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The 39th Annual Meeting of the JCSS (2022) **Presenter Award-winning Paper**

Awareness of cardiac/gastric interoception and its individual differences modulate the neural dynamics

Yusuke Haruki * Keisuke Suzuki Kenji Ogawa

Hokkaido University, Japan

(Award winner's words)

I am very honored to have been selected for the conference presentation award at the 39th annual meeting of the Japanese Cognitive Science Society. I would like to express my deepest gratitude to everyone involved in the conference and the audience. The Center for Human Nature, Artificial Intelligence, and Neuroscience (CHAIN) at Hokkaido University, to which I belong, aims to answer fundamental questions of human nature through the collaboration of students and faculty with backgrounds in the humanities, neuroscience, and artificial intelligence. As a part of this ambitious program, the present fMRI study showed how the brain encodes senses arising from within the body (i.e., interoception) and its individual differences, particularly in bridging everyday behavior and subjective experience of interoception. In future studies, I would like to further deepen my interdisciplinarity and ensure that research from CHAIN at Hokudai contributes to various fields of cognitive science. (Yusuke Haruki)

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1. Introduction

Interoception refers to senses that arise from within the body. For example, hunger, heartbeat sensations, dizziness, urination, fever, and many other phenomenal experiences are subject to interoception. Empirical studies on interoception, however, have been unable to incorporate such diversity due to the difficulty of measuring and manipulating bodily signals.

Awareness of cardiac signals has been extensively used to investigate the characteristics of interoception. Behavioral tasks on heartbeat perception (e.g., counting own heartbeat) have revealed a large individual difference in cardiac interoception (or its sensitivity) (Garfinkel et al., 2015). Although those tasks have been widely used and well-validated, cardiac sensitivity does not necessarily correspond to bodily awareness in a broader sense. Subjective sensibility to interoception measured via questionnaire and cardiac sensitivity usually do not correlate with each other (Garfinkel et al., 2015). Another study has shown that a meditation practitioner does not have sensitive cardiac interoception (Khalsa et al., 2020).

One seminal opinion regarding the neural substrates of interoception suggests that the insular cortex, particularly the right anterior insula, plays a critical role in generating phenomenal interoception (Craig, 2009). This idea has been supported by fMRI studies using cardiac interoception (Critchley et al., 2004). However, given the variety of phenomenal interoception, the opinion could be suspicious without a direct comparison of brain activity between cardiac and other types of interoception. Several fMRI studies have already used gastric (senses related to stomach sensation) and urinary (related to the bladder) interoception to capture the neural basis of interoception (Simmons et al., 2013), but none of them compared the neural activation by the types of interoception.

Here, we directly compared neural activation during cardiac and gastric interoception to test whether the different types of phenomenal interoception evoke particular patterns of brain activation. Furthermore, we assessed individual differences in cardiac and gastric sensitivity and tried to associate them with the intrinsic, task-free functional connectivity in the insular cortex. Through a series of analyses, we showed that the

Yusuke Haruki is also at Japan Society for the Promotion of Science and École Polytechnique Fédérale de Lausanne.
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∗ Corresponding Author. E-mail: haruki@let.hokudai.ac.jp

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brain dynamics underlying cardiac and gastric interoception largely differ, highlighting the importance of submodalities of interoception.

2. Materials and Methods

2.1 fMRI Experiments

A total of 30 healthy volunteers (12 women, 21.61 ± 2.45 years old) participated in the experiment on two occasions, at least a week apart. On day 1, we asked participants to experience fMRI scanning to obtain brain activation during rest and performing tasks. Participants first underwent a five-minute resting-state fMRI scan in which they looked at a fixation crossbar with their eyes open and did not think anything in particular.

Subsequently, we asked participants to perform an interoceptive attention task in the scanner (DeVille et al., 2020; Simmons et al., 2013), which was modified for our purposes. The task had three conditions: HEART (related to cardiac), STOMACH (related to gastric), and VISUAL (control). In each condition, participants tried to perceive sensations from the instructed source (i.e., heart, stomach, and slight color change of words) by directing their attention. There were five trials for each condition per run, with five runs repetition (a total of 125 scans per condition).

All scans were performed on a Siemens 3-Tesla Prisma scanner (Erlangen, Germany) with a 64-channel head coil at Hokkaido University. The scanning parameters for functional data were as follows: repetition time, 2,000 ms; field of view, 192 × 192 mm; matrix, 94 × 94; 32 axial slices; and slice thickness, 3.500 mm with a 0.875-mm gap. Thus, the voxel size was 2.042 × 2.042 × 4.375 mm.

