometer (Neuromag Ltd., Finland). The recording passband was 0.1–200 Hz and the sampling rate was 591 Hz. The automatic rejection level of 3000 fT/cm was applied for excluding the magnetic artifacts. Electrooculograms were recorded and epochs > 150 μV were rejected online. The measurements from 50 ms before to 600 ms after the stimulus onset were averaged 150–200 times. A low-pass filter was used at 40 Hz and a high pass filter was used at 2 Hz in the offline analysis. A single dipole model was applied. Equivalent current dipole (ECD) was calculated from 30–40 adjacent temporal channels for the N100m component of the auditory evoked field peaking at about 100 ms after stimulus onset, using an iterative least squares minimization algorithm. The calculated ECDs were selected on the basis of a goodness-of-fit (GOF) > 90%.

To superimpose the estimated generator sources of N100m on the head MRI, the position of each subject’s head relative to the MEG instrument was determined by measuring magnetic fields produced by four marker coils attached to the scalp. Before the measurements, the location of the marker coils in relation to cardinal points of the head (nasion, left and right pre-auricular points) were determined using an Isotrak 3D-digitizer (Polhemus Inc., USA). Multiplanar head 3D-MRIs were obtained with a Sigma 1.5T MRI system (G.E. Medical Systems, USA). Statistical comparisons were made using three-way ANOVA.

RESULTS
In all subjects the N100m was elicited and located in the bilateral auditory cortices in every session. Figure 1 shows an example of the magnetic fields of the representative absolute pitch possessor recorded from the temporal sensors that showed N100m most clearly. Figure 2 shows an example of isocontour maps of the magnetic fields and the N100m dipole superimposed on the head MRI of the representative absolute pitch possessor in the labeling session. Table 1 shows the averaged strength of the right and left N100m dipole moment. The F values and \( p \) values of ANOVAs are summarized in Table 2.

![Fig. 1. An example of the magnetic fields of a representative absolute pitch possessor recorded from the bilateral temporal sensors that showed N100m most clearly.](image)
DISCUSSION

There was a significant main effect for the condition (single tone/labeling sessions) in the ANOVA with the condition and hemisphere (left/right) only in the absolute pitch possessors (Fig. 3, Table 2). This result means that there were significant increases in the bilateral N100m dipole moments of the absolute pitch possessors in the labeling session. The dipole in the labeling session of the absolute pitch possessors was located in the bilateral auditory cortices (Fig. 2). The dipole moment indicates the total strength of the cortical activation, that is, the number of neurons involved in the cortical response. Therefore, the present results showed that, ~100 ms after the stimulus onset, there were significantly greater activations in the bilateral auditory cortices while the absolute pitch possessors were labeling the tones.

In the attentive condition, the N100m dipole moment increased in contrast with that in the non-attentive condition while performing the auditory selective attention task [23]. It was also reported that the primary auditory cortex played a major role in the auditory attention as early as 100 ms after the stimulus onset [23]. This suggests that attention is not carried out in a unique module independently, but must be a function that consists of a dispersed system including the primary auditory cortex, being indivisible from the perception process. In the acquisition of cognitive ability such as absolute pitch, it is suggested that the attention process might be transfigured from an intentional to automatic process during the sensitive period as seen in other learning processes such as language acquisition. In other words, absolute pitch possessors appear to acquire the labeling ability through the minimization of the intentional attention together with automation of the attention process at the auditory cortex that was previously suggested to be engaged mainly in the auditory perception.

The significant interaction between condition and group (absolute pitch/non-absolute pitch) in the ANOVA with the condition and group in the right hemisphere. There was also a marginal main effect for the condition in the ANOVA with the condition and group in the left hemisphere (Table 2). Although there was no significant interaction between the group and hemisphere in the ANOVA with the group and hemisphere in the labeling session (Table 2), these results suggested that, in the non-absolute pitch possessors, the left N100m dipole moment alone tended to increase in the labeling session.

Previous studies [22] reported that the right auditory cortex had an important role in the perception of pitch.

