- 1 Interoceptive sensitivity modulates heart rate and insula activity
- 2 when listening to music

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Abstract

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Interoception plays an important role in emotion processing, but the relationship between the physiological responses associated with emotional experience and interoception is unclear. In this study, we measured interoceptive sensitivity using the heartbeat discrimination task and investigated the effects of individual differences in interoceptive sensitivity on changes in heart rate and insula activity in response to musicinduced emotions. We found that the heart rate increased when listening to the music pieces rated as emotionally high-touching in the high interoceptive sensitivity group only. Compared to the emotionally low-touching music, listening to the emotionally hightouching music was associated with higher insula activity. Furthermore, relative to individuals with low interoceptive sensitivity, the region of interest analysis of the insula subregions for individuals with high interoceptive sensitivity revealed significant activity in the bilateral dorsal granular insula, the right ventral dysgranular insula, and the right granular and dorsal dysgranular insula while listening to the high-touching music pieces. Our results suggest that individuals with high interoceptive sensitivity use their physical condition to assess their emotional level when listening to music. Furthermore, the insula activity may reflect the use of interoception to estimate emotions.

Keywords: Emotions, Heart rate, Insula activity, Interoceptive sensitivity, Music

1. Introduction

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Interoception refers to the sense of the internal state of the body (Craig, 2002; Ceunen et al., 2016) and has attracted attention due to its important role in emotions, decision making, and social interaction (Pollatos et al., 2005; Craig, 2008; Seth, 2013; Critchley and Garfinkel, 2017; Khalsa et al., 2018). One of the objective ways to investigate the relationship between emotions and interoception is to examine physiological responses when experiencing emotions. Pollatos et al. (2007) and Pollatos and Schandry (2008) reported a significant decrease in the heart rate after the presentation of emotional images to participants with high interoceptive sensitivity. Herbert et al. (2010) also showed that the heart rate and cardiovascular parameters during emotional image observation differ depending on the level of interoceptive sensitivity. These results indicate that the physiological response to emotional images changes according to interoceptive sensitivity. In contrast, a previous study reported no differences in heart rate and SCR in response to the presentation of emotional videos between the high and low interoceptive sensitivity groups (Wiens et al., 2000). Therefore, the relationship between emotional and physiological responses and interoceptive sensitivity is not always consistent. In the study of interoception, heartbeats are widely used to examine individual differences in interoceptive sensitivity. The most popular method is the heartbeat counting task (Schandry, 1981), in which participants count their heartbeat in mind within a certain period. The previous studies of emotion and physiological response used the heartbeat counting task to estimate the interoceptive sensitivity. However, this method has been criticized as the participants' knowledge of heart rate affects their scores (Murphy et al., 2018; Zamariola et al., 2018). To address these issues, some studies have used the heartbeat discrimination task (Garfinkel et al., 2015; Ring and Brener, 2018) in which

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participants listen to the sound stimulus and respond whether it matches the timing of their heartbeat. In this task, it is thought that the participants' knowledge and strategy do not affect the results, and the participants' sensitivity to the heartbeat can be measured more accurately than with the heartbeat counting task (Ring and Brener, 2018). Neuroimaging studies have strongly suggested a link between interoception and emotion (Quigley et al., 2021). The insula is considered central to interoceptive processing, and insula activity during interoceptive tasks (Critchley et al., 2004; Simmons et al., 2013) and the relationship between insula activity and individual differences in interoceptive sensitivity (Kuehn et al., 2016; Tan et al., 2018) have been demonstrated. The insula is also considered to be an important area for linking interoception with emotion or social interaction (Gu et al., 2013), and overlapping activations of emotional and interoceptive tasks have been reported (Zaki et al., 2012). The insula is categorized into three types according to its cytoarchitectural organization: agranular cortex located in the anterior region, dysgranular cortex located in the dorsal-mid region, and granular cortex located in the posterior region (Mesulam and Mufson, 1982). A meta-analysis of insula activity showed that the social-emotional, cognitive, and sensorimotor tasks activated the anterior-ventral, the anterior-dorsal, and the mid-posterior insula, respectively (Kurth et al., 2010). However, consistent results have not been obtained regarding the relationship between individual differences in interoceptive sensitivity and the activities of the insula subregions. Previous studies have reported a correlation between the activity of the right anterior insula and interoceptive sensitivity (Critchley et al., 2004; Haruki and Ogawa, 2021), a correlation between the activity of the mid insula and interoceptive sensitivity (Tan et al., 2018), and decreased network centrality in the right posterior insula in the high interoceptive sensitivity group

(Kuehn et al., 2016). These inconsistencies might be due to the difference in experimental tasks. A meta-analysis of the brain activity during various interoception-related tasks reported that the commonly activated regions are the mid and posterior insula (Schulz, 2016). However, the relationship between the physiological responses associated with emotional experience and individual differences in interoception has not been fully clarified. Based on these previous findings, we made the following hypotheses: (1) the physiological response during the emotional experience of music correlates with individual differences in interoceptive sensitivity; (2) the interoceptive sensitivity measured by the heartbeat discrimination task is related to the physiological response; and (3) the activity of the posterior insula during an emotional experience correlates with individual differences in interoceptive sensitivity. To test these hypotheses, we conducted an experiment in which participants listened to various music pieces while measuring brain activity using functional magnetic resonance imaging (fMRI) and heart rate as a physiological response. Music is often used as a visual stimulus for emotion induction (Gilet, 2008). A comparison of visual and auditory emotional induction showed that emotional recognition of visual stimuli is more accurate, whereas musical stimuli induce larger changes in electrodermal activity (EDA), heart rate, and brain wave amplitude than visual stimuli (Baumgartner et al., 2006). Therefore, it is expected that the relationship between emotions and interoception will be more prominent when music is used to induce

2. Methods

emotions.

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Participants

The study involved 52 participants (31 females, 21 males, age range: 18–35 years,

average age: 22.6 ± 2.81 years). All participants were right-handed, not professional musicians, and had never majored in music. One participant was excluded from the analysis due to a malfunction in the physiological recording. The participants provided written informed consent in accordance with the Declaration of Helsinki and received a monetary reward for participating. The research ethics committee of Hiroshima University approved this study (approval number: E-965).

Heartbeat counting task

In the heartbeat counting task, the participants counted and reported the number of heartbeats between two beep sounds. The sound intervals comprised 6 conditions of 25, 30, 35, 40, 45, and 50 s, and once for each condition. During the task, a 3-lead electrocardiograph (ECG) was attached to the chest of the participants and the ECG was recorded at 1000 Hz using a Biopac MP160 System (Biopac Systems, Goleta, CA).