2.2 Behavioral Experiments

On day 2, we asked participants to complete a heartbeat counting task (Garfinkel et al., 2015) and water load test (Herbert et al., 2012) out of the MRI scanner to assess individual differences in cardiac and gastric sensitivity behaviorally. The heartbeat counting task required participants to silently count the number of their heartbeats in a certain period by focusing on the internal bodily sensation. Estimating the number and taking pulse outside the body was prohibited. We evaluated individual sensitivity of cardiac interoception by comparing the counted number to the actual number of heartbeats. The calculation yielded a score ranging from 0 to 1, with 1 indicating the highest sensitivity.

In the water load test, participants were asked to drink room temperature, non-carbonated water ad libitum using a straw and to stop drinking when they first felt the sign of subjective fullness. A total of 1.5 liters of water was filled in a five-liter capacity container whose contents were invisible from the outside; thus, participants did not know the water volume they consumed. The difference between the total volume and consumed volume was used as an estimation of individual sensitivity of gastric interoception.

2.3 fMRI Data Analysis

All image processing was performed using SPM12 (Welcome Department of Cognitive Neurology [1)]). The standard procedure of preprocessing (realignment, normalization to Montreal Numerological Institute [MNI] space, and smoothing with 6 mm cube Gaussian kernel) was performed before statistical inference. A high-pass filter was applied with a cutoff of 128 s, and serial correlations among scans were estimated using an autoregressive model to exclude signal noise.

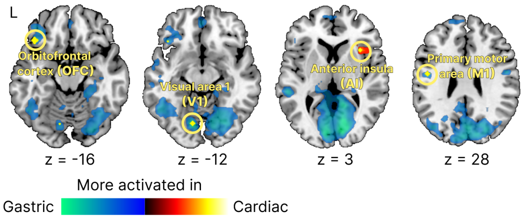
Individual level generalized linear model included each task trial block as separate box-car regressors that were convolved with the canonical hemodynamic response function. To reduce motion-related artifacts, six motion parameters were included as nuisance regressors.

We then performed two independent group analyses: random effects analysis to directly compare brain activation and correlation analysis for the resting-state fMRI data. First, we performed one sample t-test on random effects using the contrast images of the HEART and STOMACH conditions. By doing so, we identified brain regions selectively activated for cardiac and gastric interoception across the whole brain.

In the second analysis, we identified the brain regions that exhibited an enhanced intrinsic (task-free) functional connectivity with the structural subdivisions of the insular cortex in people with high cardiac/gastric sensitivity. We adopted the ROIs from the Hammersmith atlas (Faillenot et al., 2017): the right middle short gyrus for the anterior insula and the anterior long gyrus for the posterior insula. The selection was based on previous findings that the middle short gyrus was the most activated when people focused on their heartbeats (Haruki & Ogawa, 2021) and that the anterior long gyrus corresponds to the primary interoceptive cortex that is first projected with visceral signals at the cortical level (Evrard, 2019). Individual correlation maps were generated by extracting the time series signal in each ROI (i.e., the right anterior and posterior insula) and calculating correlation coefficients with the signals of each voxel throughout the whole brain. We

1) http://www.fil.ion.ucl.ac.uk/spm

Figure 1
Selectively activated brain regions for cardiac and gastric interoception.



Note: The symbol z denotes the axial slice in MNI space. L: left hemisphere.

then tested the group level effects of cardiac/gastric sensitivity on the intrinsic functional connectivity of the insula by performing one sample t-tests.

3. Results

3.1 Behavioral Result

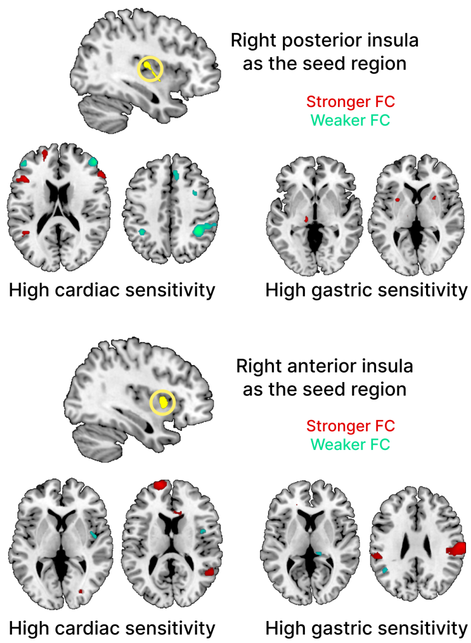
The mean score of cardiac sensitivity measured by the heartbeat counting task was 0.43 ± 0.25 while the average volume left in the bottle in the water load test was 1179 ± 189.54 ml.

