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To cite this article: Masayuki Satoh, Natsuko Kato, Ken-ichi Tabei, Chizuru Nakano, Makiko Abe, Risa Fujita, Hirotaka Kida, Hidekazu Tomimoto & Kiyohiko Kondo (2016): A case of musical anhedonia due to right putaminal hemorrhage: a disconnection syndrome between the auditory cortex and insula, *Neurocase*

To link to this article: <http://dx.doi.org/10.1080/13554794.2016.1264609>



Published online: 07 Dec 2016.



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A case of musical anhedonia due to right putaminal hemorrhage: a disconnection syndrome between the auditory cortex and insula

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ABSTRACT

A 63-year-old, right-handed professional chorus conductor developed right putaminal hemorrhage, and became unable to experience emotion while listening to music. Two years later, neurological examination revealed slight left hemiparesis. Neuromusiological assessments revealed impaired judgment of “musical sense,” and the inability to discriminate the sound of chords in pure intervals from those in equal temperament. Brain MRI and tractography identified the old hemorrhagic lesion in the right putamen and impaired fiber connectivity between the right insula and superior temporal lobe. These findings suggest that *musical anhedonia* might be caused by a disconnection between the insula and auditory cortex.

ARTICLE HISTORY

Received 25 May 2016
Accepted 17 November 2016

KEYWORDS

musical anhedonia;
putaminal hemorrhage;
insula; auditory cortex;
disconnection

Introduction

It is generally accepted that the emotional processing of music has two components: emotion perception and emotional experience (Juslin & Västfjäll, 2008). Emotion perception means the recognition of expressed emotions in music without necessarily feeling an emotion (Juslin & Västfjäll, 2008). Emotional experience is the subjective experience of emotion (Juslin & Västfjäll, 2008). The reported literature on the impairment of emotion perception and emotional experience of music reveals a double dissociation, in other words, these two cognitive domains have, at least in part, independent neural networks in the brain (Satoh, Nakase, Nagata, & Tomimoto, 2011). Cases have been reported in which one of these two domains was impaired and another preserved (Griffiths, Warren, Dean, & Howard, 2004; Hirel et al., 2014; Matthews, Chang, May, Engstrom, & Miller, 2009; Mazzoni, Moretti, Pardossi, Vista, & Muratorio, 1993; Peretz & Gagnon, 1999; Satoh et al., 2011).

Selective loss of the emotional experience of music was named *musical anhedonia* by the present author (Satoh et al., 2011). Musical anhedonia is characterized by the following: (i) normal otolaryngological function, (ii) normal perception of elementary musical components and emotion perception of music, (iii) impaired capacity to respond emotionally to music, and (iv) normal emotional experience to other auditory stimuli and sensory modalities such as environmental sounds and vision. Musical anhedonia was first presented as an acquired disorder, but this concept was widened to include congenital impairment of the emotional experience of music (Mas-Herrero, Zatorre, Rodriguez-Fornells, & Marco-Pallares, 2014; Zatorre, 2015). In this article, we use the term “musical anhedonia” in its original meaning, namely the acquired impairment of emotional experience of music due to cerebral

damage. Until now, only four cases of musical anhedonia had been reported. The first case was a 24-year-old amateur guitarist (Mazzoni et al., 1993). After a hemorrhage due to an arteriovenous malformation at the right temporoparietal lobe, he lost the esthetic pleasure of listening to music. The second case was a 52-year-old radio announcer (Griffiths et al., 2004). Due to an infarction of the left insula partly extending into the frontal lobe and amygdala, emotional response to specific music was lost. The third case was a 71-year-old retired teacher (Satoh et al., 2011), who developed an infarction of the right temporoparietal lobe. After the cerebrovascular event, he found himself unable to experience emotion while listening to music even that which he had enjoyed prior to the illness. The fourth case was recently reported in French (Hirel et al., 2014). The patient was a 43-year-old amateur musician; due to an ischemic lesion of the right superior temporal lobe, the patient showed musical anhedonia. While the neural basis of musical anhedonia is controversial, according to a similar symptom in the vision system called “visual hypoemotionality” (Bauer, 1982; Habib, 1986), it is hypothesized that an auditory-limbic disconnection is responsible.