From the participants' responses, the interoceptive accuracy (IA) score was calculated using the following formula:

$$IA = 1/6 \sum_{i=1}^{n} 1 - \left| nbeats_{recorded} - nbeats_{recorded} \right| / nbeats_{recorded}$$

Here, $nbeat_{recorded}$ represents the correct number of heartbeats, and $nbeat_{reported}$ represents the number of heartbeats reported by the participant.

Heartbeat discrimination task

The heartbeat discrimination task is used to determine whether the timing of the beep sound and one's own heartbeat are synchronized when a beep sound is slightly delayed from the actual heartbeat (Whitehead *et al.*, 1977). A beep sound was presented immediately after the participant's R-peak detected by the ECG (0 ms condition), or with 150 ms (150 ms condition), 300 ms (300 ms condition), and 450 ms (450 ms condition)

delay from the R-peak timing. In each trial, participants listened 10 beep sounds and answered whether the beep timing matched or did not match their heartbeat. Six trials under each condition were performed, totaling 24 trials.

In the heartbeat discrimination task, participants do not always feel that their heartbeats are simultaneous with the sounds when the delay time is 0 ms (Ring and Brener, 2018). In addition, since the heartbeat is periodic, it might be impossible to distinguish whether the stimulus is delayed or advanced in some cases. Therefore, we created a novel heartbeat discrimination index. To characterize the performance of the participants, we approximated the Gaussian function to the simultaneous judgment ratio (Figure 1). In this fitting, the periodicity of the heartbeat was dealt with as follows: In the case of a participant with an R-R interval of 800 ms, as an example, because the heartbeat occurs in an almost constant cycle, the delay of the sound of 450 ms is indistinguishable from the advance of the sound of 350 ms (= 800–450 ms). Therefore, the response data under the 450 ms delay condition can also be treated as relevant data when the sounds are presented 350 ms earlier than the heartbeats. Each participant's data at five points, (450 – RRI) ms, 0 ms, 150 ms, 300 ms, and 450 ms, were fitted to the following Gaussian function.

Simultaneous judgement ratio =
$$A \times exp\left(-\frac{(delay - \mu)^2}{\sigma^2}\right) + b$$

There are four fitting parameters: A, μ , σ , and b. If a participant has a good heartbeat sensitivity, the Gaussian shape should be higher and sharper. Therefore, we used amplitude A and variance σ as indicators of interoceptive sensitivity (IS) for subsequent analyses.

Music task

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Participants listened to a music piece for 30 s using an MRI scanner and evaluated emotional touching. Musical stimuli were selected from the music used by Proverbio et al. (2015). To widen the range of touching, we selected 10 tonal music pieces as highemotionally touching music and 10 atonal music pieces as low-emotionally touching music (Table 1). In addition, for the 10 tonal music pieces, two variations were made by changing the pitches to one half note higher and three half notes lower; then, a music piece was created by synthesizing them (Koelsch et al., 2006). Most of these synthesized music pieces were dissonant and unpleasant; thus, the touching level was expected to be low. Therefore, a total of 30 music pieces were used, including 10 tonal, 10 atonal, and 10 pitch-shifted tonal music pieces. Participants listened to a music piece while undergoing the fMRI. They wore earplugs and headphones with a noise-canceling function (OptoActive, Optoacoustics Ltd, Or Yehuda, Israel). In addition, a photoplethysmogram was recorded from the participants' left index finger at 1000 Hz using Biopac MP 150 system. In each trial, after a presentation of a fixation cross for 5 s, participants listened a music piece for 30 s and rated touching level by a visual analog scale. Each music piece was presented once, and participants performed 30 trials. The experiment was divided into two sessions of 15 trials, with a 10-minute break between sessions.

fMRI data acquisition and analysis

A 20-channel head coil 3T MRI system (Siemens MAGNETOM Skyra, Siemens LTD., Erlangen) was used for data acquisition. Before the experiment, a high-resolution T1-weighted structural scan was obtained using a three-dimensional magnetization prepared rapid gradient echo imaging sequence (TR = 2300 ms, TE = 2.98 ms, flip

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angle = 9°, field of view = 256 mm, voxel size $1 \times 1 \times 1$ mm, 176 slices). The functional images were obtained using an echo-planar T2*-weighted multiband gradient echo sequence (TR = 1000 ms, TE = 30 ms, flip angle = 80 degrees, field of view = 192 mm, voxel size $3.0 \times 3.0 \times 3.2$ mm, 42 slices, acceleration factor 3). The experiment was divided into two blocks, and 707-902 functional image data were obtained for each block. The first 10 functional images for each block were excluded from the analysis to allow for T1-equilibration. The movement of the head during the task was corrected, normalized using the Montreal Neurological Institute (MNI) template, and smoothed with a 3D Gaussian filter (full width at half maximum 8 mm). After preprocessing, the first-level analysis was conducted using a general linear model (GLM) for each participant. The GLM comprised regressors for the periods during the presentation of music, presentation of fixation before music was played, presentation of music rated as high-touching, and presentation of music rated as low-touching score, as well as during a response, including pressing buttons. We then obtained the contrast between high-touching trials and low-touching trials. The statistical significance of the contrast was verified by a t-test in the group analysis. The significance level was p < 0.001without correction at the voxel-level and p < 0.05 with family wise error correction at the cluster level. Next, we conducted a region of interest (ROI) analysis to investigate the effects of individual differences in interoceptive sensitivity. We defined six subregions of the insula for each hemisphere using the Brainnetome Atlas (Fan et al., 2016). For each subregion, we examined whether there was any difference in activity between the high and low groups of interoceptive sensitivity.