Table 1. The average strength of the right and left N100m dipole moment (s.d.)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Side</th>
<th>Single tone</th>
<th>Labeling</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>Rt</td>
<td>24.53 (14.67)</td>
<td>37.09 (21.13)</td>
</tr>
<tr>
<td></td>
<td>Lt</td>
<td>25.74 (13.54)</td>
<td>31.47 (11.33)</td>
</tr>
<tr>
<td>Non-AP</td>
<td>Rt</td>
<td>33.67 (13.41)</td>
<td>32.36 (12.45)</td>
</tr>
<tr>
<td></td>
<td>Lt</td>
<td>33.49 (13.59)</td>
<td>40.49 (18.72)</td>
</tr>
</tbody>
</table>

AP: absolute pitch (nAm).

Table 2. Results of ANOVAs for the N100m dipole moment.

<table>
<thead>
<tr>
<th>1) in each group</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condition (C)</td>
<td>10.159*</td>
</tr>
<tr>
<td>Hemisphere (H)</td>
<td>0.042</td>
</tr>
<tr>
<td>C × H</td>
<td>0.646</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2) in each hemisphere</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condition (C)</td>
<td>4.489***</td>
</tr>
<tr>
<td>Group (G)</td>
<td>1.453</td>
</tr>
<tr>
<td>C × G</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>6.867**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3) in each session</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (G)</td>
<td>2.976</td>
</tr>
<tr>
<td>Hemisphere (H)</td>
<td>0.011</td>
</tr>
<tr>
<td>G × H</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*p < 0.01, ** p < 0.05, *** p = 0.05.
Ayotte et al. [24] showed that in the recognition process of music, right hemisphere played a perceptive role and the left hemisphere played an associative role. In other words, the perception of music was executed in the right hemisphere and the association of the music with the long-term memory representations (e.g. the name of the music piece, the name of the players and the name of the tone) were executed in the left hemisphere. Zatorre et al. [25] showed that the right and left STG developed in a functionally and anatomically different way; the right developed for pitch perception, the left for the language understanding. It is not certain whether the right STG is genetically determined for labeling or it is organized for labeling by the early commencement of musical training. Considering recent studies [7–9] which suggested that genetic factors were predominant over environmental and educational factors in the acquisition of the absolute pitch, the former seems more plausible. Difficulty in the absolute pitch acquisition after the sensitive period [7–9] might also be related to the age-dependency of the innate neuronal circuit for labeling, thus, the early commencement of musical training is indispensable for the absolute pitch acquisition. So, the absolute pitch possessors appear to analyze the height of the tone in the right hemisphere and assign the name of the pitch to the tone in the left hemisphere. This suggests that they executed the labeling task through interhemispheric cooperation.

In contrast to the absolute pitch possessors, the right N100m dipole moment of the non-absolute pitch possessors did not increase in the labeling session. This suggests that the interhemispheric cooperation in the non-absolute pitch possessors did not operate properly. Of course, the non-absolute pitch possessors made best efforts to pay attention in executing the labeling task. Therefore, if any auditory attention increased the N100m dipole moment, the right N100m dipole moment of the non-absolute pitch possessors should have increased during the labeling session. Furthermore, because the kinds of tones were only one in the single tone session and eight in the labeling session, a greater neuron population might be activated in the labeling session even in the non-absolute pitch possessors. However this hypothesis is quite unlikely because the non-absolute pitch possessors did not have a neuronal circuit to analyze the height of the tone in the right hemisphere. They could not link their attention to the analytical circuit of the height and consequently their right N100m dipole moment remained almost unchanged among sessions. Thus, the auditory attention appeared to be effectively operational only if a neural circuit for labeling was given. The non-absolute pitch possessors, however, tried to assign the name of the pitch in the left hemisphere. Therefore, their left N100m dipole moment alone increased in the labeling session, though not significantly.

CONCLUSIONS
We examined only the N100m dipole. Further analyses are required in the long latency after 100 ms. The investigation of the spatiotemporal distribution of dipoles in the whole labeling session will uncover the complete mechanism of labeling.

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REFERENCES