We present a patient with musical anhedonia who was a professional chorus conductor. He suffered from a right putaminal hemorrhage, and subsequently lost the esthetic pleasure of listening to music. Neuroimaging studies suggest that a disconnection between the insula and auditory cortex is, in part, responsible for the occurrence of musical anhedonia.

Case report

History

In May, 2011, a 63-year-old professional chorus conductor being treated for hypertension developed a right putaminal

hemorrhage. He was treated conservatively, and 1 month later was transferred to a rehabilitation hospital. At the end of July, he returned home with slight left hemiparesis which was measured by manual muscle testing, and mild hypoesthesia on the left side of his body. He was able to independently perform activities of daily life, such as dressing, eating, bathing, going out using public transportation, and shopping. When he returned to his musical profession, he found himself unable to have any emotional experience while listening to music. He could not elicit interest from any type music, even his favorite genre. When he conducted his chorus group, he felt much different than prior to the cerebrovascular event; these changes are described below. Before the illness he felt great joy and “chills” when the harmony sounded complete. He subsequently lost this sensation, and thus lacked self-confidence as to whether the harmony was good or not. He felt that the sound was dull and lacked freshness, though he could acoustically recognize that the harmony was correct in its physical sound properties. He could recognize familiar music and discriminate subtle differences in the timbre of voices, although it had become somewhat difficult to separately identify the alto and tenor voices in soprano-alto-tenor-base (SATB) chorus. He also found it difficult to speak in noisy situations. These symptoms suggested the existence of the disturbance of cocktail party effect. None of his chorus members noticed this impairment. During rehearsals, the patient frequently sang melodies and phrases in order to make choir members understand his willing. His singing was musically appropriate, so the members could easily understand that. His musical performances were excellent as before the illness, and the audience was satisfied when attending his concerts. No hearing deficit was found during consultation with an otolaryngologist. He was able to enjoy pictures in an art museum, movies in the theater, watching comic dialogues on television, and eating delicious foods, as he did before the cerebrovascular event. His symptoms remained unchanged for 2 years. In April, 2013, he was referred to us for assessment of his impaired musical appreciation.

Neurological and neuropsychological examinations

Neurological examination revealed slight left hemiparesis and mild hypoesthesia on the left side of his body, but there was no evidence of unilateral neglect, aphasia, apraxia, dyscalculia, or visual discrimination difficulties. No hearing deficit was found during consultations with an otolaryngologist. Neuropsychological assessments revealed a normal score on the Mini-Mental State Examination (27/30) and a perfect score on a Japanese version of Raven’s Colored Progressive Matrices (36/36) (Raven, 1995). To assess memory function, we performed the Japanese version of the Rivermead Behavioral Memory Test (RBMT). The RBMT yielded a normal score: a standard profile score of 22 (mean \pm SD; 19.73 \pm 2.93) and a screening score of 10 (9.15 \pm 1.78). He clearly remembered daily and social events. Therefore, we reasonably concluded that the patient had normally functioning short- and long-term memory. He could correctly copy the figure of a cube. When the patient was asked to verbally name as many different animals as he could in 1 min, the patient responded with

25 words where the lower limit of normal is between 8 and 10 (Satoh, Takeda, & Kuzuhara, 2009). His letter fluency beginning with “ka” was also excellent (17 words/min.). The results of the Trail Making Test – A and B were also normal (A 146 sec., mean \pm SD; 173.2 \pm 65.8; B 143 sec., mean \pm SD; 230.2 \pm 89.5). Given that the quality of his musical performance was at the same level as before the cerebrovascular event, we can conclude that his frontal and executive function was also preserved. Speech audiometry revealed a normal score on single sounds (146/148). To assess recognition of environmental sounds, a previously described test was used (Satoh, Takeda, & Kuzuhara, 2007; Satoh et al., 2005, 2011). Twenty-four familiar environmental sounds were presented, and the patient correctly stated what each sound meant (24/24). Assessment of responses to other sounds showed that he felt comfortable when listening to recorded natural sounds. Unpleasant stimuli such as disgusting smells, the sound of scratching a blackboard, pictures of wars or disasters, and physical pain caused him discomfort. We may say that these negative stimuli normally caused in negative feeling to the patient. For the assessment of emotional experience we used the International Affective Picture System (IAPS) which is a set of normative emotional stimuli for experimental investigations of emotion and attention (Center for the Study of Emotion and Attention, 1999). The two primary components are affective valance (ranging from pleasant to unpleasant) and arousal (ranging from calm to excited). To assess these dimensions, the Self-Assessment Manikin, which is an affective rating system, was used. According to the guidelines of Meagher’s report (Meagher, Arnau, & Rhudy, 2001), we used 39 IAPS slides (pleasant 10; unpleasant 9; neutral 20), when compared to the mean value of the IAPS, the patient scored within normal limits: total valence 5.0 \pm 1.9 (mean \pm SD; 5.2 \pm 1.5) and total arousal 4.7 \pm 2.0 (mean \pm SD; 4.1 \pm 1.7). The results of pleasant, unpleasant, and neutral visual stimuli were also normal: pleasant valence 7.1 (mean \pm SD; 7.4 \pm 1.6) and arousal 6.2 (mean \pm SD; 4.4 \pm 2.2), unpleasant valence 2.1 (mean \pm SD; 3.4 \pm 1.7) and arousal 6.6 (mean \pm SD; 6.6 \pm 1.9), and neutral valence 5.3 (mean \pm SD; 4.9 \pm 1.3) and arousal 3.1 (mean \pm SD; 2.7 \pm 1.7). Thus, he was able to normally experience emotion to visual stimuli, and the preservation of pleasure towards a variety of other stimuli suggested that his loss of pleasure was restricted to listening to music.