3. Results

Heartbeat tasks

The average IA score for the heartbeat counting task was 0.72 ± 0.22 . For the heartbeat discrimination task, Gaussian parameters were estimated for each participant, and the average values for each parameter were as follows: A: 0.72 ± 0.16 , μ : 197 ± 265 ms, σ : 671 ± 520 ms, and b: 0.26 ± 0.17 . We then calculated the correlation between IA and the heartbeat discrimination task parameters. This revealed a weak positive correlation between the amplitude parameter (A) only and IA (A: r = 0.27, t (49) = 1.94, p = 0.05, μ : r = -0.03, t (49) = 0.21, p = 0.86, σ : r = -0.12, t (49) = 0.82, p = 0.41, t: t = t

Heart rate during the music task

First, we examined whether the heart rate during the presentation of the music piece would differ depending on the ratings of touching. For each trial, we calculated the average heart rate during the presentation of the fixation cross before the start of the presentation of a music piece as the baseline, and the difference from the baseline as the heart rate. Then, for each participant, we divided 30 trials into three touching-level groups based on the rated scores of touching: high-touching trials, 10 trials in which the touching score was the lowest; and middle-touching trials, 10 trials in which the touching score was between low and high. We then averaged the heart rate during the presentation of the music piece for trials in each group. Figure 2 shows the average heart rate for all participants. A one-way repeated-measures analysis of variance (ANOVA) with a factor of touching level group (high-touching, middle-touching, and low-touching trials) was performed on the average heart rate for 30 s while listening to the music piece. This revealed a significant main

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effect of touching (F(1, 50) = 5.69, p = 0.02). The post-hoc test with Bonferroni correction revealed a significantly higher heart rate in the high-touching trials than in the low-touching trials (p = 0.05). However, a one-way repeated-measures ANOVA with a factor of music type (tonal, atonal, and discorded) revealed no significant main effect (F (1, 50) = 0.45, p = 0.83. Next, we divided the participants into two groups according to the heartbeat discrimination task amplitude, that is, fitting parameter A. Based on the median of A, 25 participants with A above the median were classified into the high interoceptive sensitivity (high-IS) group. The remaining 26 participants were classified into the low interoceptive sensitivity (low-IS) group. The average heart rate for each interoceptive sensitivity group is shown in Figure 3. A two-way repeated measures ANOVA revealed a significant interaction between the interoceptive sensitivity group and the touching level group with regard to the average heart rate (IS group: F(1, 49) = 0.04, p = 0.95; touching level group: F(1, 49) = 5.89, p = 0.02; IS×touching interaction: F(1, 49) = 4.53, p = 0.020.04). The post-hoc test with Bonferroni correction revealed a significant difference between the high-touching trials and the low-touching trials in the high-IS group only (p = 0.01). We performed the same analyses based on grouping according to the heartbeat counting task score (IS group: F(1, 49) = 1.55, p = 0.22; touching level group: F(1, 49)= 5.56, p = 0.02; IS×touching interaction: F(1, 49) = 1.07, p = 0.31) and the variance parameter (σ) of the heartbeat discrimination task (IS group: F(1, 49) = 0.18, p = 0.67; touching level group: F(1, 49) = 5.85, p = 0.02; IS×touching interaction: F(1, 49) = 1.41, p = 0.24), but none of them showed a significant interaction. Therefore, we used the heartbeat discrimination task amplitude parameter (A) as an index of interoceptive sensitivity.

Next, we examined whether the touching score was affected by individual differences in interoceptive sensitivity. This analysis revealed a weak but significant positive correlation between interoceptive sensitivity and touching score (r = 0.27, t (49) = 1.92, p = 0.05, Figure 4). In contrast, no significant correlation was found between interoceptive sensitivity and the standard deviation (SD) or the variance of the touching score (SD: r = 0.16, t (49) = 1.11, p = 0.27, variance: r = 0.23, t (49) = 1.62, p = 0.09). Furthermore, to determine whether the heart rate changed due to interoceptive sensitivity regardless of the touching level, we examined the relationship between heart rate changes and interoceptive sensitivity. However, no significant correlation was found between interoceptive sensitivity and average, SD, or variance of the heart rate changes (average: r = -0.03, t (49) = 0.21, p = 0.83; SD: r = -0.02, t (49) = 0.14, t = 0.88; variance: t = 0.06, t (49) = 0.41, t = 0.67).

fMRI activity and interoceptive sensitivity

First, to investigate the activity related to the emotional experience induced by music, we compared whole-brain activity in the high-touching and low-touching trials. We observed significantly higher activation in the bilateral auditory cortices (superior temporal gyrus and inferior frontal gyrus), supplementary motor area, striatum (caudate nucleus, putamen, and globus pallidus), left primary motor area, left anterior insula, and left ventral inferior frontal cortex (Broca's area) in the high-touching trials than in the low-touching trials (Figure 5, Table 2).

Next, to investigate the relationship between individual differences in interoceptive sensitivity and activity in the insula subregions, we divided the participants into two groups, high-IS and low-IS groups, according to the heartbeat discrimination task

parameter (A), as in the analysis of physiological responses. We conducted an ROI analysis of six insula subregions: hypergranular insula, ventral agranular insula, dorsal agranular insula, ventral dysgranular and granular insula, dorsal granular insula, and dorsal dysgranular insula, defined by the Human Brainnetome Atlas (Fan $et\ al.$, 2016; Table 3). For the ROI analysis, we used contrast images of high-touching and low-touching trials. We performed a t-test for the activities in the high-IS and low-IS groups. The P-value threshold was corrected with false discovery rate correction for multiple comparisons (p < 0.05). This analysis revealed that the activity in the dorsal granular insula in both hemispheres and ventral dysgranular and granular insula and dorsal dysgranular insula in the right hemisphere were significantly higher in the high-IS group than in the low-IS group (Figure 6, Table 3).

4. Discussion

In this study, we assessed three hypotheses about emotional experience, physiological and brain activities, and the effect of individual differences in interoceptive sensitivity. (1) The physiological response during the emotional experience of music correlates with individual differences in interoceptive sensitivity. (2) The interoceptive sensitivity measured by the heartbeat discrimination task is related to the physiological response. (3) The activity of the posterior insula during emotional experience correlates with individual differences in interoceptive sensitivity. To estimate the participants' interoceptive sensitivity, we used heartbeat discrimination and heartbeat counting tasks. Based on the newly created index (amplitude parameter, *A*) of the interoceptive sensitivity derived from the heartbeat discrimination task, the heart rate increased when listening to a high-touching music piece (high-touching trials) in the high interoceptive sensitivity group only (high-IS group). These findings support the first and second hypothesis that the

physiological response during an emotional experience correlates with individual differences in interoceptive sensitivity, which was estimated by heartbeat discrimination task. The fMRI analysis showed that the left anterior insula was more active in the high-touching trials than in the low-touching trials. Furthermore, the ROI analysis of the insula subregions revealed that the high-IS individuals showed high activity in the mid-posterior insula in the high-touching trials. These results indicate that the posterior insula activity during an emotional experience correlates with the individual difference in the interoceptive sensitivity estimated by the heartbeat discrimination task, supporting the third hypothesis.