3.2 fMRI Result

We report all the results surviving peak level threshold $p < .001$ (uncorrected) and cluster level threshold $15 < k$. Firstly, we found that cardiac interoception enhanced the neural activation in the right anterior insula compared to gastric interoception. In contrast, the activated regions in the gastric contrasted to cardiac interoception encompassed the larger brain areas, including the visual area, sensorimotor region, hippocampus, superior frontal and orbitofrontal cortex (Fig. 1).

We also found that individual differences in cardiac and gastric sensitivity were differently associated with the intrinsic (task-free) functional connectivity in the insula (Fig. 2). In people with higher cardiac sensitivity, the right primary interoceptive cortex (posterior insula) showed a stronger intrinsic functional connectivity with the bilateral frontal operculum, temporoparietal junction, left frontal pole, and left inferior frontal gyrus but decreased connectivity with the bilateral dorsolateral prefrontal cortex and superior parietal lobule. Such people also had the increased intrinsic connectivity of the right anterior insula with the bilateral ventromedial prefrontal cortex and right temporoparietal junction but decreased with the right middle insula. Conversely, higher gastric sensitivity contributed to stronger intrinsic connectivity of the right dorsal posterior insula with the bilateral putamen and left thalamus.

Figure 2
Subdivisions of the insula showing altered intrinsic functional connectivity depending on individual difference in cardiac/gastric sensitivity.



Note: FC: functional connectivity.

The right anterior insula was more connected with the bilateral temporoparietal junction in people with higher gastric sensitivity.

4. Discussion

In this study, we show that focusing on cardiac and gastric interoception activated different brain regions. Moreover, intrinsic (task-free) functional connectivity in the insular cortex with other brain regions was associated with individual differences in cardiac/gastric sensitivity measured via behavioral tasks. These results reveal that the different types of phenomenal interoception are associated with particular neural dynamics in the human brain, suggesting that interoception is not a unimodal sensory experience even at the neural level.

A previous meta-analysis on fMRI studies using cardiac interoception identified the consistently activated brain regions in the right insula and supplementary motor area (Schulz, 2016). These results strongly supported the dominance of the right insula in interoception (Craig, 2009; Critchley et al., 2004; Simmons et al., 2013). However, the present study showed gastric interoception activated a widespread region across the sensorimotor region and frontal region in gastric interoception, while cardiac interoception enhanced the activation in the right insula. Therefore, the role of the right insula for interoception may be cardiac-specific rather than interoception in general.

It is interesting to note that gastric interoception showed enhanced activations in the primary visual and sensorimotor area. It appears puzzling that activations in the primary sensory cortex differed between conditions because any visual or sensorimotor signals were absent in the present interoceptive attention task. This could be explained by differences in the functional roles of each phenomenal interoception. For example, the functional role of gastric interoception has been proposed to modulate feeding and foraging behavior in which agents must properly regulate their sensorimotor ability (Suarez et al., 2019). In line with this, it could be reasoned that gastric interoception that is likely to occur during food intake may be more relevant to the visual and sensorimotor regions than cardiac interoception.

Furthermore, individual differences in intrinsic functional connectivity in the right anterior and posterior insula were associated with interoceptive sensitivity. Particularly, higher sensitivity in cardiac interoception contributed to the increased connectivity in both the anterior and posterior insula with the frontal and temporal regions. Sensitive cardiac interoception was also characterized by the decreased connectivity in the posterior insula with the superior parietal region and the anterior insula with the ipsilateral middle insula. In contrast, high gastric sensitivity enhanced the intrinsic functional connectivity in the anterior insula with the bilateral temporoparietal junction and in the posterior insula with the putamen. Together, the functional connectivity between the right anterior insula and temporoparietal junction may be necessary for sensitive interoception over modalities. However, cardiac sensitivity may require the (de)coupling of the insula with the regions orienting attention (the superior parietal and frontal regions) compared to gastric interoception.

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Yusuke Haruki (Student Member)

Currently a Ph.D. student at the Graduate School of Humanities and Human Sciences and at the Center for Human Nature, Artificial Intelligence, and Neuroscience (CHAIN), Hokkaido University. From April 2022, he holds a post as Research Fellow (DC1) of the Japan Society for the Promotion of Science and from November 2022, he is concurrently a visiting researcher at the École Polytechnique Fédérale de Lausanne (EPFL). His research focuses on elucidating the mechanism of how the internal bodily sensation (interoception) comes to an awareness.