Neuromusicological assessments

Perception and expression of music were investigated by tests used in our previous studies of amusic patients (Satoh et al., 2005, 2007, 2011) and by “The Montreal Battery of Evaluation of Amusia (MBEA) (Peretz, Champod, & Hyde, 2003). For the former tests (Satoh et al., 2005, 2007, 2011), we performed the following tasks regarding musical perception: pitch discrimination, discrimination and recognition of familiar songs, discrimination of unfamiliar phrases, rhythm discrimination, meter discrimination, discrimination of isolated chords, and judgment of tonality (Table 1). For further details, please see the aforementioned papers (Satoh et al., 2005, 2007, Satoh et al., 2011). The results are summarized in Table 2, the patient’s score was within the normal range for all

Table 1. Assessment of musical abilities.

| | |
|--|---|
| <i>Perception of music</i> | |
| Pitch discrimination (Hz) | After presenting a pure tone of 440 Hz as the standard, we presented a second tone and measured the range in which the standard and second tones were heard as the same pitch. |
| Discrimination and recognition of familiar songs (/30) | Thirty familiar nursery songs, all in a major key, were chosen and in twenty of these songs, a part of the melody was locally altered. Two different response modes were used: (i) song decision; (ii) "familiar-unfamiliar" decision. |
| Discrimination of unfamiliar phrases (/30) | The tonal memory test of Seashore's measures of musical talents (Seashore, Lewis, & Saetveit, 1960) was used. Subjects were presented with two serial phrases and were asked which tone was altered in the second phrase. |
| Rhythm discrimination (/30) | The rhythm test from Seashore's measures of musical talents (Seashore et al., 1960) was used. Thirty pairs of rhythm patterns were presented, and subjects were asked to make a same-difference discrimination. |
| Meter discrimination (/4) | We used items from the meter test of an assessment of musical capacity for school children (Mashino, Hamano, & Moteji, 1979). Following an example of two pieces of music that had double or triple time, the examiner presented four pieces of music that had double or triple time. The subject was then required to answer "two" or "three" for each piece of music. |
| Discrimination of isolated chords (/14) | A pair of chords in which the interval was 1 s was presented and subjects were asked to make a same-different discrimination. We used an item from the harmony test from an assessment of musical capacity for schoolchildren (Mashino et al., 1979). |
| Judgment of tonality (/20) | We made 20 kinds of sequences of 3 chords in which 2 chords had subdominant to dominant seventh progression. The last chords of eight tasks were the tonic chords of each key which induced a natural feeling of an end. In 12 tasks, the last chords were irrelevant to the preceding 2 chords, which induced an unfinished, peculiar feeling. Subjects were asked to make a finished/unfinished response for each task. |
| <i>Expression of music</i> | |
| Singing familiar songs | The patient and control subjects were asked to sing 10 well-known Japanese nursery songs without accompaniment with the help of written lyrics. |
| Reproduction of single sounds | Subjects were required to vocally reproduce single tones presented by the examiner. The examination was performed under two conditions: (i) while the tone was sounding, and (ii) immediately following the end of the tone presentation. |
| Reproduction of two-note phrases | Subjects were presented with three two-note phrases and were asked to sing each phrase. The phrases consisted of two notes whose pitches were separated by 3, 4, or 5 degrees (e.g., D-F sharp, D-G, and D-A). |
| Reproduction of simple rhythm | Ten simple rhythm patterns 2 bars long in 4/4 time were presented and subjects were required to reproduce the rhythm by hand clapping. |