Method for measuring interoceptive sensitivity

In this study, heartbeat counting and heartbeat discrimination tasks were performed by the same participants. In the comparison between the two tasks, a weak positive correlation (r = 0.27) was found between the IA and amplitude of the heartbeat discrimination task only. In previous studies, the correlation between heartbeat counting and heartbeat discrimination tasks has been controversial; some researchers have reported positive correlations (Garfinkel *et al.*, 2015; Garfinkel *et al.*, 2016; Kandasamy *et al.*, 2016; Rae *et al.*, 2019), whereas others have reported no correlation (Forkmann *et al.*, 2016; Ring and Brener, 2018; Herman *et al.*, 2019). An integrative review of these studies suggests a weak correlation of 0.20 (Hickman *et al.*, 2020), which is close to that of the present study. Contrary to the previous studies, we devised two new heartbeat discrimination indices (A and σ). The amplitude may represent the sensitivity to the heartbeat intensity, and the variance may reflect the goodness of the temporal resolution of heartbeat perception. Since the IA of the heartbeat counting task was correlated with the amplitude of the heartbeat discrimination task, our results suggest that the heartbeat

counting task can estimate the sensitivity to heartbeat intensity.

Regarding the relationship between the music listening task and the heartbeat tasks, a significant difference in heart rate was observed only when the participants were grouped according to the heartbeat discrimination task amplitude. One reason for this finding is that the heartbeat discrimination task amplitude may have been more strongly related to the touching of the music. The heartbeat counting task requires good interoceptive sensitivity because it merely counts the heartbeat. In contrast, to perform the heartbeat discrimination task, participants must compare their heart beats with the sounds presented concurrently. Therefore, the heartbeat discrimination task requires integrated processing of interoception and exteroception. Notably, the generation of emotions requires the integration of interoception and exteroception (Barrett *et al.*, 2004; Barrett and Simmons, 2015); thus, the ability to integrate interoception and exteroception may be strongly associated with the physiological response to music.

Individual differences in interoceptive sensitivity and physiological response

A comparison of the heart rates when listening to music among the high-touching, middle-touching, and low-touching trials showed that the higher the touching rating, the higher the heart rate. This is consistent with the typical tendency observed when listening to music or feeling emotions induced by music (Koelsch and Jäncke, 2015). Furthermore, regarding the relationship between changes in heart rate and individual differences in interoceptive sensitivity, it was only in the high-IS group that the heart rate was higher when listening to the high-touching music piece. This finding is consistent with those of previous studies comparing interoceptive sensitivity with the magnitude of the physiological response caused by visually induced emotions (Pollatos *et al.*, 2007; Pollatos and Schandry, 2008; Herbert *et al.*, 2010; De Witte *et al.*, 2016). However, no

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significant change in the heart rate was observed when we divided trials by the type of music pieces (tonal, atonal, and dissonance). This suggests that subjective evaluation is related to the heart rate. In addition, there was a weak positive correlation between interoceptive sensitivity and the average touching score, but no significant correlation between interoceptive sensitivity and the variance of touching score, the average heart rate, and the variance of heart rate was observed. This indicates that participants with low and high interoceptive sensitivity showed similar changes in touching scores and heart rate. The finding that only the high-IS group had a relationship between the touching score and the heart rate has two possible interpretations. First, the heart rate of the high-IS individuals fluctuate greatly depending on the emotions. Second, the high-IS individuals refer to the heart rate when assessing emotions. If the first hypothesis was true, participants in the low-IS group would show less heart rate changes among the trials. However, no difference in the variance of heart rate changes between the high- and low-IS groups was observed. Thus, the second interpretation is more appropriate. Based on our findings, we can speculate that individuals with high interoceptive sensitivity use their physical condition to assess their emotional level when listening to music, while those with low interoceptive sensitivity use their knowledge of moving and non-moving music or experience of emotional music. Dunn et al. (2010) showed that participants with high interoceptive sensitivity had a greater effect of anticipatory EDA on risk-aversion behavior. However, there was no difference in the magnitude of EDA depending on interoceptive sensitivity. In other words, when making a risky selection, EDA occurs in the same way regardless of the interoceptive sensitivity, but an individual with a high interoceptive sensitivity can

effectively utilize it for selection behavior. Consistent with this result, in the present study, individuals in the high-IS group showed a large heart rate change during the high-touching trials, but the magnitude of heart rate change did not differ according to interoceptive sensitivity. Therefore, although the magnitude of the physiological response does not change depending on individual differences in interoceptive sensitivity, a difference in the use of the physiological response is apparent.

Brain activity and interoceptive sensitivity

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During the high-touching trials, we found significant activations in the bilateral auditory cortices, supplementary motor area, striatum, left primary motor area, anterior insula, and Broca's area. The anterior insula and supplementary motor area are generally considered to be activated by emotional arousal (Lee et al., 2015; Lindquist et al., 2015). In addition, the brain activity related to music-induced emotions was observed in the striatum, amygdala, hypothalamus, cingulate cortex, insula, primary motor cortex, and prefrontal cortex (Koelsch, 2014). The activated areas in these previous studies are consistent with our findings, suggesting that the activity observed in our study was also caused by music-induced emotions. Furthermore, the activated areas involved in interoceptive processing overlap with those involved in emotion processing (Adolfi et al., 2017; Quigley et al., 2021), including the insula, inferior frontal gyrus, prefrontal cortex, striatum, supplementary motor area, and cingulate cortex. The activated areas in our study are consistent with these areas, which further supports the view that interoceptive activity in the brain is related to emotional activity. Next, the ROI analysis of the insula subregions showed a significant difference between the high-IS group and low-IS group in the activity of the bilateral dorsal granular insula and the right ventral dysgranular and granular insula, as well as the right dorsal

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dysgranular insula. The anterior insula is thought to be responsible for cognitive and emotional functions, while the posterior insula is thought to be responsible for bodily sensorimotor functions, including internal organs. The anterior insula is connected to the orbitofrontal cortex, the cingulate cortex, and the limbic cortex, while the posterior insula is connected to the parietal area, such as the somatosensory and the motor cortices (Deen et al., 2010; Cauda et al., 2011; Cerliani et al., 2012; Cloutman et al., 2012), which correspond to their respective functions. Barrett and Simmons (2015) proposed a model of interoceptive processing focusing on the composition of the insula subregion and argued that the agranular cortex receives the interoceptive sensory input, while the granular cortex provides interoceptive predictions and is assigned an emotional function. Since the posterior insula, which showed a significant difference in activity between the high- and low-IS groups, receives sensory input, it is presumed that participants with high interoceptive sensitivity received more interoceptive sensory input during the emotional experience. From the result of physiological responses, we can speculate that participants with high interoceptive sensitivity received strong heartbeat sensory input and used it for emotional evaluation, and the strong sensory input may have been reflected in the activity of the posterior insula. The mid-insula connects the anterior and posterior regions, and it has been suggested that the brain waves generated by pain are transmitted from the posterior insula to the anterior insula via the mid insula (Frot et al., 2014). Kuehn et al. (2016) also showed that interoceptive sensitivity is related to the strength of the connection between the posterior insula and the mid/anterior insula. In this study, the strength of the connection between the anterior and posterior insula may be reflected in the activity of the mid insula.