Table 2. Results for musical abilities.

| | Present case | Control |
|--|---------------------------------|-----------------------------------|
| <i>Perception of music</i> | | |
| Pitch discrimination (Hz) | 439–441 (–3.939–3.930 cents) | 434–446 (–23.770–23.448 cents) |
| Discrimination and recognition of familiar songs (/30) | 30 | 27.7 (26–30) |
| Discrimination of unfamiliar phrases (/30) | 30 | 21.8 (17–27) |
| Rhythm discrimination (/30) | 26 | 24.8 (20–29) |
| Meter discrimination (/4) | 4 | 3.8 (3–4) |
| Discrimination of isolated chords (/14) | 14 | 12.6 (11–14) |
| Judgment of tonality (/20) | 20 | 15.6 (12–19) |
| <i>Expression of music</i> | | |
| Singing familiar songs | Well | Well |
| Reproduction of single sounds | Well | Well |
| Reproduction of two-note phrases | Well | Well |
| Reproduction of simple rhythm | Well | Well |

components. For the evaluation of music perception, we also used "The MBEA (Peretz et al., 2003). The MBEA aims to assess musical ability in brain-damaged patients and consists of six tasks: scale, contour interval, rhythm, meter, and memory task. Our patient scored within normal limits on all tasks: Scale 27 (mean \pm SD; 27 \pm 2.3, cutoff 22), Different contour 29 (mean \pm SD; 27 \pm 2.2, cutoff 22), Same contour 30 (mean \pm SD; 26 \pm 2.4, cutoff 21), Rhythmic contour 29 (mean \pm SD; 27 \pm 2.1, cutoff 23), Metric 30 (mean \pm SD; 26 \pm 2.9, cutoff 20), and Incidental memory 27 (mean \pm SD; 27 \pm 2.3, cutoff 23).

In order to evaluate the perceptual capacity of musical characteristics, we performed portions of the Musical Aptitude Profile (Gordon, 1995), a test to assess musical sensitivity, including: Part I, Phrasing; Part II, Balance; Part III, Style. These tests were designed to evaluate the musical aptitudes of elementary, junior, and senior high school students, and consisted of 30 pairs of identical musical phrases which were played by a violin and/or a cello. In each pair, one performance sounded more musically accomplished than the other. Differences between the two performances consisted of timbre, legato or staccato, crescendo or decrescendo, accelerando or ritardando, playing carefully or crudely, the way of finishing the phrase, and the "agogic" which is the term for a type of accent based on duration (lingering on a note in order to stress it) (Sadie, 1994). The subject was asked to determine which of the two renditions of the same musical phrase made better "musical sense." The word "musical sense" means appropriate and suitable characteristics of music including intonation, articulation, melodic contour, tempo, timbre, phrasing, ending, and style (Gordon, 1995). These tests can reveal a more subtle and complex capacity for perception of the musical characteristics which produce emotional experiences. For the normative data, we used results from senior high school students that were highest among the tested elementary, junior, and senior high school students. If the patient scored below the normative average, we could assume that his ability to perceive esthetical characteristics of music

was impaired. The results of these tests were as follows: Part I-Phrasing test 23 (mean \pm SD; 23 ± 3.79 , percentile 44%), Part II-Balance 19 (mean \pm SD; 23.2 ± 3.96 , percentile 15%), and Part III Style 23 (mean \pm SD; 23 ± 4.13 , percentile 44%). The scores of the patient fell within or below the normative means. Given that our patient was a professional musician and the normative data were those of nonmusicians, we can reasonably conclude that the ability to perceive the subtle characteristics of “musical sense” was impaired in this patient.

The patient complained that while conducting a chorus he could not judge if the harmony was acoustically correct or not. To assess this ability, we performed a chord-type discrimination task. There are several types of chords in music. A chord with pure intervals consists of tones whose pitches are completely equal to their physiological properties based on the fundamental tone. For example, an octave is a tone whose pitch has double frequency, and a tone with a 5-degree interval (ex. “G” on “C,” 701.955 cents) has a one and a half difference of frequency (Table 3). The standard Western temperament today is equal temperament, in which the octave is divided into 12 uniform semitones (Sadie, 1994). In equal temperament, the pitch interval with 5 degrees is slightly narrower than pure interval which is acoustically correct (Table 3). Therefore, the sound of chords with equal temperament is not as clear as those with pure intervals, and professional musicians usually can discriminate whether a chord is of pure intervals or not. For the assessment, we played a pair of chords, one was pure and the other was equal temperament. Using Musical Instrument Digital Interface (MIDI) function of Cubase Essential 4 (Steinberg), we made triad of C major in the timber of AKOUSTIK PIANO (Native Instruments). By using the tuning function, we made C

major triads with pure intervals and in equal temperament (Table 3), and stored in the personal computer in Wave files. We prepared four kinds of stimuli with pair of triads: pure interval-pure interval, pure interval-equal temperament, equal temperament-pure interval, and equal temperament-equal temperament. These stimuli were randomly arranged, and sounded two times (total number of stimuli was eight). We asked the patient whether the chord was in the pure interval, or not. Five professional musicians could easily and completely discriminate the chords with pure interval and equal temperament. The ratio of correct answers given by the patient was 62.5% (correct 5). Among three incorrect answers, one was replied as different though the pair of chords was the same with pure intervals, and two replied as the same, though they were different. We thus concluded that the patient had impaired perception of the subtle differences in the sound of chords.

Neuroimaging assessments

Duvernoy’s atlas (Duvernoy, 1991) was used to estimate the location of the patient’s brain lesion. Two years after the onset of the cerebrovascular event, fluid attenuated inversion recovery images of MRI scans revealed that the old hemorrhagic lesion was situated in the right putamen (Figure 1). Subcortical fiber degeneration was observed between the superior temporal gyrus and the posterior two thirds of the right insula. *N*-isopropyl-*p*-[¹²³I] iodoamphetamine (¹²³I-IMP) single photon emission computed tomography imaging showed decreased regional cerebral blood flow (rCBF) in the right insula and temporal lobe (Figure 2).

For the tractography by diffusion tensor imaging (DTI), the resulting averaged DTI dataset was preprocessed (non-brain tissue removal, eddy current (an induced electric current formed within the body of a conductor when it is exposed to a time varying magnetic field) and motion correction) and then analyzed using FMRIB Diffusion Toolbox (FDT 3.0) from FSL 5.0.9 (Smith et al., 2004; Woolrich et al., 2009). The processing step we need to take is to correct for eddy currents, which occur due to the changing gradient field directions, and head motion.

Table 3. Triad on C in pure interval and equal temperament.

| | Pure interval | | Equal temperament | |
|---|---------------|---------|-------------------|---------|
| | Hz | Cent | Hz | Cent |
| C | 264.0 | 0 | 261.6 | 0 |
| E | 330.0 | 386.314 | 329.6 | 400.024 |
| G | 396.0 | 701.955 | 392.0 | 700.189 |

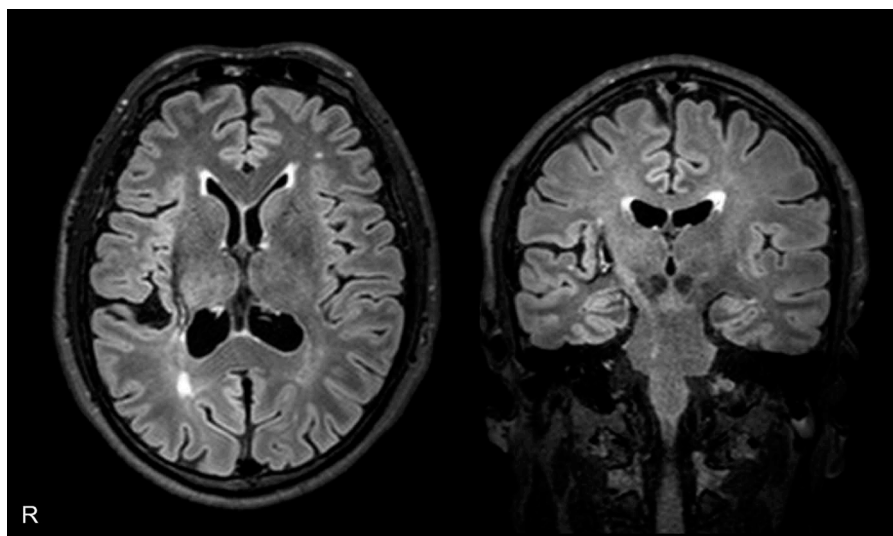


Figure 1. FLAIR MRI two years after the cerebrovascular event. FLAIR: fluid attenuated inversion recovery, R: right.