Conclusions

In this study, we investigated the relationship between individual differences in interoceptive sensitivity and ratings of emotional touch and heart rate when listening to music. We found increased heart rate in the high-touching trials for the high-IS group only, which was defined by the amplitude parameter of the heartbeat discrimination task. This finding suggests that individuals with high interoceptive sensitivity use their physical condition to assess their emotional level when listening to music. In addition, we found no significant change in the heart rate for cases where interoceptive sensitivity was defined by the heartbeat counting task, suggesting that the heartbeat discrimination task could be more strongly associated with the physiological response of emotional experience. Furthermore, our ROI analysis showed that the activities of the mid and posterior insula during the emotional experience were correlated with interoceptive sensitivity. This suggests that insula activity may reflect the use of interoception for estimating emotions. These results may extend the knowledge of interoceptive processing and elucidate the role of interoception in emotions.

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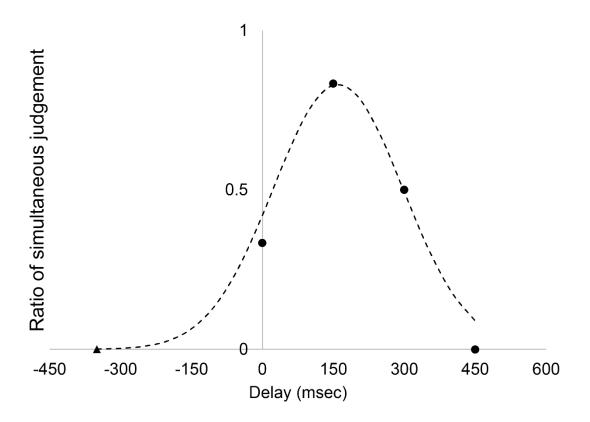


Figure 1. A schematic diagram of the analysis of the heartbeat discrimination task. The horizontal axis shows the delay time of the beep from R-peak, while the vertical axis shows the percentage of trials in which participants responded that the timing was matched. The triangular symbol indicates the extrapolated condition considering the periodicity of the heartbeat (see details in the text). The dotted line shows the Gaussian approximation.

Table 1

List of music used in the experiment.

Type	Composer	Title								
Tonal	Beethoven, Ludwig	Fourth Movement of Symphony No. 5 in C major (op. 67) (last minute of The coda: Allegro)								
	Mozart, Wolfgang Amadeus	The Marriage of Figaro – Overture in D major (K492)								
	Mendelssohn, Bartholdy Felix	First Movement of Symphony No.4 "Italian" in A major (op.90)								
	Mahler, Gustav	Symphony no. 5 in F major (Adagietto)								
	Ravel, Maurice	Second movement of concert in G major								
	Bach, Johann Sebastian	Second Movement of Concert for two Violins in D minor (BWV 1043) (from measure 10)								
	Mahler, Gustav	Der Abschied from "The Song of the Earth" in C-minor								
	Holst, Gustave	The Planets: Mars, the bringer of war in C minor (op. 32)								
	Beethoven, Ludwig van	Piano sonata No. 14 in C-sharp minor, First Movement. (op.27, No.2)								
	Beethoven, Ludwig van	Symphony No. 5, First Movement in C minor (op. 67)								
	Cage, John	Fontana Mix, for magnetic tape								
	Maderna, Bruno	Serenade for a satellite								
	Pärt, Arvo	Cantus in Memoriam of Benjamin Britten (the opening passage, after the first 15 s)								
	Ives, Charles	The Unanswered question								
Atonol	Berg, Alban	Last orchestra interlude from the last scene of Wozzeck								
Atonal	Ligeti, György	Concert for cello and orchestra								
	Donatoni, Franco	Duo Pour Bruno (ninth panel, from 14× 37××)								
	Petrassi, Goffredo	(Chorus of the Dead) Coro di morti								
	Boulez, Pierre	Second piano sonata								
	Kurtag, Gyorgy	String Quartet No. 1								

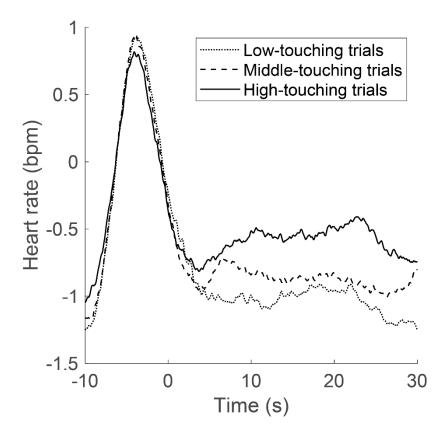


Figure 2. Changes in heart rate when listening to music in the music task. The vertical axis shows the change in heart rate based on the fixation time before the trial. The zero on the horizontal axis indicates the time when the music started.

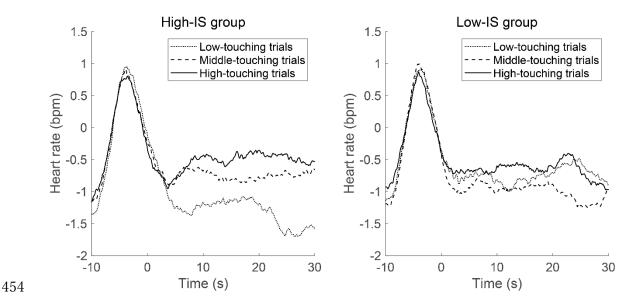


Figure 3. Changes in heart rate grouped according to the interoceptive sensitivity defined by the performance of the heartbeat discrimination task (HDT). Participants were divided into two groups based on the HDT amplitude parameter. The left figure shows the average result of the high-IS group, while the right figure shows the average result of the low-IS group.