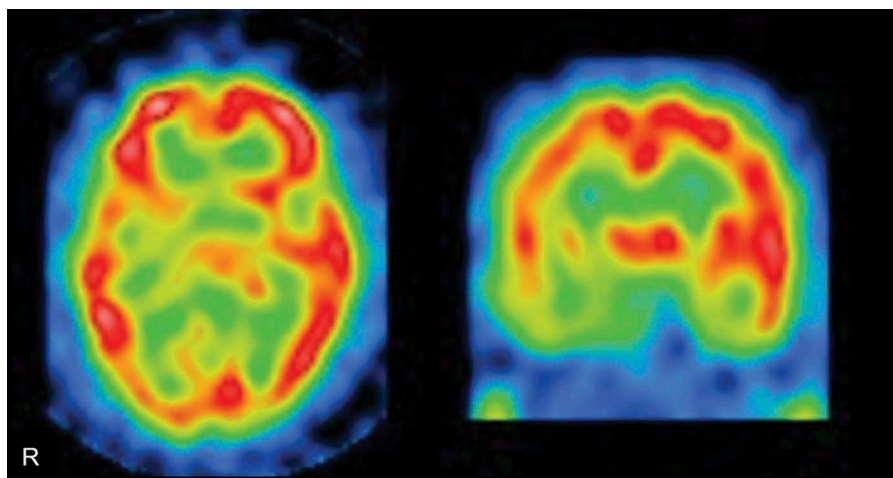


Figure 2. ^{123}I -IMP SPECT imaging shows decreased rCBF in the right insula and temporal lobe. ^{123}I -IMP: N-isopropyl-p- ^{123}I iodoamphetamine, rCBF: regional cerebral blood flow, R: right, SPECT: single photon emission computed tomography.

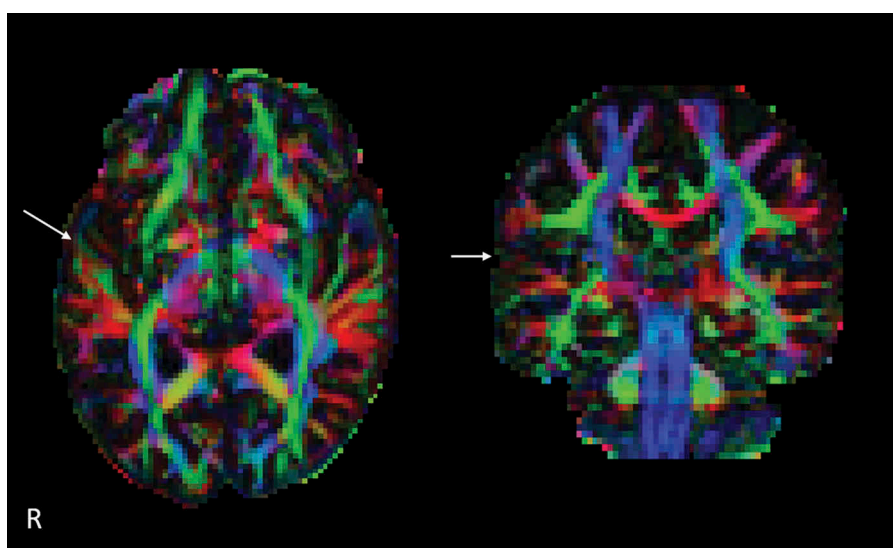


Figure 3. Colored encoding diffusion tensor imaging (CEDTI) map using FMRIB Diffusion Toolbox. Red, green, and blue color show right-left, anterior-posterior, and rostral-caudal fibers, respectively. The image level of (x, y, z) is (66, 51, 25). The depicted fiber tracking between the insula and superior temporal gyrus is decreased in the right hemisphere (white arrows). R: right.