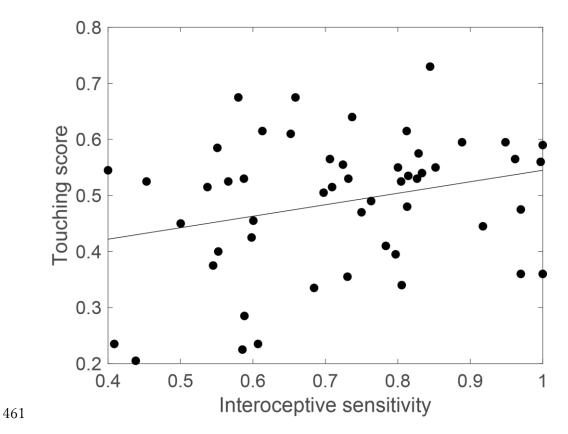


Figure 4. The relationship between the average touching score for all music pieces and interoceptive sensitivity defined by the amplitude parameter of the HDT. Each point indicates each participant's data. The solid line shows a result of linear regression. HDT, heartbeat discrimination task.

Table 2

Anatomical locations and coordinates of brain regions showing significant activations in the high-touching trials

		Left hemisphere			Right hemisphere				
Cluster	Region	t-score	X	у	Z	t-score	X	у	Z
Auditory cortex									
	Superior temporal gyrus	7.42	-51	-16	4	8.17	51	-13	0
	Inferior frontal gyrus	5.07	-42	-31	13	4.08	54	-22	13
Primary motor cortex									
	Precentral gyrus	5.33	-51	-1	48				
Supplementary motor area									
	Frontal superior gyrus	5.20	-9	17	48	3.92	3	5	64
Broca's area /									
Insular cortex	Frontal middle gyrus	4.28	-45	23	32				
	Anterior insula cortex	3.76	-36	23	-6				
Striatum									
	Caudate	4.38	-12	2	10	4.66	15	2	13
	Pallidum	4.47	-18	5	0	5.26	15	8	-3
	Putamen	4.54	-18	8	0	5.11	21	5	-3

The areas that were more active when listening to music in the high-touching trials than in the low-touching trials. Coordinates are derived from the standard brain of the Montreal Neurological Institute (MNI). The significance level is p < 0.001 without correction at voxel-level and p < 0.05, with family wise error (FWE) correction at the cluster level.

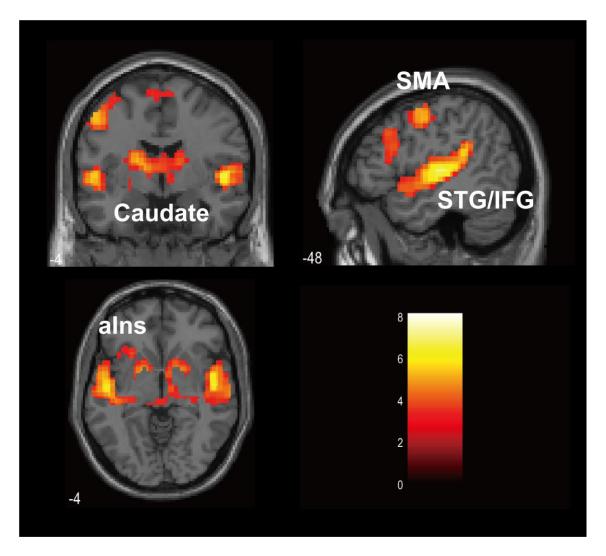


Figure 5. The brain regions that were more active when listening to music in the high-touching trials than in the low-touching trials (uncorrected p < 0.001 at voxel-level, FWE corrected p < 0.05 at cluster-level). SMA, Supplementary motor area; STG, Superior temporal gyrus; IFG, Inferior frontal gyrus; aIns, anterior Insula.

Table 3

Anatomical coordinates of insula subregions and t-value of ROI analysis

	Left						Right					
	t	sig.	X	У	Z		t	sig.	X	У	Z	
hypergranular insula	1.46		-36	-20	10		1.99		37	-18	8	
ventral agranular insula	0.56		-32	14	-13		1.85		33	14	-13	
dorsal agranular insula	1.38		-34	18	1		1.24		36	18	1	
ventral dysgranular and granular insula	1.18		-38	-4	-9		2.31	*	39	-2	-9	
dorsal granular insula	2.37	*	-38	-8	8		2.77	*	39	-7	8	
dorsal dysgranular insula	1.56		-38	5	5		2.27	*	38	5	5	

The regions of interest were defined using the Brainnetome Atlas. The t-value indicates the result of a one-sided t-test on whether the activity in the high-touching trials is larger in the high-IS group than in the low-IS group. The asterisk in the table shows p < 0.05 at the significance level corrected with false discovery rate correction for multiple comparisons. ROI,

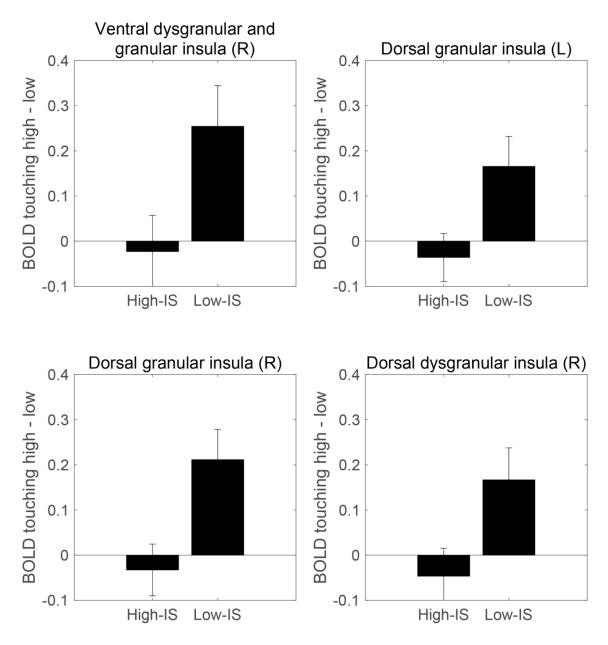


Figure 6. BOLD responses in the insula subregion for the low and high interoceptive sensitivity groups. Each figure represents the insula subregions showing significant differences between the high- and low-IS groups in the ROI analysis. The vertical axis represents the difference in the BOLD responses between the activity when listening to music in the high-touching trials and in the low-touching trials. The error bars represent ±1 standard error.

References

- Adolfi, F., Couto, B., Richter, F., Decety, J., Lopez, J., Sigman, M., Manes, F. & Ibáñez, A.
- 487 (2017) 'Convergence of interoception, emotion, and social cognition: a twofold fMRI meta-
- analysis and lesion approach', *Cortex*, **88**, pp. 124-142.
- Barrett, L. F., Quigley, K. S., Bliss-Moreau, E. & Aronson, K. R. (2004) 'Interoceptive
- sensitivity and self-reports of emotional experience', Journal of Personality and Social Psychology,
- 491 **87**(5), p. 684.

- Barrett, L. F. & Simmons, W. K. (2015) 'Interoceptive predictions in the brain', Nature Reviews
- 493 Neuroscience, **16**(7), pp. 419-429.
- Baumgartner, T., Esslen, M. & Jäncke, L. (2006) 'From emotion perception to emotion
- 495 experience: Emotions evoked by pictures and classical music', International Journal of
- 496 *Psychophysiology*, **60**(1), pp. 34-43.
- Cauda, F., D'Agata, F., Sacco, K., Duca, S., Geminiani, G. & Vercelli, A. (2011) 'Functional
- connectivity of the insula in the resting brain', *Neuroimage*, **55**(1), pp. 8-23.
- Cerliani, L., Thomas, R. M., Jbabdi, S., Siero, J. C. W., Nanetti, L., Crippa, A., Gazzola, V.,
- 500 D'Arceuil, H. & Keysers, C. (2012) 'Probabilistic tractography recovers a rostrocaudal trajectory
- of connectivity variability in the human insular cortex', Human Brain Mapping, 33(9), pp. 2005-
- 502 2034.
- Ceunen, E., Vlaeyen, J. W. & Van Diest, I. (2016) 'On the origin of interoception', Frontiers in
- 504 *Psychology*, **7**, p. 743.
- Cloutman, L. L., Binney, R. J., Drakesmith, M., Parker, G. J. M. & Lambon Ralph, M. A. (2012)
- The variation of function across the human insula mirrors its patterns of structural connectivity:
- 507 Evidence from in vivo probabilistic tractography', *Neuroimage*, **59**(4), pp. 3514-3521.
- 508 Craig, A. (2008) 'Interoception and emotion: a neuroanatomical perspective', Handbook of
- 509 *emotions*, **3**(602), pp. 272-288.
- 510 Craig, A. D. (2002) 'How do you feel? Interoception: the sense of the physiological condition
- of the body', *Nature Reviews Neuroscience*, **3**(8), pp. 655-666.
- 512 Critchley, H. D. & Garfinkel, S. N. (2017) 'Interoception and emotion', Current opinion in
- 513 *psychology*, **17**, pp. 7-14.
- Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A. & Dolan, R. J. (2004) 'Neural systems
- supporting interoceptive awareness', *Nature Neuroscience*, **7**(2), pp. 189-195.
- De Witte, N. A. J., Sütterlin, S., Braet, C. & Mueller, S. C. (2016) 'Getting to the Heart of
- 517 Emotion Regulation in Youth: The Role of Interoceptive Sensitivity, Heart Rate Variability, and
- Parental Psychopathology', *PloS One*, **11**(10), p. e0164615.
- Deen, B., Pitskel, N. B. & Pelphrey, K. A. (2010) 'Three Systems of Insular Functional
- 520 Connectivity Identified with Cluster Analysis', Cerebral Cortex, 21(7), pp. 1498-1506.
- 521 Dunn, B. D., Galton, H. C., Morgan, R., Evans, D., Oliver, C., Meyer, M., Cusack, R., Lawrence,
- 522 A. D. & Dalgleish, T. (2010) 'Listening to your heart how interoception shapes emotion experience

- and intuitive decision making', *Psychological Science*, **21**(12), pp. 1835-1844.
- 524 Fan, L., Li, H., Zhuo, J., Zhang, Y., Wang, J., Chen, L., Yang, Z., Chu, C., Xie, S., Laird, A. R.,
- 525 Fox, P. T., Eickhoff, S. B., Yu, C. & Jiang, T. (2016) 'The Human Brainnetome Atlas: A New Brain
- 526 Atlas Based on Connectional Architecture', Cerebral Cortex, 26(8), pp. 3508-3526.
- Forkmann, T., Scherer, A., Meessen, J., Michal, M., Schächinger, H., Vögele, C. & Schulz, A.
- 528 (2016) 'Making sense of what you sense: Disentangling interoceptive awareness, sensibility and
- accuracy', *International Journal of Psychophysiology*, **109**, pp. 71-80.
- Frot, M., Faillenot, I. & Mauguière, F. (2014) 'Processing of nociceptive input from posterior
- to anterior insula in humans', *Human Brain Mapping*, **35**(11), pp. 5486-5499.
- Garfinkel, S. N., Seth, A. K., Barrett, A. B., Suzuki, K. & Critchley, H. D. (2015) 'Knowing your
- 533 own heart: distinguishing interoceptive accuracy from interoceptive awareness', Biological
- 534 *Psychology*, **104**, pp. 65-74.
- Garfinkel, S. N., Tiley, C., O'Keeffe, S., Harrison, N. A., Seth, A. K. & Critchley, H. D. (2016)
- 536 'Discrepancies between dimensions of interoception in autism: implications for emotion and
- anxiety', Biological Psychology, 114, pp. 117-126.
- Gilet, A. L. (2008) 'Mood induction procedures: a critical review', Encephale, 34(3), pp. 233-
- 539 239.
- Gu, X., Hof, P. R., Friston, K. J. & Fan, J. (2013) 'Anterior insular cortex and emotional
- awareness', Journal of Comparative Neurology, 521(15), pp. 3371-3388.
- Haruki, Y. & Ogawa, K. (2021) 'Role of anatomical insular subdivisions in interoception:
- 543 Interoceptive attention and accuracy have dissociable substrates', European Journal of
- 544 *Neuroscience*, **53**(8), pp. 2669-2680.
- Herbert, B. M., Pollatos, O., Flor, H., Enck, P. & Schandry, R. (2010) 'Cardiac awareness and
- 546 autonomic cardiac reactivity during emotional picture viewing and mental stress',
- 547 *Psychophysiology*, **47**(2), pp. 342-354.
- Herman, A. M., Rae, C. L., Critchley, H. D. & Duka, T. (2019) 'Interoceptive accuracy predicts
- nonplanning trait impulsivity', *Psychophysiology*, **56**(6), p. e13339.
- Hickman, L., Seyedsalehi, A., Cook, J. L., Bird, G. & Murphy, J. (2020) 'The relationship
- between heartbeat counting and heartbeat discrimination: A meta-analysis', Biological Psychology,
- 552 **156**, p. 107949.
- Kandasamy, N., Garfinkel, S. N., Page, L., Hardy, B., Critchley, H. D., Gurnell, M. & Coates,
- J. M. (2016) 'Interoceptive Ability Predicts Survival on a London Trading Floor', Scientific Reports,
- 555 **6**(1), p. 32986.
- Khalsa, S. S., Adolphs, R., Cameron, O. G., Critchley, H. D., Davenport, P. W., Feinstein, J. S.,
- Feusner, J. D., Garfinkel, S. N., Lane, R. D. & Mehling, W. E. (2018) 'Interoception and mental
- health: a roadmap', Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 3(6), pp.
- 559 501-513.
- Koelsch, S. (2014) 'Brain correlates of music-evoked emotions', *Nature Reviews Neuroscience*,
- 561 **15**(3), p. 170.