Following eddy current correction we can now use DTIFit to fit tensors to the data and determine a variety of values include the fractional anisotropy at each voxel as well as the principle diffusion direction (Figure. 3).

Discussion

The patient was a professional musician that, due to a putaminal hemorrhage in the right hemisphere, lost the esthetic pleasure of listening to music. This symptom was formerly named “musical anhedonia” (Sato et al., 2011), and is to our knowledge only the fifth case presenting with this symptom (Table 4). The abilities of our patient are summarized as follows: (i) normal perception and expression of music, specifically, the quality of his performances was unchanged, (ii) normal speech audiometry and environmental sound recognition, (iii) impairment of judgment of “musical

sense,” (iv) inability to discriminate the sound of chords in pure versus equal temperament, (v) impairment listening to the inner vocal parts, such as alto and tenor, while conducting a chorus, and when experiencing the cocktail party effect during conversation, (vi) right putaminal hemorrhage and impairment of fiber connections between the insula and superior temporal lobe including the auditory cortex, and (vii) intact response to visual and other auditory stimuli and sensory modalities. In the following section, we discuss the mechanism of musical anhedonia as a disconnection syndrome between the insula and auditory cortex.

In recent years, the function of the insula has been an important topic in neurology. The insula, as a multimodal area, has a major role as a convergence zone implicated in the coordination between internal and external information through emotional subjective awareness (Ibañez, Gleichgerrcht, & Manes, 2010). The insular cortex has

Table 4. Summary of reported cases of musical anhedonia with associated pattern of symptoms.

| Author | Year | Journal | Age (year-old) | Sex | Handedness | Musical history | Musical emotion | | Site of lesion | Diagnosis |
|--------------|------|-------------------------------|----------------|-----|--------------|-------------------------------|-----------------|------------|---|----------------------|
| | | | | | | | Perception | Experience | | |
| Mazzoni | 1993 | J Neurol Neurosurg Psychiatry | 24 | M | Ambidextrous | Amateur guitarist | | × | Right temporoparietal | AVM, hemorrhage |
| Griffiths | 2004 | J Neurol Neurosurg Psychiatry | 52 | M | R | np | | ○ | Left frontal region, amygdala, insula | Infarction |
| Satoh | 2011 | Neurocase | 71 | M | R | np | | ○ | Right temporoparietal | Infarction |
| Hirel | 2014 | Rev Neurologique | 43 | M | R | Amateur | | ○ | Right superior temporal lobe | Infarction |
| Present case | 2015 | Neurocase | 63 | M | R | Professional chorus conductor | | ○ | Subcortical region of right temporal lobe | Putaminal hemorrhage |
| Peretz | 1999 | Neurocase | 40 | F | R | np | | × | Bilateral temporal and left frontal | Infarction |
| Matthews | 2009 | Neurocase | 30 | M | R | np | | × | Bilateral temporal | Egeneration |

○: preserved; ×: impaired; AVM: arteriovenous malformation; F: female; M: male; np: not particular; R: right.

connections with the primary and secondary somatosensory areas, anterior cingulate cortex, amygdala, prefrontal cortex, superior temporal gyrus, temporal pole, orbitofrontal cortex, frontal operculum, parietal operculum, primary auditory cortex, auditory association cortex, visual association cortex, olfactory bulb, hippocampus, entorhinal cortex, thalamus, medial geniculate body, and motor cortex (Craig, 2009; Ibañez et al., 2010; Mutschler et al., 2009; Nagai, Kishi, & Kato, 2007). The insula is known as a multi-sensory integration site (Figure 4) (Ibañez et al., 2010; Nagai et al., 2007). The insular cortex affects autonomic function, and involved in interoceptive awareness, pain, temperature perception, olfactory, gustatory, vestibular sensation, auditory processing, language, and emotional processing (Mutschler et al., 2009). Koelsch (2014) reported that grey matter loss of posterior insula was associated with impaired recognition of emotions expressed by music in the patient with frontotemporal lobar degeneration. This finding reinforced the opinion that the insula has a causal role in music-evoked emotions (Koelsch, 2014).

The neural architecture for encoding the biological value of music consists of a neural network for perceptual coding of music, emotion and reward processing, and higher-order cognitive processing (Clark, Downey, & Warren, 2014). Based on the present and reported literature, musical anhedonia might be caused by a disconnection between the insula and auditory cortex. The Griffiths's case had an infarction of the left insula (Griffiths et al., 2004). In contrast, our first case with musical anhedonia (Satoh et al., 2011) and Mazzoni's case (Mazzoni et al., 1993) had a lesion at the subcortical area of the right temporoparietal region, possibly including the fibers from/to the auditory cortex. The present case of musical anhedonia is the first to clearly demonstrate impairment of the fiber connections between the insula and auditory cortex using tractography. The esthetic pleasure in listening to music, for example, the deep impression consisting of shivering and/or tearing, is related to emotional and autonomic nervous responses. All cases of musical anhedonia have presented with a lesion at the insula and/or its subcortical region, which impaired the input of information from the auditory cortex to the insula resulting in disrupted integration of auditory, emotional, and autonomic nervous function. The lateralization of musical anhedonia is unknown. Among the five cases mentioned above, four cases (Hirel et al., 2014; Mazzoni et al., 1993; Satoh et al., 2011; and the present Satoh case) had the responsible brain lesion in the right cerebral hemisphere; only the case reported by Griffiths et al. (2004) had a lesion in the left hemisphere. Of the pre-illness musical abilities, only the present case was a professional musician. In terms of handedness, four patients were right-handed (Griffiths et al., 2004; Hirel et al., 2014; Satoh et al., 2011; and the present Satoh case), while the Mazzoni et al. (1993) case was ambidextrous. Much remains to be learned about the relationship between the cognitive processing of esthetic pleasure and hemispheric lateralization, pre-illness musical ability, and handedness.

What is the role of the insula in the occurrence of musical anhedonia? While this is an ongoing question, the insula might participate in the high level esthetic perception of

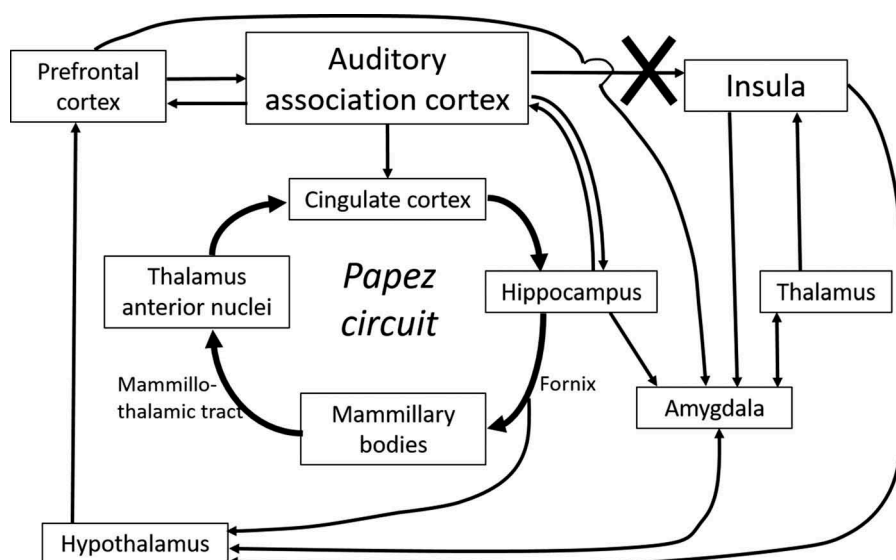


Figure 4. Diagram showing the neural circuit between the association cortex, limbic system (representing the emotional system), hypothalamus (representing the autonomic nervous system), thalamus (forming the sensory input), and the insula (acting as the multi-sensory integration site). The "X" shows the region thought to be impaired in the present case. Figure adapted from Lippincott's Illustrated Reviews: *Neuroscience*.

listening to music. The present patient showed impaired judgment of "musical sense" and the perception of chords with pure intervals, both of which are very sensitive finely honed abilities obtained by long-term professional training. Thus, as a multi-sensory integration site which connects many kinds of information, the insula might play a key role in the deep impressions of artistic appreciation.

In summary, we reported a case of musical anhedonia caused by right putaminal hemorrhage. Neuroimaging showed a disconnection between the insula and auditory cortex in the right hemisphere. Recent understanding of the insula suggests that this region plays an important role in integrating multi-sensory information. Thus, we can interpret the present and reported cases of musical anhedonia as a disconnection syndrome between the insula and auditory cortex.

Disclosure statement

No potential conflict of interest was reported by the authors.

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