- Koelsch, S., Fritz, T., v. Cramon, D. Y., Müller, K. & Friederici, A. D. (2006) 'Investigating
- emotion with music: an fMRI study', *Human Brain Mapping*, **27**(3), pp. 239-250.
- Koelsch, S. & Jäncke, L. (2015) 'Music and the heart', European Heart Journal, 36(44), pp.
- 565 3043-3049.
- Kuehn, E., Mueller, K., Lohmann, G. & Schuetz-Bosbach, S. (2016) 'Interoceptive awareness
- changes the posterior insula functional connectivity profile', Brain Structure and Function, **221**(3),
- 568 pp. 1555-1571.
- Kurth, F., Zilles, K., Fox, P. T., Laird, A. R. & Eickhoff, S. B. (2010) 'A link between the systems:
- 570 functional differentiation and integration within the human insula revealed by meta-analysis',
- 571 Brain Structure and Function, **214**(5-6), pp. 519-534.
- Lee, S. W., O'Doherty, J. P. & Shimojo, S. (2015) 'Neural computations mediating one-shot
- learning in the human brain', *PLoS Biology*, **13**(4), p. e1002137.
- Lindquist, K. A., Satpute, A. B., Wager, T. D., Weber, J. & Barrett, L. F. (2015) 'The Brain
- Basis of Positive and Negative Affect: Evidence from a Meta-Analysis of the Human Neuroimaging
- 576 Literature', *Cerebral Cortex*, **26**(5), pp. 1910-1922.
- Mesulam, M. M. & Mufson, E. J. (1982) 'Insula of the old world monkey. Architectonics in the
- 578 insulo orbito temporal component of the paralimbic brain', Journal of Comparative Neurology,
- 579 **212**(1), pp. 1-22.
- Murphy, J., Millgate, E., Geary, H., Ichijo, E., Coll, M.-P., Brewer, R., Catmur, C. & Bird, G.
- 581 (2018) 'Knowledge of resting heart rate mediates the relationship between intelligence and the
- heartbeat counting task', *Biological Psychology*, **133**, pp. 1-3.
- Pollatos, O., Herbert, B. M., Matthias, E. & Schandry, R. (2007) 'Heart rate response after
- emotional picture presentation is modulated by interoceptive awareness', International Journal of
- 585 *Psychophysiology*, **63**(1), pp. 117-124.
- Pollatos, O., Kirsch, W. & Schandry, R. (2005) 'On the relationship between interoceptive
- awareness, emotional experience, and brain processes', Cognitive Brain Research, 25(3), pp. 948-
- 588 962.
- Pollatos, O. & Schandry, R. (2008) 'Emotional processing and emotional memory are
- modulated by interoceptive awareness', Cognition & Emotion, 22(2), pp. 272-287.
- Proverbio, A. M., Manfrin, L., Arcari, L. A., De Benedetto, F., Gazzola, M., Guardamagna, M.,
- 592 Lozano Nasi, V. & Zani, A. (2015) 'Non-expert listeners show decreased heart rate and increased
- 593 blood pressure (fear bradycardia) in response to atonal music', Frontiers in Psychology, 6, p. 1646.
- 594 Ouigley, K. S., Kanoski, S., Grill, W. M., Barrett, L. F. & Tsakiris, M. (2021) 'Functions of
- Interoception: From Energy Regulation to Experience of the Self', *Trends in Neurosciences*, **44**(1),
- 596 pp. 29-38.
- Rae, C., Ahmad, A., Larsson, D., Silva, M., van Praag, C. G., Garfinkel, S. & Critchley, H.
- 598 (2019) 'Impact of cardiac interoception cues on voluntary decisions to make or withhold action in
- an intentional inhibition task'.
- Ring, C. & Brener, J. (2018) 'Heartbeat counting is unrelated to heartbeat detection: A

- comparison of methods to quantify interoception', *Psychophysiology*, **55**(9), p. e13084.
- Schandry, R. (1981) 'Heart beat perception and emotional experience', *Psychophysiology*,
- 603 **18**(4), pp. 483-488.
- Schulz, S. M. (2016) 'Neural correlates of heart-focused interoception: a functional magnetic
- 605 resonance imaging meta-analysis', Philosophical Transactions of the Royal Society B: Biological
- 606 Sciences, **371**(1708), p. 20160018.
- Seth, A. K. (2013) 'Interoceptive inference, emotion, and the embodied self', Trends in
- 608 *Cognitive Sciences,* **17**(11), pp. 565-573.
- 609 Simmons, W. K., Avery, J. A., Barcalow, J. C., Bodurka, J., Drevets, W. C. & Bellgowan, P.
- 610 (2013) 'Keeping the body in mind: insula functional organization and functional connectivity
- integrate interoceptive, exteroceptive, and emotional awareness', Human Brain Mapping, 34(11),
- 612 pp. 2944-2958.

- Tan, Y., Wei, D., Zhang, M., Yang, J., Jelinčić, V. & Qiu, J. (2018) 'The role of mid-insula in
- the relationship between cardiac interoceptive attention and anxiety: evidence from an fMRI study',
- 615 Scientific Reports, **8**(1), p. 17280.
- Whitehead, W. E., Drescher, V. M., Heiman, P. & Blackwell, B. (1977) 'Relation of heart rate
- control to heartbeat perception', *Biofeedback and Self-regulation*, **2**(4), pp. 371-392.
- Wiens, S., Mezzacappa, E. S. & Katkin, E. S. (2000) 'Heartbeat detection and the experience of
- 619 emotions', *Cognition and Emotion*, **14**(3), pp. 417-427.
- Zaki, J., Davis, J. I. & Ochsner, K. N. (2012) 'Overlapping activity in anterior insula during
- interoception and emotional experience', *Neuroimage*, **62**(1), pp. 493-499.
- Zamariola, G., Maurage, P., Luminet, O. & Corneille, O. (2018) 'Interoceptive accuracy scores
- from the heartbeat counting task are problematic: Evidence from simple bivariate correlations',
- 624 Biological Psychology, 137, pp. 12-17.